AN OVERVIEW OF URINARY TRACT INFECTION

Authors

Dr. Rajesh Sarkar
Ph.D.,
Assistant Professor in Medical Microbiology and Immunology
Department of Medical Microbiology and Immunology
College of Health and Medical Sciences
Haramaya University, Ethiopia.
academicmb021@outlook.com

Dr. Biniyam Wondwosen
MD Resident
Department of Obstetrics and Gynecology
Hiwotfana Comprehensive Specialized University Hospital
College of Health and Medical Sciences
Haramaya University Harar, Ethiopia.

Dr. Abdi Fikru
MD Resident
Department of Obstetrics and Gynecology
Hiwotfana Comprehensive Specialized University Hospital
College of Health and Medical Sciences
Haramaya University, Harar, Ethiopia.

Tadesse Shume
M.Sc.
Lecturer in Medical Microbiology and Immunology
Department of Medical Microbiology and Immunology
College of Health and Medical Sciences
Haramaya University
Harar, Ethiopia.

I. INTRODUCTION

The urogenital tract is the union of the reproductive and urinary tract systems. Both systems are susceptible to disease because of their openness to the external environment. Among the most prevalent bacterial infections, urinary tract infections (UTIs) impact 150 million individuals globally (Mlugu *et al.*, 2023). Uropathogenic *E. Coli* (UPEC), the most frequent cause of UTIs, can form a biofilm associated with antibiotic resistance (AMR) (Mlugu *et al.*, 2023). A microbiome that is out of balance can cause some infections, while external exposure can cause others (Kim and Lee, 2023). When STIs traverse the reproductive organs, they can result in severe morbidity and reduced fertility. Due to variations in urogenital anatomy, males and females may be affected by urogenital infections in different ways (Van Gerwen, Muzny, and Marrazzo, 2022). Although both men and women can have infections, UTIs are more common in women, with approximately 50% of cases happening in women throughout their lives (Health Exchange, 2024).

Among women in particular, the urinary tract is one of the most prevalent locations of bacterial infection; three percent of those who have had a UTI in the same period will also acquire one within six months, and between 20 and 30 percent will get recurrence (Foxman B, 1990). Men are less likely to get UTIs, and they usually start after the age of 50 (Tan and Chlebicki, 2016). Despite the fact that most infections are acute and transient, they can cause a considerable amount of morbidity in a population. Serious long-term consequences including a loss of renal function are brought on by severe infection. There is a difference between vaginitis, urethritis, and cystitis in females. However, there is a continuum in the gastro-urinary tract, and symptoms frequently coexist. (Sabih A, 2024a). The mid-stream

urine (MSU) of women experiencing UTI symptoms often remains negative (Sathiananthamoorthy *et al.*, 2019; McKertich and Hanegbi, 2021).

Since treatment with antibiotics for an acute illness does not stop relapses and multidrug-resistant urinary pathogens are becoming more common, current treatments are not ideal. For both men and women who are afflicted, these resistant illnesses can worsen their quality of life and develop into serious health issues (Aggarwal N, Leslie SW, 2024a). The common condition known as "bacteriuria," or bacterial colonization of the urine in this tract, can occasionally lead to microbial invasion of the tissues that produce, transport, and store urine (Tullus and Shaikh, 2020).

Pyelonephritis is an infection of the upper urinary system, which includes the kidney and its pelvis. The male urethra's first segment, the sexual organ that surrounds and communicates with it, the bladder (cystitis), the urethra (urethritis), or the prostate (prostatitis) can all be affected by a lower tract infection (Figure:1) (CDC, 2024). The recent development in urogenital infection will be covered in this chapter, along with its etiology, epidemiology, pathogenesis, virulence factors, clinical manifestation, laboratory diagnosis, and its subsequent treatment.

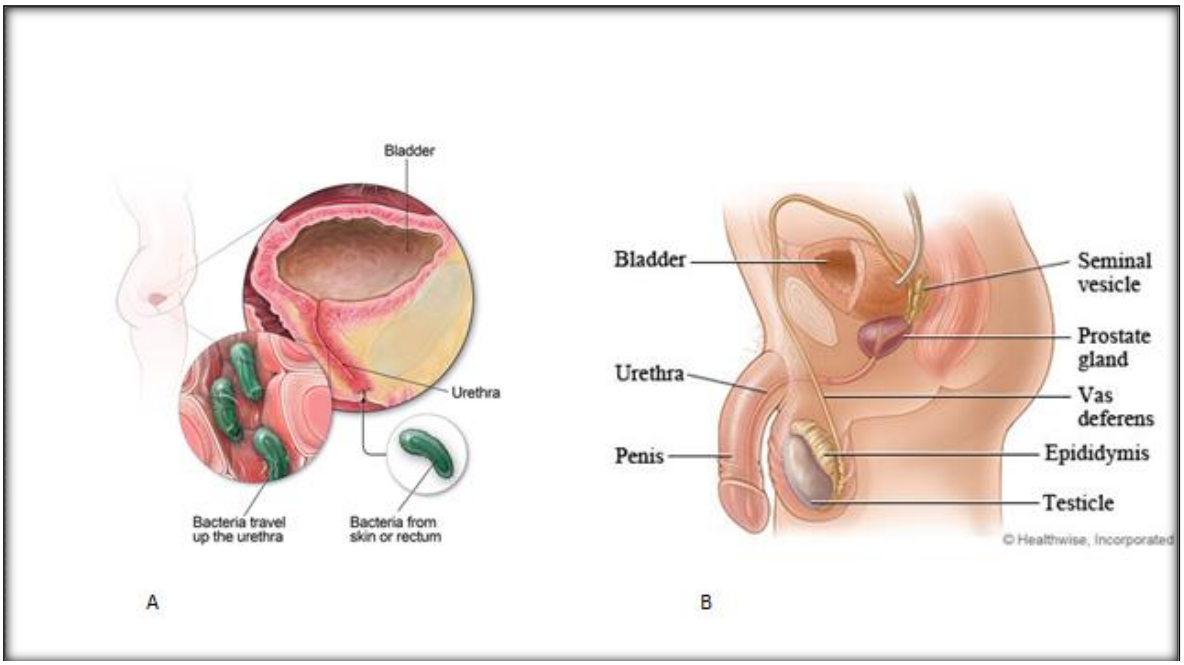
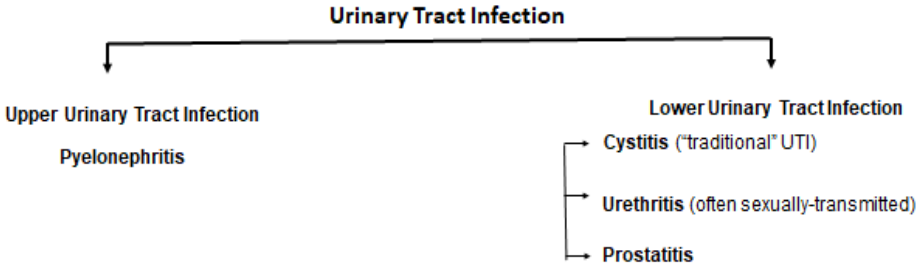


Figure 1: *A. The female urinary tract consists of the bladder and urethra. This diagram shows how bacteria from the skin or the rectum can travel up the urethra and cause an infection in the bladder. Picture sourced from the CDC. B. The male urinary tract is made up of the bladder (cystitis), urethra (urethritis), and prostate (prostatitis). Image courtesy of MyHealth.Alberta.Ca.*

1. **Types of Urinary Tract Infection:** Urinary tract infections come in two main varieties, and which urinary tract segment is infected determines the type of infection. Several urinary tract sections, such as the following ones, may be affected by a urinary tract infection (Figure: 2).



- **Upper Urinary Tract Infection**

  - **Pyelonephritis:** An infection of the kidneys, usually brought on by an obstruction in the urinary tract or an infection that has progressed up the tract. Urine backflow into the ureters and kidneys is caused by a blockage in the urinary system.

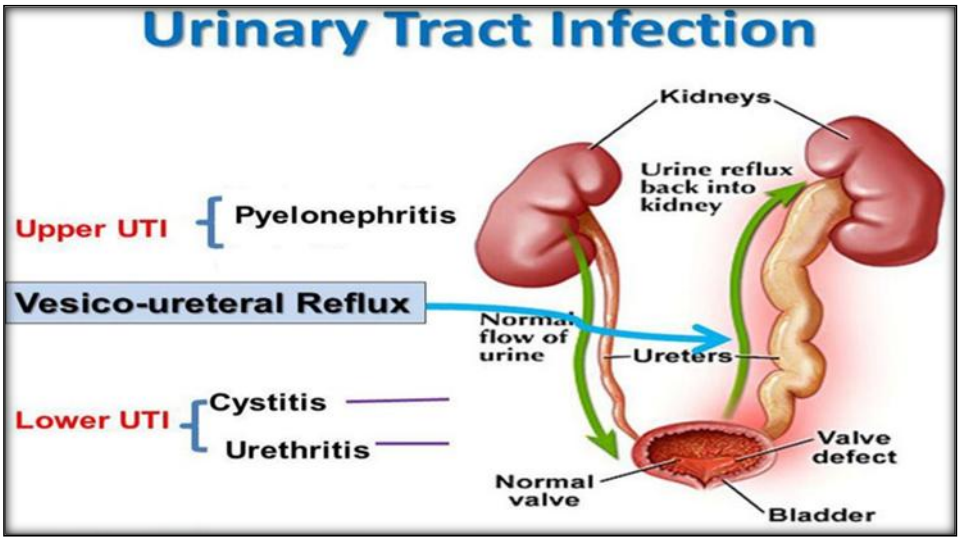


Figure 2: *An Overview of UTI infection image courtesy CDC*

- **Lower Urinary Tract Infection**

  - **Urethritis:** Urinary bladder discharge to the external environment is accomplished by the urethra, a hollow tube. Urethritis is an infection of this tube.
  - **Cystitis:** An infection of the bladder caused by bacteria that frequently travels up from the urethra.
  - **Prostatitis:** Inflammation of male prostate Glands Pain in the testicles, perirectum, and lower back are common symptoms of prostate infection...

2. **Etiology:** The bladder is the main source of bacterial infections, though it can also spread to the kidney. Septicemia can occasionally be brought on by urinary tract infection germs that enter the bloodstream. Less frequently, infection can arise from an organism spreading hematopoietic to the kidney, with the renal tissue becoming infected first (J. J. Belyayeva M, Leslie SW, 2024). According to epidemiology, UTIs happen in two contexts (Medina and Castillo-Pino, 2019):
   - Community-acquired
   - Hospital-acquired

   Although less frequent than community-acquired UTIs, hospital-acquired UTIs account for 40% of all nosocomial infections (Table 1) (Kalsi et al., 2003).

   The gram-negative rod is a kind of bacteria. The most common reason for ascending UTIs is *E. coli* (Zhou et al., 2023). Other Enterobacteriaceae, including *Proteus mirabilis*, are frequently linked to calculi in the urine. This is most likely due to the organism's strong urease, which reacts with urea to form ammonia, which makes the urine alkaline (Schaffer and Pearson, 2015). In hospital-acquired infections, more often found pathogens include *P. aeruginosa, Serratia spp., Enterobacter spp., and Klebsiella spp*. (Guentzel, 1996) (Figure 3).

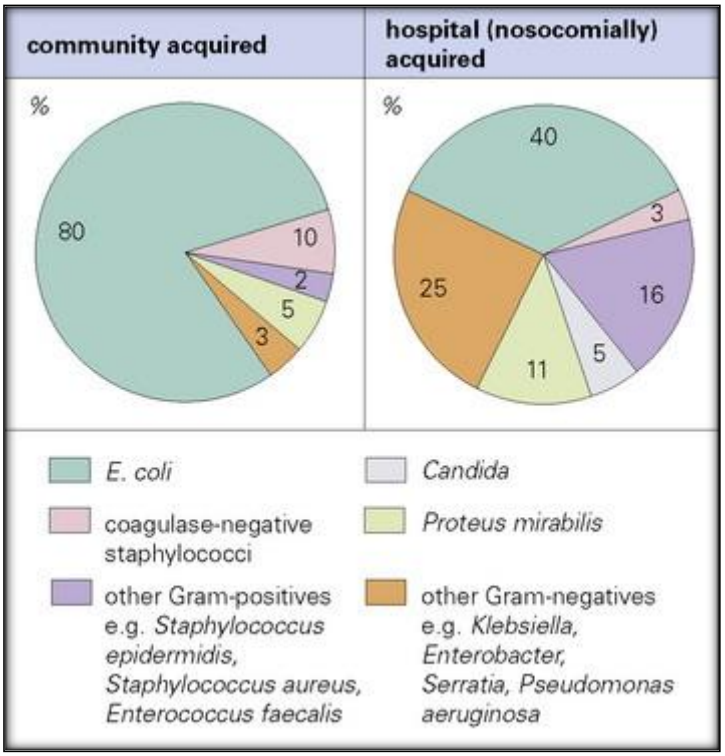
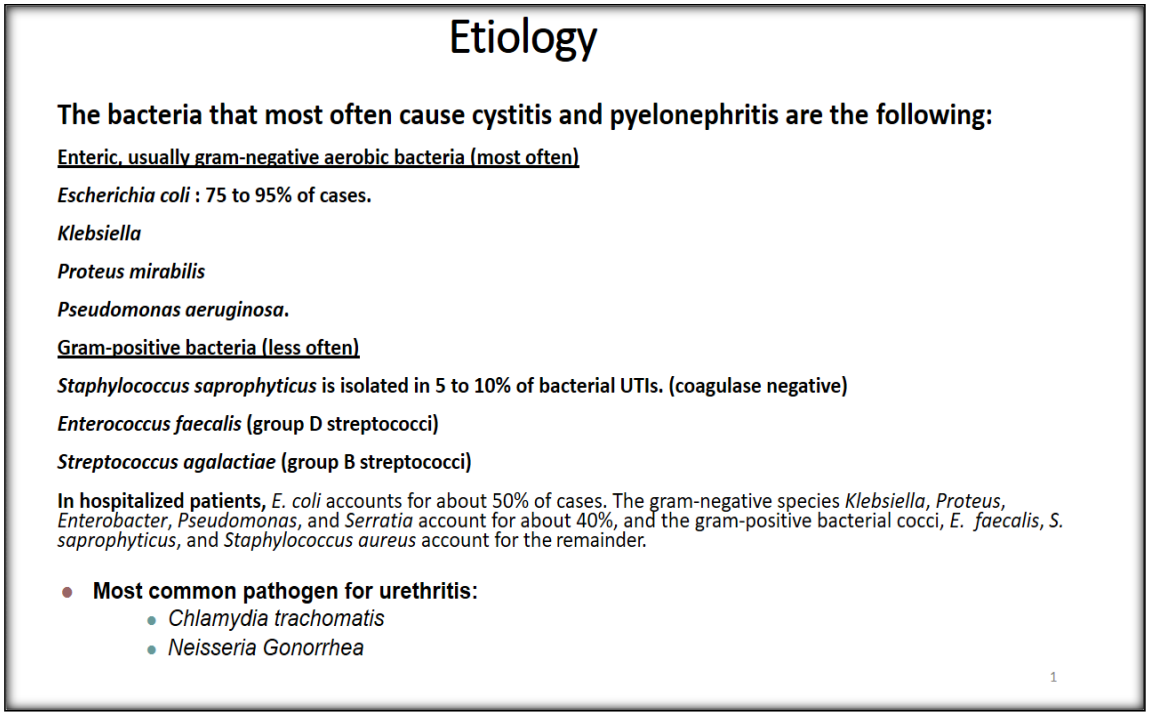


Figure 3: *Urinary tract infections' typical causes. The rates of hospital inpatients and outpatients with infections brought on by various bacteria are displayed. Although E. coli is the most prevalent isolate in both patient groups, keep note of the variations in the proportion of infections brought on via additional gram-negative rods. Hospital patients are colonized by these isolates, which frequently have multiple drug resistance. Image courtesy of Medical Microbiology by (Richard Goering, Hazel Dockrell, Mark Zuckerman, and Ivan Roitt, 2013).*

Staphylococcus saprophyticus is one example of a gram-positive bacteria that is more prone to infection, particularly in females who are young and infected sexually (Ehlers S and Merrill SA, 2023). Hospitalized patients' UTIs are caused by *Staphylococcus epidermis* and *Enterococcus spp* among AIDs patients. (Ehlers S and Merrill SA, 2023; Kahsay et al., 2024). Hospitalized individuals experience treatment challenges as a result of multiple antibiotic resistance. Lactobacilli and Corneybacteria are examples of species that grow in carbon dioxide, or capnophilic organisms. Seldom are obligatory anaerobes implicated (Wolfe et al., 2012; Mohd Khairul, Nurzam, and Hamat, 2022). *Mycobacterium tuberculosis*, *Candida spp,* and *Staphylococcus aureus* in UTI have been linked to hematogenous spread (Sabih and Leslie, 2024; Lo et al., 2013).

The bacteria that most often cause cystitis and pyelonephritis

Table 1: The Bacteria that Most Frequently Result in Pyelonephritis and Cystitis



Even in the absence of a UTI, certain viruses can be isolated from urine. Human polyomaviruses, JC, and BK enter the body through the respiratory system, travel throughout the body, and infect renal tubules and the ureter's epithelial cells, which creates the viral genome's latency and persistence (Luciani and Mattevi, 2022; Paduch, 2007). The viruses may reawaken asymptomatically during a typical pregnancy if there is a noticeable increase in the amount of virus in the urine (Brillo V; Tosto E, 2021). In patients with impaired immune systems, reactivation may result in hemorrhagic cystitis (Luciani and Mattevi, 2022; Hussain et al., 2020).

Congenitally infected infants may have high titers of rubella and CMV in their urine without any symptoms (Shukla S and Maraqa NF., 2024; Pass, 2008). Hemorrhagic cystitis is linked to asymptomatic adenovirus shedding (Klein et al., 2015). Renal syndrome with proteinuria is caused by a rodent-borne hantavirus that infects kidney

capillary blood vessels and causes Korean hemorrhagic fever (Tariq and Kim, 2022). Other viruses: mumps and HIV can cause kidney infections (Helin and Carstensen, 1983). Electron microscopy, viral isolation, immunological, and genomic detection techniques can all be used to examine urine samples(Goldsmith and Miller, 2009).

UTIs are rarely caused by parasites (Khurana et al., 2018). The following are added fungal causes of UTIs: Candida spp and *Histoplasma capsulatum* (Kauffman, 2014). In addition, Protozoa: Both men and women may develop urethritis as a result of *Trichomonas vaginalis* (Schumann JA and Plasner S., 2023). Infection with *Schistosoma haematobium,* which typically results in hematuria and bladder irritation Hematuria is caused by an egg penetrating the bladder. The eggs pierce the wall of the bladder and, in cases of severe infection, may result in a significant granulomatous reaction and calcification of the eggs. Chronic infections are linked to bladder cancer, while the exact mechanism is unknown. Hydronephrosis can also develop from ureter obstruction brought on by inflammatory alterations produced by eggs. (Lyon (FR): International Agency for Research on Cancer, 1994).

The condition known as urethral inflammation is known as urethritis. Clinical signs and symptoms include dysuria or urethral pruritus, as well as the discharge of mucopurulent or purulent material. *Neisseria gonorrhoeae* is the traditional bacterial pathogen of acute urethritis (Lewis, 2020). The collective term for urethral infection resulting from any other source is nongonococcal urethritis (NGU). *Chlamydia trachomatis* is the bacteria most obviously connected to conditions other than stomach ulcers (15–55% of instances). (Lewis, 2020). *Mycoplasma genitalium*, HSV, *Trichomonas vaginalis*, and *Ureaplasma urealyticum* are the microorganisms that cause Chlamydia-negative NGU. Most cases of non-chlamydial NGU have an unclear cause (Cinti, Malani, and Riddell, 2008a).

3. Epidemiology

Commonly Infected are Young Women: The prevalence varies with age and gender. In children urinary tract infections and UTIs, anatomical abnormalities are a significant concern. According to studies, structural abnormalities such as vesicoureteral reflux, ureteropelvic blockage, or duplicated ureters are present in more than 30–50% of children with UTIs. If left untreated, these anomalies might raise the risk of recurring urinary tract infections and result in complications like renal scarring and chronic kidney disorders (Garcia-Roig and Kirsch, 2016). UTIs are frequent, especially as people age. Compared to men, women are more likely to be suffering from a UTI. Approximately one in three women will experience a UTI before the age of 24 that necessitates medical care. Women's short, straight urethras make it easier for bacteria to enter the bladder (Bono MJ, Leslie SW, no date). Roughly 20–30% of women have recurrent infections, and 60% of every woman has experienced at least one UTI in her lifetime. (Foxman *et al.*, 2000; Foxman *et al.*, 2000; Patton, Nash, and Abrutyn, 1991) . Women's sexual activity has been connected to a higher risk of UTI infections and recurrences. Fifty to sixty percent of women will get urinary tract infections at some point in their life. Most cases of UTIs are caused by Escherichia coli. Recurrent UTIs (RUTIs) are primarily caused by reinfection with the same pathogen. Frequent intercourse is one of the main risk factors for RUTIs (Al-Badr and Al-Shaikh, 2013). Urinary incontinence is another risk factor for

UTIs in postmenopausal women (Ajith *et al.,* 2019). The chance of an infection returning may also be impacted by the virulence characteristics of the bacteria (Mancuso *et al.,* 2023).

Epidemiology of Hospital Acquired (HAUTIs) and Community Acquired (CAUTIs) UTIs: UTIs can be acquired in two broad environments, according to epidemiology: hospitals and communities. Hospital-acquired UTIs (HAUTIs) are typically linked to catheter use. Hospital-acquired UTIs make up 40% of all nosocomial infection rates while being less common than community-acquired UTIs. Thirty to forty percent of all infections related to healthcare are hospital-acquired illnesses, of which UTIs are one of the most prevalent (Kalsi *et al.,* 2003). The majority of UTIs are caused by *E. coli,* followed by *K. pneumoniae* and *Enterococcus species* (Kalsi *et al.,* 2003). Indwelling urinary catheters are the primary risk factor for HAUTIs, accounting for 70–80% of cases (Kalsi *et al.,* 2003). Extended hospital stays raise the risk of contracting hospital infections in UTIs (Simmering *et al.,* 2017). Individuals with chronic illnesses or those receiving chemotherapy who have compromised immune systems are particularly vulnerable (Sabih A, 2024b). Community-acquired UTIs (CAUTIs) are more common than hospital-acquired UTIs and affect primarily women, especially those who are sexually active, pregnant, or postmenopausal (Wawrysiuk *et al.,* 2019; Seid *et al.,* 2023). Recurrent infections are more common in women who have had UTIs in the past (Al-Badr and Al-Shaikh, 2013). Mechanical contraceptive of spermicides can change the flora in the vagina, which makes it easier for bacteria to colonize(Achilles *et al.,* 2018). One risk factor for UTIs is a family history of the condition (Scholes *et al.,* 2010).

Although *E. coli* is the primary cause of both HAUTIs and CAUTIs, the hospital setting and the administration of wide-spectrum antibiotics increase the occurrence of multidrug resistance organisms in HAUTIs (Medina-Polo, Naber and Bjerklund Johansen, 2021). CAUTIs predominantly affect young sexually active women, whereas HAUTIs are more common in elderly patients, those with prolonged hospital stays, and individuals with catheters (Rowe and Juthani-Mehta, 2013).

Male Diseases are Associated with Prostate Enlargement: Men are less likely than women to get UTIs because of anatomical differences. When they do, however, usually stem from underlying disorders. Men experience UTIs more frequently as they age, particularly after the age of 50. For adult males under 50, the incidence of genuine UTI is rather modest (5-8 per year per 10,000). Infections of the urethra (such as gonococcal and nongonococcal urethritis) and prostate associated with sexually transmitted diseases (STDs) are typically the cause of dysuria or frequent urination in this population (Foxman, 2002).

When compared to women, young men experience UTIs far less frequently (Tan and Chlebicki, 2016). Similar to UTIs in women, *E. coli* is the most frequent bacterium in male UTIs. About 25% of cases in men are caused by *E. Coli*, and the remainder of infections are mostly caused by Proteus and Providencia; Enterococci, Klebsiella, Pseudomonas, and Serratia are less common (John L Brusch, MD, 2024). Prostate enlargement is one risk factor associated with male UTIs. A bacterial breeding environment can be created by conditions such as BPH, which can cause incomplete bladder emptying(Aronson, 2023). Men who use urinary catheters are at higher risk for

UTIs due to the direct introduction of bacteria into the urinary tract. (Chenoweth, Gould, and Saint, 2014). Kidney stones and other obstructions can prevent normal urine flow, leading to infections. Urine flow can be disrupted by kidney stones and other blockages, which can result in infections (Thakore P, no date). HIV and diabetes are two conditions that can make a person more vulnerable to UTI infections (Skrzat-Klapaczyńska *et al.*, 2018).

Male infections continue to be rare until the fifth decade of life, at which point bladder emptying becomes difficult due to prostate hypertrophy (John L Brusch, MD, 2024). Incontinence following gynecologic or prostatic surgery, prolonged urethral catheterization and instrumentation drive the risk of UTIs in the elderly to 30 to 40% in both sexes (Ouslander, Greengold, and Chen, 1987). The infectious risk associated with a single bladder catheterization is 1%, and at least 10% of those who have in-home catheters develop an infection (Sedor and Mulholland, 1999).

4. **Pathogenesis of UTI and Associated Risk Factors:** Due to a few risk factors, the lower urinary tract becomes contaminated with the initial bacteria (Figure: 4). In this context, *E. coli*, which is a gram-negative bacterium that causes UTIs in 80–90% of cases (Flores-Mireles *et al.*, 2015). Initially, they colonize the bladder and urethra, which causes the lower UTI to become inflamed. In this region, neutrophils are then recruited. Hence, bacteria and neutrophils will invade the bladder (Klein and Hultgren, 2020). Certain virulence factors allow bacteria to proliferate and make it easier for them to elude the immune system. For instance, *E. coli* binds to lower urinary tract cells to conceal itself from immune cells (Peterson JW, 1996). Bacteria can create biofilms. Any collection of microorganisms that are symbiotic and rely on one another to stick to surfaces to thrive is called a biofilm (Sharma *et al.*, 2023). Upper urinary tract infections (UTIs) can result from bacteria that ascend toward the kidney and colonize it if the infection worsens, is left untreated, or the patient has a damaged immune system (JM., Jeong, Belyayeva M, 2024). Bacteria can then, in the worst-case scenario of septic shock, spread to circulation through the renal veins if left untreated (Hsiao *et al.*, 2015).

   One of the main risk factors for urinary tract infections is urinary tract catheterization, particularly in women (Nicolle, 2014; Field, Harris, and Pollock, 2010) (Figure: 5). Similarly, if catheterization is not done hygienically, it might bring infection directly into the bladder. When germs invade the bladder, a protective inflammatory immune response is triggered. A perfect habitat for uropathogens that express fibrinogen binding to attach protein is created when fibrinogen builds up in the catheter (Flores-Mireles, Hreha, and Hunstad, 2019). Following their first attachment to the catheter, bacteria can grow and create a biofilm, which increases the risk of epithelial cell damage and kidney seed infection. Urinary tract infections are frequent during pregnancy (Lila *et al.*, 2023). The urethra is shorter in pregnant women, however this is not the only factor contributing to the nearly universal incidence of UTIs following catheterization. Progesterone causes the production of urine by relaxing smooth muscles, which permits colonization, particularly up to the kidney. Progesterone relaxes smooth muscle, and the gravid uterus compresses the bladder, lowering its capacity. Stasis in the urine may be observed, as vesicoureteral reflux increases the amount of leftover urine in the bladder. Pregnancy-related UTI risk increases with any of these changes (Habak PJ, Carlson K, Griggs, 2024). Urine analysis is crucial during pregnancy since UTI infections are not

only common but also silent. Untreated urinary tract infections during pregnancy can have negative effects on the developing fetus (Habak PJ, Carlson K, Griggs, 2024).

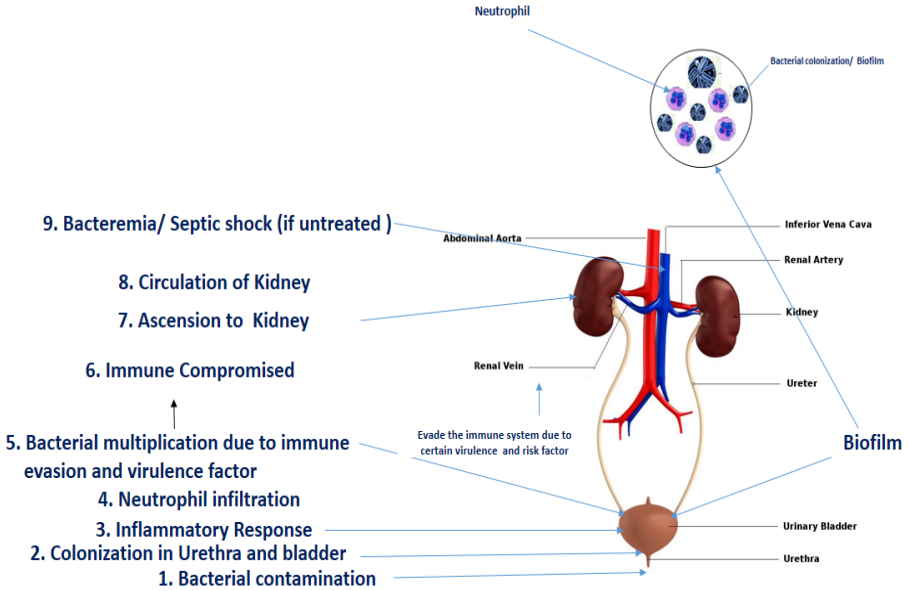


Figure 4: *Sequential events of the pathogenesis of urinary tract infections*

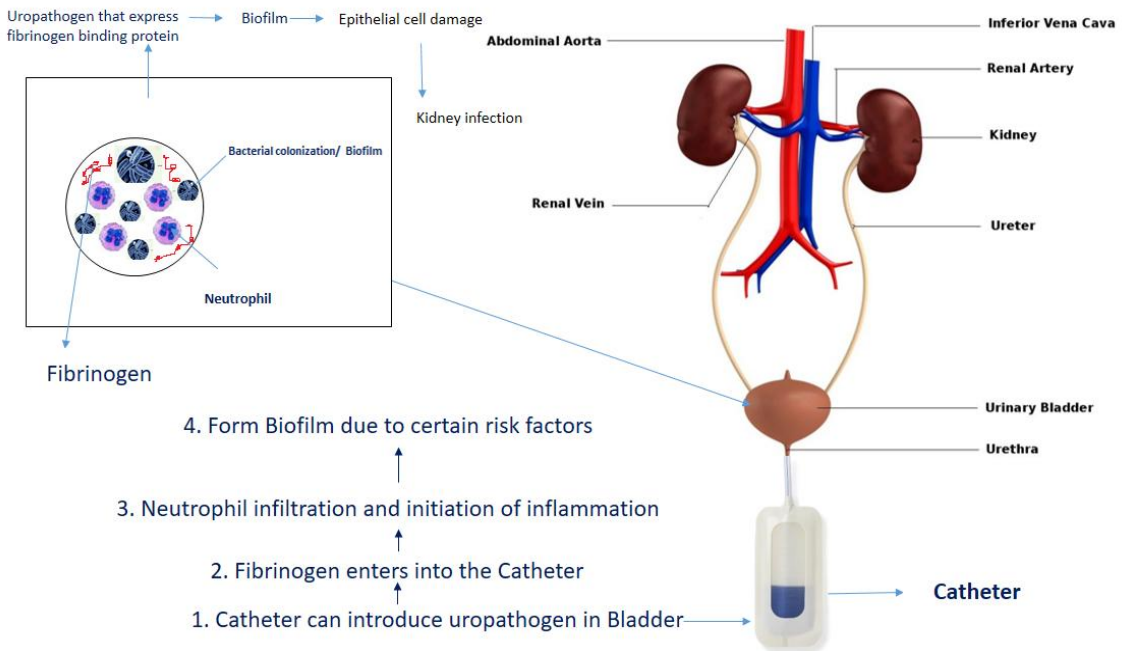


Figure 5: *The Catheterization a risk factor for Urinary tract infection*

- **The Perineal Flora is the Source of Bacteria:** The urine that the kidney creates travels through the ureters and renal pelvis to the sterile bladder in a healthy state (Mancuso G, 2023). Bacteria that can survive in this environment cause infection.

Bacteria belonging to the perineal flora, whether permanent or temporary, mainly follow an ascending pathway of access (Bono MJ, 2023).

- **Physical Elements:** Anything that prevents the bladder from completely emptying, interferes with the passage of urine or makes it easier for organisms to enter the bladder (Hooton and Stamm, 1997). Women's shorter urethras are more prone to infection (Hooton and Stamm, 1997). Because sexual activity makes it easier for organisms to pass up the urethra, especially in females, sexually active women have a higher prevalence of UTI. It could be significant to occur before bacteria colonize the vaginal periurethral region (Sihra *et al.*, 2018; Foxman, 2014; Hannan *et al.*, 2012). Fecal organism colonization of the prepuce and urethra is linked to the higher incidence of urinary tract infections (UTIs) in male infants who are not circumcised (Barola S, Grossman OK, 2024).

- **Sexual Activity is Typically Associated with UTI:** Uncomfortably close to the gut flora is where these organisms originate (Barola S, Grossman OK, 2024). Sexual activity is the most significant factor in establishing access since it has been demonstrated to temporarily transfer bacteria into the bladder. Due to the small urethral distance, this puts the female companion at risk (Czaja *et al.*, 2009; Buckley, McGuckin, and MacGregor, 1978; Rosen *et al.*, 2007; Hooton and Stamm, 1997).

- **The Risk is Higher with Catheters:** There is risk associated with other urethral interventions as well, especially those that are therapeutic, such as catheterization. Microorganisms can enter the bladder directly during a catheter infection, and while the catheter is in place, it can also help germs enter the bladder by tracking up between the urethral wall and the catheter's lumen. A urinary catheter interferes with the bladder's natural defense mechanism, giving bacteria an advantage. Therefore, the length of catheterization is directly linked to a higher risk of infection (Hariati, Suza, and Tarigan, 2019; Agodi, A. and Barchitta, 2011; Meddings and Saint, 2011; Assanga, 2016). Approximately 3-7% more people have UTI infections every day they are catheterized (McGuckin, 2012; Lo *et al.*, 2014).

- **Clinical Complication:** The most common causes of blockage to full bladder emptying are pregnancy, prostatic hypertrophy, renal calculi, tumors, and strictures (Leslie SW, Sajjad H, 2024; Klahr, 2008; Rasmussen and Nielsen, 1988). One significant risk factor for urinary tract infections (UTIs) is thought to be residual urine (Merritt, 1981, The Journal of the American Paraplegia Society, 1992). When an infection is combined with a blockage in the urinary tract, it can spread to the kidney and quickly destroy renal tissue.

- **Anatomical Abnormalities:** A common condition in children with anatomical anomalies, vesicoureteral reflux (reflux of urine from the bladder cavity up the ureters, sometimes into the renal pelvis or parenchyma) may put a child at risk for ascending infection and kidney injury (Lotfollahzadeh S, Leslie SW, 2024). In children without underlying problems, reflux may also be associated with infection; however, this tends to go away as the child gets older (Lotfollahzadeh S, Leslie SW, 2024, Mattoo, 2007).

- **Association of UTI with Disease State:** Clinical surveys conducted after mortality have revealed less evidence of a connection between diabetes mellitus and pyelonephritis. However, their clinical results are less obvious than those of non-diabetic patients, diabetic CA-APN patients require longer hospital stays and more severe disease symptoms (Kim *et al.*, 2014). Nonetheless, UTIs can be more severe in diabetic mellitus patients, and recurring UTIs are likely if diabetic neuropathy impairs normal bladder function (Nitzan *et al.*, 2015).

  Additionally, bacteria from the circulation may enter the urinary tract. This is far less common, as it necessitates an uncontrolled infection at a different location (Mancuso *et al.*, 2023).

Virulence Factors in the Bacteria Causing UTI: An individual is more vulnerable to infection if something interferes with the regular flow of urine, prevents the bladder from emptying, or makes it easier for organisms to enter the bladder. There are several factors associated with UTI infection illustrated in the figure (Figure 4).

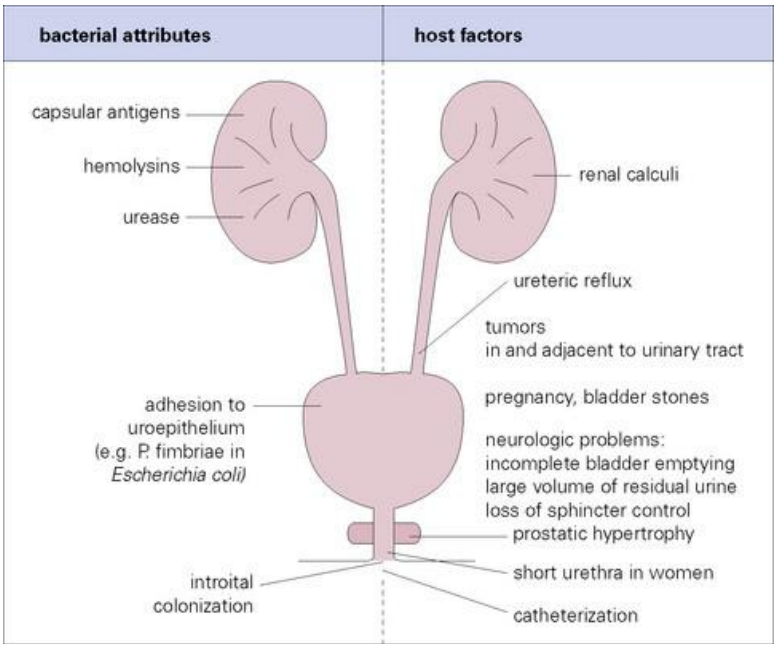


Figure 6: *Characteristics of the bacteria and the host that promote urinary tract infections (UTIs). Urinary tract abnormalities often increase the risk of infection. There has been extensive research on bacterial adhesion factors, but not as much is known about other bacterial virulence factors. Image courtesy of Medical Microbiology by (Richard Goering, Hazel Dockrell, Mark Zuckerman, Ivan Roitt, 2013)*

Escherichia Coli: The only species with the necessary characteristics to colonize and infect the urinary tract are facultative and aerobic bacteria. UTIs are generally brought on by two serogroups of *E. coli* (Johnson *et al.*, 2005*;* Domingos *et al.*, 2022*;* Agarwal, J., Srivastava, S. and Singh, 2012):

- O (Semantic serotypes, somatic antigen)- (O1,O2,O4,O6,O7 and O75)

- K (Capsular serotypes)- (K1,K2,K3,K5,K12 and K13)

The *E. coli* serotypes linked to gastrointestinal tract infections (EPEC) are not the same as these. "Uropathogenic *E. coli*" (UPEC) is described as *E. coli* that causes UTI. The primary cause of UTIs in the community is UPEC. Based on the expression of toxins and surface polysaccharides, iron acquisition mechanism, adhesion, and toxins, four major UPEC phylogroups (A, B1, B2, and D) have been identified (Terlizzi, Gribaudo and Maffei, 2017). When mannose is present in a variety of human cells, type-1 fimbriae can facilitate adhesion. These strains are a range of genes in chromosomal pathogenicity islands that are absent from fecal *E. coli.* For instance, genes linked to the colonization of the periurethral regions are usually present in UPEC(Kaper, J. B., Nataro, J. P., & Mobley, 2004).

These strains are a range of genes in chromosomal pathogenicity islands that are absent from fecal *E. coli* (Kaper, J. B., Nataro, J. P., & Mobley, 2004). For instance, genes linked to the colonization of the periurethral regions are usually present in UPEC. One such instance is the adhesion that permits UPEC to selectively cling to the urethral and bladder epithelium, known as p. fimbriae (pyelonephritis-associated pili, or PAP) pili. While Type-1 fimbriae interbacterial interaction and biofilm formation in the lumen's center cause antibiotic resistance, P fimbriae binds bacteria to epithelial cells. Similar adhesions for uroepithelial cells have been demonstrated by studies with different types of urinary tract infections. Adhesion of this kind may play a role in pathogenicity; instances of this Mannose-resistant haemagglutination are caused by filamentous structures that resemble fimbriae, and these structures are crucial to the pathophysiology of UTI infection(Lane and Mobley, 2007).

Additional characteristics of *E. coli* that seem to contribute to the location of organisms in the kidney and renal injury include:

By preventing phagocytosis, the capsular acid polysaccharide (K) antigens are known to allow *E. coli* strains to evade host defenses and are linked to the development of pyelonephritis. The ability of *E. coli* to harm kidneys has been connected to its production of hemolysins; several hemolysins function more generally as toxins that destroy membranes (Riley, 2014; Cress *et al.*, 2014; Bingen *et al.*, 1997; Kaijser, 1973).

Additionally, the flagellar antigen, which is a component of bacterial flagella, is referred to as the H antigen. These antigens are used to categorize various *E. coli* strains. The identification of particular strains—which is vital to comprehending their virulence and resistance patterns—requires the use of the H antigens (Ratiner *et al.*, 2003). One well-known pathogenic strain that can cause serious foodborne illness is *E. coli* O157:H7(Ameer MA, Wasey A, 2023). Sequence type 131 (ST131) of *E. coli* is a multidrug-resistant clone that is worldwide prominent and linked to bloodstream and urinary tract infections. The majority of ST131 strains produce illnesses for which there are few available treatments and show resistance to several medicines. The biggest sub-clonal ST131 lineage expresses an H4 flagella antigen, has the type 1 fimbria fimH30 allele, and is resistant to fluoroquinolones. In general, the behaviors of H4, H1, and H7 flagella are conserved in terms of invasion, motility, adherence of epithelial cells, and absorption by macrophages. As opposed to H1 and H7 flagella, H4 flagella cause greater

activation of the anti-inflammatory cytokine IL-10; this characteristic might help explain ST131 fitness in the urinary system (Kakkanat *et al.*, 2015).

Klebsiella Pneumoniae: Many Klebsiella species, most notably *K. pneumoniae*, are important UTI causes. Their capacity to spread illness is facilitated by their virulence factors. lipopolysaccharides, Siderophores, fimbriae, and capsules are important virulence agents (Riwu *et al.*, 2022). Numerous Klebsiella bacteria are resistant to antibiotics because they generate carbapenemase or extended-spectrum beta-lactamases (ESBLs) (Parveen *et al.*, 2011).

Proteus Mirabilis: One frequent cause of UTIs is *Proteus mirabilis*. Possess several virulence factors that enhance pathogenicity, including (Coker, C., Poore, C.A., Li, X. and Mobley, H.L., 2000; Norsworthy and Pearson, 2017)

- **Urease Production:** Urine acidification and the development of struvite stones, which can worsen urinary tract injury, are caused by this enzyme's hydrolysis of urea into ammonia and carbon dioxide. *P. mirabilis* is thought to be more susceptible to urolithiasis, pyelonephritis, and upper urinary tract infections due to its capacity to produce urease.

- **Fimbriae and Adhesins:** These features make it possible for the bacteria to stick to the uroepithelium, which promotes colonization and infection (E., T., and M., 2018).

- **Flagella:** Due to their ability to move, these bacteria can go up the urinary canal from the urethra to the bladder and possibly even the kidneys (Schaffer and Pearson, 2015).

- **Biofilm Formation:** This contributes to the persistence of infection by strengthening the bacteria's resistance to host immune responses and medications. The *P. mirabilis* biofilms found in the urinary tract, especially on the surface of catheters, have been studied the most. The crystallized biofilms that cause catheter incrustation and blockage are the major problems. They may contain two primary forms of crystals: apatite (hydroxyl calcium phosphate) and struvite (magnesium ammonium phosphate). They develop in the biofilms of the urinary system and obstruct the flow of urine (Jacobsen and Shirtliff, 2011). Bladder obstruction, bacteriuria episodes, fever, sepsis, and shock are possible side effects(Jones *et al.*, 2007).

- **Hemolysins:** The toxin can lyse red blood cells, which releases nutrients and damages surrounding tissue (Weaver, T. M., Hocking, J. M., Bailey, L. J., Wawrzyn, G. T., Howard, D. R., Sikkink, L. A., Ramirez-Alvarado, M., & Thompson, 2009).

- **Proteases:** proteins from the host that are broken down by enzymes to help evade the immune system and absorb nutrients. Proteus mirabilis ZapA Metalloprotease breaks down a variety of substrates, including peptides that fight microbes (Belas, Manos, and Suvanasuthi, 2004)

Because of these, Proteus mirabilis is a notoriously difficult pathogen to treat in situations of urinary tract infections (UTIs), particularly when patients are catheterized or have complex infections (Jamil RT, Foris LA, 2024). In addition to being the causative agent

of a greater proportion of individuals with complex urinary tract infections, Proteus mirabilis is an occasional source of urinary tract infections in normal hosts. This covers those with persistent medical equipment, such as urine catheters that are indwelling, or those who have functional or anatomical problems(Fox-Moon and Shirtliff, 2015).

Pseudomonas Aeruginosa: An important opportunistic pathogen, *Pseudomonas aeruginosa* is well-known for its involvement in urinary tract infections (UTIs), especially in patients with weakened immune systems or urinary catheters. *P. aeruginosa* pathogenic process involves a variety of virulence factors that are crucial for immune evasion, host immunological suppression, and bacterial adherence and colonization. There are multiple reasons why *P. aeruginosa* is so virulent when it comes to UTIs (Liao *et al.*, 2022):

- **Biofilm Formation:** On surfaces like catheters, *P. aeruginosa* can build biofilms that shield the bacterium from antibiotic therapy and the host immune system (de Sousa *et al.*, 2023).

- **Motility:** The ability of the bacteria to move and stick to the urinary tract epithelium is provided by its flagella and pili (Reynolds and Kollef, 2021).

- **Exotoxin and Enzymes:** Exotoxins (such as ExoS, ExoT, ExoU, and ExoY) and enzymes (such as protease and elastase) produced by *P. aeruginosa* harm host tissue and impair immune responses (Reynolds and Kollef, 2021).

- **Quorum Sensing:** *P. aeruginosa* can synchronize the production of virulence factors and the creation of biofilms through the mechanism of cell-to-cell communication (Qin *et al.*, 2022).

- **Antibiotic Resistance:** *P. aeruginosa* has a high level of intrinsic resistance to a variety of antibiotics, and it can pick up more resistance through horizontal gene transfer and mutation (Pang, Z., 2018).

- **Iron Acquisition:** For *P. aeruginosa* to thrive and become pathogenic, it needs iron from the host, which it scavenges using a variety of methods. Pyoverdines are among the several virulence factors secreted by *P. aeruginosa* to live inside its host. Bacteria create and release siderophores, which are tiny chemical molecules that help them obtain iron, a crucial nutrient for bacterial growth and pathogenicity (Chimiak, A., 1984).

P. aeruginosa can cause infections, endure in the urinary tract, and be resistant to therapy due to a combination of these features.

Staphylococcus Saprophyticus: UTIs are frequently caused by *Staphylococcus saprophyticus*, particularly in young, sexually active women. It is most virulent in sexually active women. Several variables are primarily responsible for its virulence (Azimi *et al.*, 2020):

- **Urease Production:** The enzyme urease, which is produced by *S. saprophyticus*, hydrolyzes urea to create carbon dioxide and ammonia. Urine's PH is raised as a result, which may encourage the growth of bacteria and cause kidney stones (Ehlers S, 2024).

- **Adhesion Factor:** Because of the surface proteins on its surface, the bacteria can stick to uroepithelial cells. For urinary tract colonization and infection, this adherence is essential.

- **Hemagglutination:** Haemagglutinin is expressed by *S. saprophyticus*, which aids in its ability to attach to the cells lining the urinary system (Ehlers S, 2024).

- **D-Serine Utilization:** *S. saprophyticus* may have an advantage over other bacteria in the urine because it can use D-serine, a substance present in urine. The only species of Staphylococcus that normally causes urinary tract infections and has a gene that codes for d-serine-deaminase (DsdA) is *S. saprophyticus*. The presence of the d-serine-deaminase gene in the genome of uropathogens is not surprising, since d-serine is a common component of urine and is poisonous or bacteriostatic to many different types of bacteria. It has been proposed that pathogenicity depends on d-serine-deaminase or the capacity to react with or metabolize d-serine (Korte-Berwanger *et al.*, 2013).

- **Biofilm Formation:** Because of these virulence characteristics, Staphylococcus saprophyticus can effectively cause urinary tract infections by persisting in the urinary tract (Martins *et al.*, 2019). *S. saprophyticus* may effectively infect and remain in the urinary tract, causing UTIs, because of their virulence characteristics.

***Enterococcus Faecalis* / Group D Streptococcus:** *Enterococcus faecalis* is a major cause of urinary tract infections (UTIs), especially in hospitalized patients or those using urinary catheters (Said MS, Tirthani E, 2024). Among its virulence factors are:

- **Biofilm Formation:** *E. faecalis* is capable of forming biofilms on surfaces similar to urinary catheters, which shield the bacteria from both the host immune system and antibiotics (Bai, B., & Chen, 67AD).

- **Adhesion Factors:** The bacteria secrete surface proteins called adhesins, which help medical equipment and urinary tract epithelial cells adhere to one another. Surface proteins, such as Esp proteins that attach to bladder cells and Ebp proteins that bind to biotic and abiotic surfaces like catheters, are what allow E. faecalis UTI bacteria to adhere to host cell surfaces. These surface proteins also play a role in the creation of biofilm (Govindarajan and Kandaswamy, 2022).

- **Cytolysin:** Red blood cell lysis by this toxin can result in tissue injury and immunological evasion. Because it causes blood hemolysis, the secreted toxin cytolysin, which is released in response to pheromones, adds to the pathogenicity of *E. faecalis* (Ike, Hashimoto, and Clewell, 1984).

- **Gelatinase and Serine protease:** These enzymes aid in the spread and persistence of bacteria by breaking down extracellular matrix elements and host tissues (Giridhara Upadhyaya, Umapathy and Ravikumar, 2010; Said MS, Tirthani E, 2024).

- **Aggregation Substance:** By encouraging the formation of biofilms and cell clumping, these surface proteins strengthen resistance to both immune response and drugs(Taglialegna *et al.*, 2020).

- **Antibiotic Resistance:** Numerous antibiotics are intrinsically resistant to *E. faecalis*, and they can pick up more resistance genes, making treatment more difficult (Miller, Munita, and Arias, 2014).

E. faecalis can cause, sustain, and worsen UTIs due to these variables, particularly in patient populations who are more susceptible.

***Streptococcus Agalactiae* / Group B Streptococcus:** Although *Streptococcus agalactiae*, commonly referred to as Group B streptococcus (GBS), is mainly associated with newborn infections, it can also cause urinary tract infections (UTIs), particularly in immunocompromised and pregnant women (Mohanty, S., 2021). The following are the virulence factors for *S. agalactiae* that cause UTIs:

- **Capsule:** By preventing pathogenesis, the polysaccharide capsule aids in the bacteria's ability to elude the host's immune system (Ulett *et al.*, 2010).

- **Adhesins:** To adhere to uroepithelial cells and colonize the urinary tract, *S. agalactiae* needs surface proteins like pilli and other adhesion molecules(Flores-Mireles *et al.*, 2015).

- **Hemolysins:** Red blood cells can be lysed by beta hemolysins or cytolysin, which can cause tissue damage and promote the infection's spread (Kulkarni *et al.*, 2013).

- **C5a Peptidase:** By breaking down the complement system's C5a component, this enzyme lessens the amount of immune cells that are drawn to the infection site(Tan *et al.*, 2011).

- **Hyaluronidase:** This enzyme promotes the transmission of germs through tissues by degrading hyaluronic acid in the extracellular matrix (Vornhagen *et al.*, 2016).

- **Immune Evasion:** The aforementioned capsule and enzymes that break down host defense components are just two of the ways the bacteria might elude the immune system (Korir, Manning, and Davies, 2017). Because of these virulence characteristics, S. agalactiae can infect the urinary system, stay in the host, and produce UTI symptoms

Serratia Species: Asymptomatic Serratia urinary tract infection patients make up between 30% and 50% of the patient population. Fever, frequent urination, dysuria, pyuria, or pain during urination are possible symptoms. Ninety percent of the patients have had recent urinary tract surgery or instrumentation. (Nicolle, 2005).

In addition to producing carbapenem antibiotics, a red pigment known as prodigiosin, and biosurfactants, *Serratia species* release several virulence factors, including DNase, lipase, gelatinase, hemolysin, proteases, chitinase, chloroperoxidase, and numerous isozymes of alkaline phosphatase(Thomson *et al.*, 2000).

Neisseria Gonorrhoeae: The bacterium that causes gonorrhea, a common sexually transmitted infection that frequently causes urethritis in males, is *Neisseria gonorrhoeae*. *Neisseria gonorrhoeal's* main virulence factors are as follows:

- **Pili (Fimbriae):** The urethral epithelial cells of *N. gonorrhoeae* can cling to these hair-like features. Their involvement in colonization is crucial, and they are necessary for the first phase of infection(Green *et al*., 2022).

- **Opacity Proteins:** The adhesion and invasion of host cells are facilitated by these proteins. Through phase variation, they enable the bacteria to turn on and off expression, aiding in its ability to elude the host immune system (Quillin and Seifert, 2018).

- **Porins (Por B):** In the bacterial membrane, these proteins create pores that permit the intake of nutrients and the outflow of waste. Inhibiting the complement system, which aids in the removal of pathogens, they also obstruct host immunological responses (Kurzyp and Harrison, 2023).

- **Lipopolysaccharide:** Lipopolysaccharide (LPS), which is present in various Gram-negative bacteria, is comparable to this enterotoxin. Lipopolysaccharides can cause a significant inflammatory response that destroys tissue and aids in immune evasion.

- **IgA1 Protease:** By cleaving immunoglobulin A1 (IgA1) antibodies from mucosal surfaces, this enzyme helps the bacteria avoid the host's defenses (Kilian and Russell, 2015).

- **Iron Acquisition Systems**: *Neisseria gonorrhoeae* relies on multiple processes for its growth and survival, including iron acquisition systems. Among these are human transferrin and lactoferrin receptors (Lee and Bryan, 1989).

- **Antigenic Variation**: It is often the case that *N. gonorrhoeae* alters its surface components, including the pill and Opa proteins, rendering it more challenging for the host immune system to identify and eradicate the bacterium (Lee and Bryan, 1989).

- **Biofilm Formation**: Antibiotics and the human immune system can cause persistent and recurrent infections; nevertheless, the organism's ability to form biofilms on mucosal surfaces shields it from these threats (Lee and Bryan, 1989).

All of these virulence factors work together to enable *N. gonorrhoeae* to infect hosts, elude the immune system, and produce gonorrhea-related symptoms including urethritis.

Chlamydia Trachomatis: Urethritis can also be caused by *Chlamydia trachomatis*, particularly in males. This particular bacterium causes chlamydia, which is among the most prevalent STDs. These are some salient points about its determinants of virulence (Young A, Toncar A, Leslie SW, 2024).

- **Elementary Body (EB) and Reticulate Body (RB):** The biphasic life cycle of Chlamydia trachomatis has two different types. The infectious form that can endure outside of host cells is called EB, and the replicative form that lives inside of host cells is called RB. This cycle facilitates the bacterium's ability to multiply and infect new cells (Y Becker, 1996).

- **Adhesion and Invasion:** *C. trachomatis* has proteins that aid in adhesion to and penetration of urethral epithelial cells. One example of this is the main membrane protein (MOMP), which facilitates attachment to host cells(Su *et al.*, 1990).

- **Inclusion Formation:** Upon entering the host cell. Inclusion is the name of the membrane-bound vacuole in which *C. trachomatis* is found. Because of their inclusion, the bacteria are shielded from host immune reactions and can influence host cell functions in a way that promotes bacterial growth (Olson-Wood *et al.*, 2021).

- **Type III Secretion System (T3SS):** The device resembles a molecular syringe and is used to inject effector proteins into the host cell to change its functionality. These effectors can modify immunological responses, cytoskeleton dynamics, and host cell signaling, and promote bacterial survival and multiplication (A.Rucks Elizabeth, 2023).

- **Heat Shock Proteins:** HSPs are produced by *C. trachomatis* and aid the bacteria in surviving in a stressful environment within the host. These proteins can cause inflammation, which exacerbates the infection's pathogenesis (Linhares and Witkin, 2010).

- **Inhibition of Apoptosis*:*** *C. trachomatis* can prolong the intracellular environment for its multiplication by preventing the host cell's planned cell death, or apoptosis(Sixt *et al.*, 2018).

- **Immune Evasion:** There are ways for *C. trachomatis* to evade the host immune system's identification and elimination. It can lessen immune cells' ability to recognize infected cells by preventing their antigens from being shown on their surface (Wang, X., Wu, H., Fang, C., & Li, 2024).

- **Inflammation Induction:** The infection incites the host's inflammatory response, resulting in symptoms including pain and discharge from the urethra when urinating. Scarring and tissue damage can result from persistent inflammation (Redgrove, K. A., & McLaughlin, 2014).

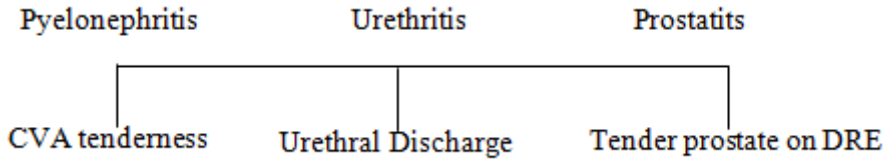
These virulence factors enable *C. trachomatis* to efficiently infect and stay within host cells, leading to various consequences if treatment is not received, including urethritis.

5. **Clinical Manifestation:** A UTI can present with a variety of clinical symptoms. Roughly half of infections result in no detectable symptoms and are unintentionally found during a routine checkup. Fevers, vomiting fits, and low vital signs are just a few of the general symptoms that newborn infections cause. When they do occur, symptoms in older kids and adults can help identify the infection and occasionally even pinpoint its exact location in the urinary system. They are categorized into two types:

- Upper urinary tract Infections:
  - **Pyelonephritis**
- Lower urinary tract infections
  - **Cystitis** ("traditional" UTI)
  - **Urethritis** (often sexually transmitted)
  - **Prostatitis**

Examination of UTI

Physical Exam



Laboratory Analysis

- **WBCs**
- **RBCs**
- **Nitrites- Abundant in Gram-negative rods**
- **Leukocyte esterase**

Culture

- **>10^5 CFU/Ml is considered a positive culture**
- **Bacteria commonly found for cystitis, prostatitis, and pyelonephritis:**
  - *Escherichia coli*
  - *Staphylococcus saprophyticus*
  - *Proteus mirabilis*
  - *Klebsiella*
  - *Enterococcus*

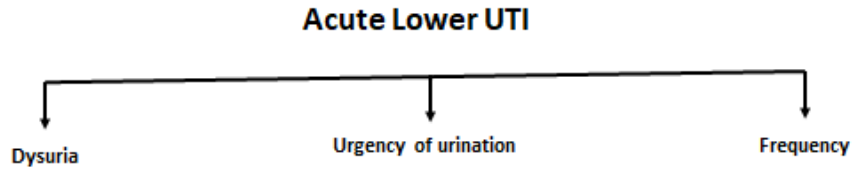
Symptoms of Urinary Tract Infection

The main clinical symptoms during UTI infections are as follows-

- Dysuria (burning pain on passing urine)
- Increased frequency of micturition
- Urgency (the urgent need to pass urine)
- Hematuria

- Fever
- Nausea/Vomiting (pyelonephritis)
- Flank pain (pyelonephritis)

Triad Lower Urinary Tract Infection



Lower Urinary Tract Infection Cystitis: Most elderly people with indwelling catheters have asymptomatic UTIs. The presence of pus cells (pyuria), bacteria (bacteriuria), and sometimes blood (hematuria) causes the urine to become hazy. These conditions are typically asymptomatic. Urine specimens must be examined in a lab to verify the diagnosis. Similar symptoms can be seen in patients with chlamydial urethritis or vaginal thrush. Pyuria in the absence of a positive culture may result from tuberculosis or chlamydia. Additionally observed in individuals getting antibiotic medication for urinary tract infections (UTIs), as the antibacterial agent inhibits or kills the bacteria before the inflammatory response subsides.

- **Simple Cystitis:** This condition affects women in good health who show no symptoms of systemic illnesses. Healthy, non-pregnant adult woman above the age of twelve. No vomiting, fever, nausea, or flank pain. Dipstick urinalysis is used to make the diagnosis; no culture or laboratory testing is required (Sabih A, 2024b). For three days, use trimethoprim/sulfamethoxazole. In regions with high frequencies of bactrim-resistant bacteria, people with sulfa allergies may benefit from the use of fluoroquinolone (ciprofloxacin or levofloxacin). Sexual activity is one of the risk factors. Patients may be advised to use prophylactic antibiotics or fluoroquinolone after coital voiding. Further, patients may be advised prophylactic antibiotic use or post-coital voiding (Jancel and Dudas, 2002).

- **Complicated Cystitis:** Men and women with concurrent medical conditions exhibit this. The patients are all male and have Foley catheters inserted. Hospitalized patients who have urospirosis. Urinalysis and urine culture play a part in diagnosis. More labs are recommended for accuracy (Shackley *et al.*, 2017).

- **Recurrent Cystitis:** Bladder inflammation is referred to as cystitis. Usually, an infection in the urine is the cause. Some women experience cystitis recurrently. Physicians classify recurrent infections as two infections in six months or as three independently verified infections in a year. Many times, a woman's recurrent bouts of cystitis appear to have no apparent cause.

  General Cause of Recurrent Cystitis
  - Recurrence brought forth by the same organism strain
  - Reinfection by different organisms

- Chronic inflammatory changes in the bladder, prostate, and periurethral glands can be caused by recurrent infections.

There are several possibilities for treatment to take into account. This could involve taking a single dosage of antibiotics after having sex (if sex seems to trigger episodes of cystitis), treating each episode quickly with a brief course of antibiotics, or starting a long-term regimen of low-dose antibiotics (Health Topic, 2024, Charles M. Kodner, MD, and Emily K. Thomas Gupton, Do, 210AD)

Bacteria: The major bacterial agents are *E. coli*, but other bacteria can also lead to cystitis(Mueller M, 2023).

Non-Contagious Agents: These include chemical cystitis (from exposure to chemicals), radiation, drug-related cystitis (from specific drugs), intestinal cystitis (a chronic illness with uncertain causation), and foreign body cystitis (typically from long-term catheter users) (Dobrek, no date).

Urinalysis is a widely used diagnostic technique that helps determine the optimal course of antibiotic medication by screening for bacteria. In cases that are severe or recurring, further imaging or a cystoscopy to examine the bladder more closely may be suggested (Bono MJ, Leslie SW, no date).

Prescription antibiotics such as amoxicillin, fosfomycin, trimethoprim/sulfamethoxazole, and nitrofurantoin are the mainstay of treatment. Making sure the infection is completely treated is essential (Zhou *et al.*, 2023).

Using heating pads, drinking lots of water, and avoiding irritants like alcohol and caffeine can all help with symptoms. Lifestyle changes, such as maintaining proper cleanliness and maybe taking preventive supplements like cranberry juice, may be advised for people who get infections frequently (Mayo Clinic HealthSystem, 2024).

Preventive measures include avoiding triggers, staying hydrated, urinating frequently, and cleaning up after bowel movements. For postmenopausal women, topical estrogen treatment may help reduce the risk of infections. A woman may benefit from switching birth control methods if she is prone to infections (Aggarwal N, Leslie SW, 2024b).

Urethritis: Both infectious and non-infectious reasons can result in urethritis, which is an inflammation of the urethra, the tube that transports urine from the bladder to the body. Here are some essential details about urethritis (Young A, Toncar A, Leslie SW, no date):

6. Contagious Agents

- Bacterial Infection
- *Neisseria gonorrhoea*- Gonococcal urethritis
- *Chlamydia trachomatis*- Non-gonococcal urethritis
- *Mycoplasma genitalium*
- *Ureaplasma urealyticum*

- *Ttrichomonas vaginalis*
- *Viral*
- *Herpes Simplex virus*
- *Cytomegalo virus*

7. Non-Contagious Agents

- Chemical irritation (e.g. Spermicide, soaps)
- Physical injuries or trauma
- Reiter's syndrome (a reactive arthritis)

Symptoms

- Dysuria Bacterial infection
  (Painful urination)
- Urinary urgency or frequency
- Urethral discharge
- Itching or irritation at the urethral opening
- In men discomfort and pain in the testicles

- *Chlamydia trachomatis* is frequently asymptomatic in females but can present with dysuria, discharge, or pelvic inflammatory disease. Diagnosis is followed by UA and urine culture (if pyuria is seen, but no bacteria, suspect Chlamydia). A pelvic exam is followed by discharge from cervical or urethral for chlamydia PCR. Chlamydia screening is now recommended for all females ≤ 25 years. Treatment is oral antibiotics with Azithromycin and doxycycline (Geisler, 2012).

- PID, discharge, and dysuria are possible symptoms of *Neisseria gonorrhoeae*. Urine culture and UA come after diagnosis. Send discharge samples for gram stain, culture, and PCR after a pelvic exam. Ceftriaxone, Ciprofloxacin, Levofloxacin, Ofloxacin, and Spectinomycin are among the oral antibiotics used in treatment. Metronidazole treatment according to the particular bacterial pathogen (Ng Lai-King and Martin, 2005; Cinti, Malani and Riddell, 2008b).

- Antiviral medication for HSV and tailored care when needed. Non-contagious agents treating the underlying causes (treatment of underlying conditions, avoiding irritants, etc.). When treating gonorrhea, patients should always receive treatment for chlamydia as well (Workowski *et al.*, 2021).

- Safe sexual behaviors, such as using condoms, getting frequent STI screenings, avoiding known irritants, and practicing excellent personal cleanliness, are the major ways to prevent STIs.

- If therapy is not received, the primary consequences could include persistent pain, constriction or narrowing of the urethra, heightened susceptibility to STDs, pelvic inflammatory disease (PID) in females, and epididymitis in males. Comprehending

the underlying cause of urethritis is crucial for optimizing treatment outcomes and averting complications (Silverberg B, Moyers A, Hinkle T, Kessler R, 2022).

Prostatitis: Acute bacterial prostatitis can result from hematogenous or ascending infections, and those who do not ordinarily have antibacterial chemicals in their prostatic fluid may be at greater risk. Despite being primarily caused by *E. coli*, chronic bacterial prostatitis is hard to treat and can lead to recurrent urinary tract infections (Davis NG, 2024).

Individuals deficient in antibacterial chemicals typically found in the prostatic fluid may be more vulnerable to ascending or hematogenous infections, which can cause acute bacterial prostatitis. While *E. coli* is typically the cause of chronic bacterial prostatitis, it can also lead to recurrent urinary tract infections and is challenging to treat (Pendergast HJ, Leslie SW, 2024).

Pain in the testicles, lower back, and perirectal area are common symptoms of prostate infection. Acute infections can cause excruciating pain along with chills, a high fever, and cystitis-like symptoms. Urinary retention and blockage of the nearby urethra might result from inflammatory swelling. The prostate is exceptionally sensitive and swollen when palpated in the rectal area (Davis NG, 2024). Inflammatory swelling can lead to obstruction of the neighboring urethra and urinary retention. On rectal palpation, the prostate is boggy and exquisitely tender. Response to antibiotic therapy is good, but occasionally abscess formation, epididymitis, and seminal vesiculitis or chronic infection develop. Typically, acute prostatitis develops in young adults; however, it can also follow the placement of an indwelling catheter in an older man. Patients with chronic prostatitis seldom give a history of an acute episode. Many are totally without symptoms; others experience low-grade pain and dysuria. Chronic disease a source for the periodic spread of prostatic organisms to the urine in the bladder produces recurrent bouts of cystitis. Chronic prostatitis is probably the major cause of recurrent bacteriuria in men. The etiologic agents are the same as in cystitis and pyelonephritis (Davis NG, 2024).

Prostatitis can cause pain in the lower abdomen, perineum, testicles, penis, and during ejaculation. It can also cause bladder irritation, blockage of the bladder outlet, and occasionally, blood in the semen. Prostatitis can cause pain in the penis, lower abdomen, testicles, and perineum, as well as discomfort during ejaculation, bladder irritation, obstruction of the bladder outlet, and occasionally blood in the semen. The key clinical history used for diagnosis includes fever, chills, dysuria, malaise, myalgias, pelvic/perineal pain, and hazy urine. The discovery during a medical examination of an edematous and sensitive prostate. There will be a higher PSA in urine. Urine cultures and urinalyses are frequently advised. For 4-6 weeks, patients are often treated with trimethoprim/sulfamethoxazole, fluoroquinolone, or another broad-spectrum antibiotic. Trauma, abstention from sexual activity, and dehydration are the risk factors (Taha *et al.*, 2020).

Upper Urinary Tract Infection or Pyelonephritis: Fever over 38.3°C and flank pain are the usual symptoms of upper urinary tract infection. Cystitis symptoms may appear before or concurrent with these findings. More critically ill patients have tachycardia, vomiting, diarrhea, and rigors. On physical examination, the back's costovertebral regions

(CVA) are painful, and there may occasionally be signs of septic shock. When there is no obstruction, the clinical signs and symptoms normally go away in a few days, leaving the kidneys fully functional. However, one of the most dangerous effects of UTI is the estimated 20–50% of pregnant women with acute pyelonephritis giving birth to preterm newborns (J. J. A. P. Belyayeva M, Leslie SW, 2024).

Chronic Pyelonephritis Is Not Linked To UTI: Clinical symptoms are more enduring when blockage, neurogenic bladder, or vesicoureteral reflux are present. This can occasionally result in renal papillae necrosis and gradual kidney function deterioration with chronic bacteriuria. Severe flank discomfort radiating to the groin is caused by a renal calculus or necrotic renal papilla that affects the ureter. The phrase "chronic pyelonephritis" refers to kidneys that are inflamed, scarred, and constricted, frequently with impaired renal function. Chronic pyelonephritis and UTI are not known to be related (Aeddula NR, 2024).

In the presence of obstruction, a neurogenic bladder, or vesicoureteral reflux, clinical manifestations are more persistent, occasionally leading to necrosis of the renal papillae and progressive impairment of kidney function with chronic bacteriuria. If a renal calculus or necrotic renal papilla impacts the ureter, severe flank pain with radiation to the groin occurs. The term chronic pyelonephritis is used to describe inflamed, scarred, contracted kidneys often in association with compromised renal function. There is no known connection between UTI and chronic pyelonephritis (Aeddula NR, 2024).

For instance, pyelonephritis is an infection of the kidney, which is associated with constitutional symptoms – fever, nausea, vomiting, and headache. Diagnosis is mainly with urinalysis, urine culture, CBC, and chemistry. Treatment is generally 2 weeks of Trimethoprim/sulfamethoxazole or fluoroquinolone, Hospitalization, and IV antibiotics if the patient is unable to take po. Complications are perinephric/renal abscess: Suspect in a patient who is not improving on antibiotic therapy. The diagnosis is CT with contrast and renal ultrasound and it may need surgical drainage (Aeddula NR, 2024; J. J. Belyayeva M, Leslie SW, 2024).

8. **Laboratory Diagnosis of Urinary Tract Infections:** Urinary tract infections (UTIs) are diagnosed in the laboratory using a multi-step process that includes determining the antibiotic susceptibility of the pathogenic organisms and precisely identifying them. The key steps are listed below (ASM Guideline, 2020; Hooton, 2012).

Sample Collection

- Midstream Clean- Catch Urine:
- Urine should be cleaned up in the genital area, the first part emptied into the toilet, and the midstream urine should be collected into a sterile container.
- Cauterized urine sample: For patients who are incapable of delivering a clean catch. Suprapubic Aspiration: Direct aspiration of urine from the bladder is the procedure used directly in neonates or when other methods are not appropriate.
- If a sexually transmitted disease (STD) is suspected, a urethral swab for STD testing is obtained before voiding.

Before voiding, a urethral sample is taken for STD testing if a sexually transmitted illness (STD) is suspected.

Macroscopic Examination

- Color and Clarity: Observing the urine for any unusual color or turbidity which may indicate infection

Microscopic Examination

- Color and clarity: Checking the urine for any turbidity or color that could point to an infection

Microscopic Examination

Urine Sediment Analysis

- Centrifuging the urine sample and looking for bacteria, red blood cells, white blood cells (pyuria), and epithelial cells in the sediment.
- **Gram Stain:** Urine sediment-stained smears can be used to see germs and direct first treatment.

Chemical Analysis

- **Dipstick Tests:** A quick screening method. Tests for nitrates, which indicate the presence of bacteria, particularly Gram-negative bacteria like E. coli, and leukocyte esterase, which indicates the presence of white blood cells.

Culture Sensitivity

- **Urine Culture:** the most reliable method for diagnosing UTIs. Plates of urine are placed on culture media (such as blood agar or MacConkey agar) and left to develop bacteria. Colony forming units (CFU) per milliliter are measured and recorded.

- **Identification of Pathogen:** Biochemical assays are used to identify bacteria followed by automated systems, and mass spectrometry (e.g., MALDI-TOF).

- **Antibiotic Sensitivity Testing:** Determine the susceptibility pattern of isolated bacteria to various antibiotics using methods like (Kirby- Bauer), both microdilution and automated systems (e.g. VITEK).

Interpretation of Results

- **Significant Bacteriuria:** commonly defined as greater than 10^5 CFU/ml in patients without symptoms. In patients with symptoms, lower numbers might be important.
- **Contaminants:** the presence of multiple types of bacteria or low CFU counts may indicate contamination

- The leukocyte esterase test is reasonably sensitive and highly specific for the presence of more than 10 WBCs/μL
- Pyuria: Patients with more than 10 WBCs/μL are considered truly infected.
- The existence of bacteria while pyuria is absent: as a result of sampling contamination.
- Although large hematuria is rare, microscopic hematuria can occur in as many as 50% of patients.
- WBC casts noninfective tubulointerstitial nephritis, glomerulonephritis, and pyelonephritis.
- In cases when individuals have nephrolithiasis, a uroepithelial tumor, appendicitis, inflammatory bowel disease, or if the sample is contaminated by vaginal WBCs, pyuria in the absence of bacteriuria and a UTI may occur.

Special Considerations

- **Recurrent UTIs:** To find underlying anomalies, additional testing, such as imaging investigations or cystoscopies, can be required.

Emerging Methods

- **Molecular Methods:** More and more assays based on nucleic acids, such as PCR, are being used to quickly identify and detect diseases, including those that are challenging to grow.

- **Automated urine Analyzers:** For quicker and more consistent findings, automated methods for urine sediment analysis and culture are being utilized more and more.

When bacteriuria is suspected or a complex UTI is indicated, cultures are advised. Typical illustrations consist of the following items:

- Pregnant women
- Postmenopausal women
- Men
- Prepubertal children
- Patients with urinary tract abnormalities or recent instrumentation
- Patients with immunosuppression or significant comorbidities
- Patients whose symptoms suggest pyelonephritis or sepsis
- Patients with recurrent UTIs (≥ 3/yr)

There are three options for urinary tract imaging: IVU, CT, and ultrasonography. Cystoscopy, retrograde urethrography, or voiding cystourethrography may be necessary on occasion.

Imaging is often needed for children with UTIs.

Most adults don't need to have their structural defects assessed unless one of the following happens: The patient has had pyelonephritis for at least two episodes.

- The patient has had pyelonephritis for at least two episodes.
- Complicated infections exist.
- It is thought to be nephrolithiasis.
- There is painless gross hematuria or new renal insufficiency.
- Febrile illness continues for ≥ 72 h.

Differential Diagnosis

- **Acute Urethral Syndrome:** The syndrome known as acute urethral syndrome, which affects women, is similar to cystitis in that it involves pyuria, frequency, and dysuria (dysuria-pyuria syndrome). Nevertheless, routine urine cultures are either negative or positive for acute urethral syndrome (unlike cystitis).

- **Urethritis:** is a potential reason since the organisms that cause the problem, Chlamydia trachomatis and Ureaplasma urealyticum, are not found in a typical urine culture.

- **Non-Communicable Causes**

  - anatomic abnormalities (e.g., urethral stenosis)
  - physiologic abnormalities (e.g, pelvic floor muscle dysfunction)
  - hormonal imbalances (e.g., atrophic urethritis)
  - localized trauma
  - GI system symptoms, and inflammation.

Screening of UTI in Pregnant Women: At the first prenatal appointment, a standard quantitative urine culture should be carried out. Use a second urine culture to confirm that bacteriuria is present in the urine (Moore *et al.*, 2018). Urine dipstick testing is insufficient to detect bacterial urinary tract infections during pregnancy. An antibiotic suitable for the isolated bacteria and the pregnant trimester should be used to treat a positive urine culture for bacteriuria in the second urine sample. Use antibiotics to treat pregnant women with asymptomatic bacteriuria (Moore *et al.*, 2018).

9. **Management:** Oral antibiotics are usually prescribed as a single dose for three days in the case of an uncomplicated UTI. The listing includes agents that are frequently prescribed. The susceptibility test or "best guess" should be used to determine the agent, at least until laboratory findings are available (Table – 3)(Finch *et al.*, 2012). Understanding potential pathogens and their susceptibility to antibiotics in the area is necessary for this.

Table 2: Common Oral Antibiotics for UTI Treatment. Image Courtesy of Medical Microbiology by (Richard Goering, Hazel Dockrell, Mark Zuckerman, and Ivan Roitt, 2013).

Antibacterial	Class of Agent	Comments
C-amoxiclav	Beta lactam+ Beta lactamase inhibitor	Increased activity against organisms resistant by virtue of β- lactamase production
Trimethoprim	Antimetabolite/ nucleic-acid synthesis inhibitor	Incidence of resistant strains increasing
CO-trimaxazole	Combination of Trimethoprim with sulfamethoxazole (also antimetabolite nucleic acid synthesis inhibitor	One of the most common 'first line' therapeutic approaches may be useful in 'blind' treatment but more toxic than trimethoprim alone an issue
Nitrofurantoin	Urinary antiseptic	For uncomplicated UTI caused by *E. coli* and Staphylococcus *saprophyticus;* not active in alkaline pH (therefore not useful for Proteus infections)
Nalidixic acid	Quinolone	For uncomplicated UTI; Gram-negative infections only; not active against Gram-positive; increasing resistance an issue
Ciprofloxacin, gatifloxacin, levofloxacin, norfloxacin, oflaxacin etc.	Quinolone	Very bad spectrum; not highly active against enterococci; increasing resistance is an issue.

Several different classes of antibacterial are available in oral formulations and suitable for the treatment of UTI. Nitrofurantoin and Nalidixic acids are useful for lower UTIs as they do not achieve adequate serum and tissue concentrations to treat upper UTIs

After the course of treatment is finished—at least two days—follow-up cultures must be conducted to verify the eradication of the pathogenic microorganisms (Leekha, Terrell, and Edson, 2011). Antibacterial therapy should be administered to children and expectant mothers with asymptomatic bacteriuria, and the infection should be monitored to ensure it has completely disappeared. A systemic antibacterial medication should be used to treat complicated UTIs (pyelonephritis). Systemic treatment should be continued until the signs and symptoms go away, and it should be recognized that the organism is responsive to the antimicrobial. Oral treatment can be used in its stead. Although ten days is the typical course of treatment, a longer course may be required to sterilize the kidney (SHEPPARD *et al.*, 2023)

Treatment Management-For Pregnant Women

- The following are the recommended medications for managing UTI pregnant women(Corrales, Corrales-Acosta and Corrales-Riveros, 2022):-
  - Fosfomycin
  - Amoxicillin
  - Nitrofurantoin
  - Cephalexin

- **Drug Contradiction**

  Fluoroquinolone harms cartilage by passing through the placenta (Loebstein *et al.*, 1998).

  TMP-SMX: Within two to three hours, TMP-SMX - Sulfonamides reaches equilibrium with maternal serum after crossing the placenta.
  When sulfonamides are given to a mother close to term (before birth), they compete with bilirubin for binding to serum albumin, which causes a spike in free bilirubin levels and the potential for jaundice and kernicterus (Li *et al.*, 2020).

II. CONCLUSION

Several aspects of host predispositions and UTI pathophysiology are unclear. It is possible to prevent recurrent infections in otherwise healthy women by routinely emptying the bladder. This removes microorganisms from the urinary tract, which is especially beneficial after sexual activity. Preventive antibiotic use may also help avoid repeated infections; nevertheless, antibiotic-resistant strains are more likely to be selected in the presence of underlying abnormalities, making illnesses more difficult to cure. There should be routine screening in public health facilities for pregnant women or women who are at risk of UTI infections. There is a need to understand UTI immunity to develop an adherence-based vaccine shortly. This site is not focused on this review. Patients on catheters frequently get infections. If at all feasible, categorization needs to be minimized or avoided.

ABBREVIATIONS

AMR	-	Antimicrobial resistance
AMR	-	Antimicrobial resistance
EPEC*E*	-	*E. coli* serotypes linked to gastrointestinal tract infections
BPH	-	Benign prostatic hyperplasia
CBC	-	*Complete blood count*
CA-APN	-	Community-acquired acute pyelonephritis
CAUTIs	-	Community-Acquired urinary tract infections
CDC	-	Centre for Disease Control
CMV	-	Cytomegalo Virus
CT	-	Computed tomography
HIV	-	Human Immunodeficiency Virus
HAUTIs	-	Hospital Acquired urinary tract infections
IV	-	Intravenous
MSU	-	Mid-stream urine
PO or p.o	-	Orally
UTIs	-	Urinary tract infections
UPEC	-	Uropathogenic Escherichia coli

REFERENCES

[1] EleyA.Rucks Elizabeth (2023) ‘Type III Secretion in Chlamydia’, *Microbiology and Molecular Biology Reviews*, 87(3), pp. e00034-23. doi: 10.1128/mmbr.00034-23.

[2] Achilles, S. L. *et al.* (2018) 'Impact of contraceptive initiation on vaginal microbiota.', *American Journal of Obstetrics and Gynecology*, 218(6), pp. 622.e1-622.e10. doi: 10.1016/j.ajog.2018.02.017.
[3] Aeddula NR, B. K. (2024) *Reflux Nephropathy. [Updated 2023 May 22]*. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-.
[4] Agarwal, J., Srivastava, S. and Singh, M. (2012) 'Pathogenomics of uropathogenic Escherichia coli.', *Indian Journal of Medical Microbiology*, 30(2), pp. 141-149.
[5] Aggarwal N, Leslie SW, L. S. (2024a) *Recurrent Urinary Tract Infections.* [Updated 2024 May 2]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing;
[6] Aggarwal N, Leslie SW, L. S. (2024b) *Recurrent Urinary Tract Infections. [Updated 2024 May 2]*. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing.
[7] Agodi, A. and Barchitta, M. (2011) *Epidemiology and control of urinary tract infections in intensive care patients. In Clinical Management of Complicated Urinary Tract Infection. IntechOpen.* In Clinical Management of Complicated Urinary Tract Infection. IntechOpen.
[8] Ajith, A. K. *et al.* (2019) 'Prevalence and Factors of Urinary Incontinence among Postmenopausal Women Attending the Obstetrics and Gynecology Outpatient Service in a Tertiary Health Care Center in Kochi, Kerala', *Indian Journal of Community Medicine*, 44(Supp 1). Available at: https://journals.lww.com/ijcm/fulltext/2019/44001/prevalence_and_factors_of_urinary_incontinence.9.aspx.
[9] Al-Badr, A. and Al-Shaikh, G. (2013) 'Recurrent Urinary Tract Infections Management in Women: A review.', *Sultan Qaboos University medical journal*, 13(3), pp. 359–367. doi: 10.12816/0003256.
[10] Ameer MA, Wasey A, S. P. (2023) *Escherichia coli (e Coli 0157 H7)*. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan.
[11] Aronson, L. R. (2023) '96 - Urosepsis', in Silverstein, D. C. and Hopper, K. B. T.-S. A. C. C. M. (Third E. (eds). W.B. Saunders, pp. 557–563. doi https://doi.org/10.1016/B978-0-323-76469-8.00105-2.
[12] ASM Guideline (2020) 'Guideline for the diagnosis of Urinary tract'.
[13] Assange, P. A. (2016) *Utilization of catheter-associated urinary tract infection bundle among critical care nurses-Kenyatta National Hospital (Doctoral dissertation, University of Nairobi)*. Doctoral dissertation, University of Nairobi.
[14] Azimi, T. *et al.* (2020) 'Coagulase-negative staphylococci (CoNS) meningitis: a narrative review of the literature from 2000 to 2020', *New Microbes and New Infections*, 37, p. 100755. doi: 10.1016/j.nmni.2020.100755.
[15] B, F. (1990) 'Recurring urinary tract infection: incidence and risk factors.', *Am J Public Health.*, 80(3), pp. 331–3. Available at: doi: 10.2105/ajph.80.3.331. PMID: 2305919.
[16] Bai, B., & Chen, Z. (2017). (67AD) 'Characterization of biofilm formation by Enterococcus faecalis isolates derived from urinary tract infections in China.', *Journal of Medical Microbiology*, 1, pp. 60–67.
[17] Barolo S, Grossman OK, A. A. (2024) *Urinary Tract Infections In Children.* In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing.
[18] Belas, R., Manos, J. and Suvanasuthi, R. (2004) 'Proteus mirabilis ZapA metalloprotease degrades a broad spectrum of substrates, including antimicrobial peptides.', *Infection and immunity*, 72(9), pp. 5159–5167. doi: 10.1128/IAI.72.9.5159-5167.2004.
[19] Belyayeva M, Leslie SW, J. J. (2024) *Acute Pyelonephritis*. Updated Ed. StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing.
[20] Belyayeva M, Leslie SW, J. J. A. P. (2024) *Acute Pyelonephritis. [Updated 2024 Feb 28]*. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-.
[21] Bingen, E. *et al.* (1997) 'Virulence patterns of Escherichia coli K1 strains associated with neonatal meningitis.', *Journal of Clinical Microbiology*, 35(11), pp. 2981–2982. doi: 10.1128/jcm.35.11.2981-2982.1997.
[22] Bono MJ, Leslie SW, R. W. (no date) *Uncomplicated Urinary Tract Infections. [Updated 2023 Nov 13]*. StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing.
[23] Bono MJ, L. S., and R. W. (2023) 'Uncomplicated Urinary Tract Infections', *In StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing*.
[24] Brillo V; Tosto E (2021) 'PREGNANCY COMPLAINTS AND COMPLICATIONS: CLINICAL PRESENTATIONS', in. Glob. libr. women's med. doi: DOI 10.3843/GLOWM.416613.
[25] Buckley, R. M. J., McGuckin, M. and MacGregor, R. R. (1978) 'Urine bacterial counts after sexual intercourse.', *The New England Journal of Medicine*, 298(6), pp. 321–324. doi: 10.1056/NEJM197802092980607.
[26] CDC (2024) 'Urinary Tract Infection Basics'. CDC.
[27] Charles M. Kodner, MD, and Emily K. Thomas Gupton, DO, M. (210AD) 'Recurrent Urinary Tract

Infections in Women: Diagnosis and Management', *Am Fam Physician.*, 82(6):638-(6), pp. 638–643.

[28] Chenoweth, C. E., Gould, C. V and Saint, S. (2014) 'Diagnosis, management, and prevention of catheter-associated urinary tract infections.', *Infectious disease Clinics of North America*, 28(1), pp. 105–119. doi: 10.1016/j.idc.2013.09.002.

[29] Chimiak, A., Hider, R.C., Liu, A., Neilands, J.B., Nomoto, K., Sugiura, Y. and Hider, R. C. (1984) 'Siderophore mediated absorption of iron.', in. Siderophores from microorganisms and plants, pp. 25–87.

[30] Cinti, S., Malani, A. and Riddell, J. (2008a) 'Chapter 11 - Infectious Diseases', in Heidelbaugh, J. J. B. T.-C. M. H. (ed.). Philadelphia: W.B. Saunders, pp. 182–206. doi https://doi.org/10.1016/B978-141603000-3.10011-5.

[31] Cinti, S., Malani, A. and Riddell, J. (2008b) 'Infectious Diseases.', *Clinical Men's Health*, pp. 182–206. doi: 10.1016/B978-141603000-3.10011-5.

[32] Coker, C., Poore, C.A., Li, X. and Mobley, H.L. (2000) 'Pathogenesis of Proteus mirabilis urinary tract infection.', *Microbes and infection*, 2(12), pp. 1497–1505.

[33] Corrales, M., Corrales-Acosta, E. and Corrales-Riveros, J. G. (2022) 'Which Antibiotic for Urinary Tract Infections in Pregnancy? A Literature Review of International Guidelines.', *Journal of Clinical Medicine*, 11(23). doi: 10.3390/jcm11237226.

[34] Cress, B. F. *et al.* (2014) 'Masquerading microbial pathogens: capsular polysaccharides mimic host-tissue molecules.', *FEMS microbiology reviews*, 38(4), pp. 660–697. doi: 10.1111/1574-6976.12056.

[35] Czaja, C. A. *et al.* (2009) 'Prospective cohort study of microbial and inflammatory events immediately preceding Escherichia coli recurrent urinary tract infection in women.', *The Journal of Infectious Diseases*, 200(4), pp. 528–536. doi: 10.1086/600385.

[36] Davis NG, S. M. (2024) *Acute Bacterial Prostatitis. [Updated 2023 May 22]*. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024.

[37] Dobrek, L. (no date) 'Lower Urinary Tract Disorders as Adverse Drug Reactions—A Literature Review.', *Pharmaceuticals*, 16(1031.). doi: https://doi.org/10.3390/ph16071031.

[38] Domingos, M. de O. *et al.* (2022) 'Escherichia coli Strains Responsible for Cystitis in Female Pediatric Patients with Normal and Abnormal Urinary Tracts Have Different Virulence Profiles.', *Pathogens (Basel, Switzerland)*, 11(2). doi: 10.3390/pathogens11020231.

[39] E., A. C., T., M. H. L. and M., P. M. (2018) 'Pathogenesis of Proteus mirabilis Infection', *EcoSal Plus*, 8(1), pp. 10.1128/ecosalplus.ESP-0009–2017. doi: 10.1128/ecosalplus.esp-0009-2017.

[40] Ehlers S and Merrill SA (2023) *Staphylococcus saprophyticus Infection.* In: StatPearls [Internet]. Treasure Island (FL):

[41] Ehlers S, M. S. (2024) *Staphylococcus saprophyticus Infection. [Updated 2023 Jun 26]*. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing;

[42] Field, M. J., Harris, D. C. and Pollock, C. A. (2010) '1 - URINARY TRACT STRUCTURE AND INFECTION', in Field, M. J., Harris, D. C., and Pollock, C. A. B. T.-T. R. S. (Second E. (eds). Churchill Livingstone, pp. 1–13. doi: https://doi.org/10.1016/B978-0-7020-3371-1.00001-4.

[43] Finch, R. *et al.* (2012) '242Urinary infections', *Antimicrobial Chemotherapy*. Edited by R. Finch et al. Oxford University Press, p. 0. doi 10.1093/med/9780199697656.003.0158.

[44] Flores-Mireles, A., Hreha, T. N. and Hunstad, D. A. (2019) 'Pathophysiology, Treatment, and Prevention of Catheter-Associated Urinary Tract Infection.', *Topics in spinal cord injury rehabilitation*, 25(3), pp. 228–240. doi: 10.1310/sci2503-228.

[45] Flores-Mireles, A. L. *et al.* (2015) 'Urinary tract infections: epidemiology, mechanisms of infection and treatment options.', *Nature Reviews. Microbiology*, 13(5), pp. 269–284. doi: 10.1038/nrmicro3432.

[46] Fox-Moon, S. M. and Shirtliff, M. E. (2015) 'Chapter 77 - Urinary Tract Infections Caused by Proteus mirabilis', in Tang, Y.-W. et al. (eds). Boston: Academic Press, pp. 1389–1400. doi https://doi.org/10.1016/B978-0-12-397169-2.00077-9.

[47] Foxman, B. *et al.* (2000) 'Urinary tract infection: self-reported incidence and associated costs.', *Annals of Epidemiology*, 10(8), pp. 509–515. doi: 10.1016/s1047-2797(00)00072-7.

[48] Foxman, B. (2002) 'Epidemiology of urinary tract infections: incidence, morbidity, and economic costs.', *The American Journal of Medicine*, 113 Suppl, pp. 5S-13S. doi: 10.1016/s0002-9343(02)01054-9.

[49] Foxman, B. (2014) 'Urinary tract infection syndromes: occurrence, recurrence, bacteriology, risk factors, and disease burden.', *Infectious disease clinics of North America*, 28(1), pp. 1–13. doi: 10.1016/j.idc.2013.09.003.

[50] Garcia-Roig, M. L. and Kirsch, A. J. (2016) 'Urinary tract infection in the setting of vesicoureteral reflux.', *F1000Research*, 5. doi: 10.12688/f1000research.8390.1.

[51] Geisler, W. M. (2012) '326 - Diseases Caused By Chlamydiae', in Goldman, L. and Schafer, A. I. B. T.-G. C. M. (Twenty F. E. (eds). Philadelphia: W.B. Saunders, pp. 1916–1922. doi https://doi.org/10.1016/B978-1-4377-1604-7.00326-2.

[52] Giridhara Upadhyaya, P. M., Umapathy, B. L. and Ravikumar, K. L. (2010) 'Comparative study for the presence of enterococcal virulence factors gelatinase, hemolysin, and biofilm among clinical and commensal isolates of enterococcus faecalis.', *Journal of laboratory physicians*, 2(2), pp. 100–104. doi: 10.4103/0974-2727.72159.

[53] Goldsmith, C. S. and Miller, S. E. (2009) 'Modern uses of electron microscopy for detection of viruses.', *Clinical microbiology reviews*, 22(4), pp. 552–563. doi: 10.1128/CMR.00027-09.

[54] Govindarajan, D. K. and Kandaswamy, K. (2022) 'Virulence factors of uropathogens and their role in host-pathogen interactions', *The Cell Surface*, 8, p. 100075. doi: https://doi.org/10.1016/j.tcsw.2022.100075.

[55] Green, L. R. *et al.* (2022) 'Chapter Two - Neisseria gonorrhoeae physiology and pathogenesis', in Poole, R. K. and Kelly, D. J. B. T.-A. in M. P. (eds). Academic Press, pp. 35–83. doi https://doi.org/10.1016/bs.ampbs.2022.01.002.

[56] Guentzel, M. (1996) *Escherichia, Klebsiella, Enterobacter, Serratia, Citrobacter, and Proteus*. 4th edition. Edited by E. In Baron S. Guentzel MN. Escherichia, Klebsiella, Enterobacter, Ser In: Baron S, edMedical Microbiology. 4th edition. Galveston (TX): University of Texas Medical Branch at Galveston; 1996. Chapter 26.

[57] Habak PJ, Carlson K, Griggs, J. R. U. (2024) *Tract Infection in Pregnancy*. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024.

[58] Hannan, T. J. *et al.* (2012) 'Host-pathogen checkpoints and population bottlenecks in persistent and intracellular uropathogenic Escherichia coli bladder infection.', *FEMS microbiology reviews*, 36(3), pp. 616–648. doi: 10.1111/j.1574-6976.2012.00339.x.

[59] Hariati, H., Suza, D. E. and Tarigan, R. (2019) 'Risk Factors Analysis for Catheter-Associated Urinary Tract Infection in Medan, Indonesia.', *Open Access Macedonian Journal of Medical Sciences*, 7(19), pp. 3189–3194. doi: 10.3889/oamjms.2019.798.

[60] Health Exchange (2024) *Urinary Tract Infection (UTI): Risk Factors, Symptoms, Treatment and Prevention*. Health Exchange. Available at: https://www.healthxchange.sg/women/urology/urinary-tract-infection-risk-factors-symptoms-treatment-prevention#:~:text=Urinary Tract Infections (UTI) are, urinary tract in significant numbers.

[61] Health Topic (2024) *Health topics Women's health Recurrent cystitis in women*.

[62] Helin, I. and Carstensen, H. (1983) 'Nephrotic Syndrome After Mumps Virus Infection', *American Journal of Diseases of Children*, 137(11), p. 1126. doi: 10.1001/archpedi.1983.02140370082026.

[63] Hooton, T. M. (2012) 'Clinical practice. Uncomplicated urinary tract infection.', *The New England Journal of Medicine*, 366(11), pp. 1028–1037. doi: 10.1056/NEJMcp1104429.

[64] Hooton, T. M. and Stamm, W. E. (1997) 'Diagnosis and treatment of uncomplicated urinary tract infection.', *Infectious disease clinics of North America*, 11(3), pp. 551–581. doi: 10.1016/s0891-5520(05)70373-1.

[65] Hsiao, C.-Y. *et al.* (2015) 'Risk Factors for Development of Septic Shock in Patients with Urinary Tract Infection.', *BioMed Research International*, 2015, p. 717094. doi: 10.1155/2015/717094.

[66] Hussain, I. *et al.* (2020) 'Human BK and JC polyomaviruses: Molecular insights and prevalence in Asia', *Virus Research*, 278, p. 197860. doi https://doi.org/10.1016/j.virusres.2020.197860.

[67] Ike, Y., Hashimoto, H. and Clewell, D. B. (1984) 'Hemolysin of Streptococcus faecalis subspecies zymogenes contributes to virulence in mice.', *Infection and immunity*, 45(2), pp. 528–530. doi: 10.1128/iai.45.2.528-530.1984.

[68] Jacobsen, S. M. and Shirtliff, M. E. (2011) 'Proteus mirabilis biofilms and catheter-associated urinary tract infections.', *Virulence*, 2(5), pp. 460–465. doi: 10.4161/viru.2.5.17783.

[69] Jamil RT, Foris LA, S. J. (2024) *Proteus mirabilis Infections*. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-.

[70] Jancel, T. and Dudas, V. (2002) 'Management of uncomplicated urinary tract infections.', *The Western Journal of Medicine*, 176(1), pp. 51–55. doi: 10.1136/ewjm.176.1.51.

[71] JM., Jeong, Belyayeva M, L. S. (2024) *Acute Pyelonephritis*. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing.

[72] John L Brusch, MD, F. (2024) 'Urinary Tract Infection (UTI) in Males Workup'. Medscape. Available at: https://emedicine.medscape.com/article/231574-workup?form=fpf.

[73] Johnson, J. R. *et al.* (2005) 'Bacterial characteristics about the clinical source of Escherichia coli isolates from women with acute cystitis or pyelonephritis and uninfected women.', *Journal of Clinical*

Microbiology, 43(12), pp. 6064–6072. doi: 10.1128/JCM.43.12.6064-6072.2005.

[74] Jones, S. M. *et al.* (2007) 'Structure of Proteus mirabilis biofilms grown in artificial urine and standard laboratory media.', *FEMS microbiology letters*, 268(1), pp. 16–21. doi: 10.1111/j.1574-6968.2006.00587.x.

[75] Kahsay, T. *et al.* (2024) 'Antimicrobial susceptibility patterns of urinary tract infections causing bacterial isolates and associated risk factors among HIV patients in Tigray, Northern Ethiopia', *BMC Microbiology*, 24(1), p. 148. doi: 10.1186/s12866-024-03297-2.

[76] Kaijser, B. (1973) 'Immunology of Escherichia coli: K antigen and its relation to urinary tract infection.', *The Journal of Infectious Diseases*, 127(6), pp. 670–677. doi: 10.1093/infdis/127.6.670.

[77] Kakkanat, A. *et al.* (2015) 'The role of H4 flagella in Escherichia coli ST131 virulence', *Scientific Reports*, 5(1), p. 16149. doi: 10.1038/srep16149.

[78] Kalsi, J. *et al.* (2003) 'Hospital-acquired urinary tract infection.', *International Journal of clinical practice*, 57(5), pp. 388–391.

[79] Kaper, J. B., Nataro, J. P., & Mobley, H. L. (2004). (2004) 'Pathogenic Escherichia coli.', *Nature Reviews Microbiology*, 2(2), pp. 123–140.

[80] Kauffman, C. A. (2014) 'Diagnosis and Management of Fungal Urinary Tract Infection', *Infectious Disease Clinics of North America*, 28(1), pp. 61–74. doi: https://doi.org/10.1016/j.idc.2013.09.004.

[81] Khurana, U. *et al.* (2018) 'Spectrum of parasitic infections in centrifuged urine sediments from a newly developed tertiary care center in Central India.', *Journal of Parasitic Diseases : official organ of the Indian Society for Parasitology*, 42(4), pp. 608–615. doi: 10.1007/s12639-018-1043-6.

[82] Kilian, M. and Russell, M. W. (2015) 'Chapter 22 - Microbial Evasion of IgA Functions', in Mestecky, J. et al. (eds). Boston: Academic Press, pp. 455–469. doi https://doi.org/10.1016/B978-0-12-415847-4.00022-7.

[83] Kim, D. S. and Lee, J. W. (2023) 'Urinary Tract Infection and Microbiome.', *Diagnostics (Basel, Switzerland)*, 13(11). doi: 10.3390/diagnostics13111921.

[84] Kim, Y. *et al.* (2014) 'Comparison of the clinical characteristics of diabetic and non-diabetic women with community-acquired acute pyelonephritis: a multicenter study.', *The Journal of Infection*, 69(3), pp. 244–251. doi: 10.1016/j.jinf.2014.05.002.

[85] Klahr, S. (2008) 'CHAPTER 80 - Obstructive Uropathy', in ALPERN, R. J. and HEBERT, S. C. B. T.-S. and G. T. K. (Fourth E. (eds). San Diego: Academic Press, pp. 2247–2282. doi: https://doi.org/10.1016/B978-012088488-9.50083-8.

[86] Klein, J. *et al.* (2015) 'Late presentation of adenovirus-induced hemorrhagic cystitis and ureteral obstruction in a kidney-pancreas transplant recipient.', *Proceedings (Baylor University. Medical Center)*. United States, pp. 488–491. doi: 10.1080/08998280.2015.11929318.

[87] Klein, R. D. and Hultgren, S. J. (2020) 'Urinary tract infections: microbial pathogenesis, host-pathogen interactions, and new treatment strategies.', *Nature Reviews. Microbiology*, 18(4), pp. 211–226. doi: 10.1038/s41579-020-0324-0.

[88] Korir, M., Manning, S. and Davies, H. (2017) 'Intrinsic Maturational Neonatal Immune Deficiencies and Susceptibility to Group B Streptococcus Infection', *Clinical Microbiology Reviews*, 30, pp. 973–989. doi: 10.1128/CMR.00019-17.

[89] Korte-Berwanger, M. *et al.* (2013) 'Significance of the d-serine-deaminase and d-serine metabolism of staphylococcus saprophyticus for virulence', *Infection and Immunity*, 81(12), pp. 4525–4533. doi: 10.1128/IAI.00599-13.

[90] Kulkarni, R. *et al.* (2013) 'β-Hemolysin/cytolysin of Group B Streptococcus enhances host inflammation but is dispensable for establishment of urinary tract infection.', *PloS one*, 8(3), p. e59091. doi: 10.1371/journal.pone.0059091.

[91] Kurzyp, K. and Harrison, O. B. (2023) 'Bacterium of one thousand and one variants: genetic diversity of Neisseria gonorrhoeae pathogenicity.', *Microbial genomics*, 9(6). doi: 10.1099/mgen.0.001040.

[92] Lane, M. C. and Mobley, H. L. T. (2007) 'Role of P-fimbrial-mediated adherence in pyelonephritis and persistence of uropathogenic Escherichia coli (UPEC) in the mammalian kidney.', *Kidney International*, 72(1), pp. 19–25. doi: 10.1038/sj.ki.5002230.

[93] Lee, B. and Bryan, L. (1989) 'Identification and comparative analysis of the lactoferrin and transferrin receptors among clinical gonococcal isolates', *Journal of Medical Microbiology*, 28, pp. 199–204. doi: 10.1099/00222615-28-3-199.

[94] Leekha, S., Terrell, C. L. and Edson, R. S. (2011) 'General principles of antimicrobial therapy.', *Mayo Clinic Proceedings*, 86(2), pp. 156–167. doi: 10.4065/mcp.2010.0639.

[95] Leslie SW, Sajjad H, M. P. (2024) *Bladder Stones. [Updated 2023 Jul 31]*. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing.

[96] Lewis, D. A. (2020) '54 - Gonorrhea', in Ryan, E. T. et al. (eds). London: Elsevier, pp. 524–527. doi https://doi.org/10.1016/B978-0-323-55512-8.00054-5.
[97] Li, P. *et al.* (2020) 'Maternal exposure to sulfonamides and adverse pregnancy outcomes: A systematic review and meta-analysis.', *PloS one*, 15(12), p. e0242523. doi: 10.1371/journal.pone.0242523.
[98] Liao, C. *et al.* (2022) 'Virulence Factors of Pseudomonas aeruginosa and Antivirulence Strategies to Combat Its Drug Resistance.', *Frontiers in cellular and infection microbiology*, 12, p. 926758. doi: 10.3389/fcimb.2022.926758.
[99] Lila, A. S. A. *et al.* (2023) 'Biofilm Lifestyle in Recurrent Urinary Tract Infections.', *Life (Basel, Switzerland)*, 13(1). doi: 10.3390/life13010148.
[100] Linhares, I. M. and Witkin, S. S. (2010) 'Immunopathogenic consequences of Chlamydia trachomatis 60 kDa heat shock protein expression in the female reproductive tract.', *Cell stress & chaperones*, 15(5), pp. 467–473. doi: 10.1007/s12192-010-0171-4.
[101] Lo, D. S. *et al.* (2013) 'Community-acquired urinary tract infection: age and gender-dependent etiology.', *Jornal brasileiro de nefrologia*, 35(2), pp. 93–98. doi: 10.5935/0101-2800.20130016.
[102] Lo, E. *et al.* (2014) 'Strategies to prevent catheter-associated urinary tract infections in acute care hospitals: 2014 update.', *Infection control and hospital epidemiology*, 35(5), pp. 464–479. doi: 10.1086/675718.
[103] Loebstein, R. *et al.* (1998) 'Pregnancy outcome following gestational exposure to fluoroquinolones: a multicenter prospective controlled study.', *Antimicrobial agents and chemotherapy*, 42(6), pp. 1336–1339. doi: 10.1128/AAC.42.6.1336.
[104] Lotfollahzadeh S, Leslie SW, A. N. (2024) *Vesicoureteral Reflux*. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan.
[105] Luciani, L. G. and Mattevi, D. (2022) 'Urinary Tract Infections: Virus.', *Encyclopedia of Infection and Immunity*, pp. 32–43. doi: 10.1016/B978-0-12-818731-9.00139-7.
[106] Lyon (FR): International Agency for Research on Cancer (1994) *IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. Schistosomes, Liver Flukes, and Helicobacter pylori.* (IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, No. 61.) INFECTION WITH SCHISTOSOMES (Schistosoma haematobium, Schistosoma mansoni and Schistosoma japonicum).
[107] Mancuso G, Midiri A, Gerace E, Marra M, Zummo S, B. C. (2023) 'Urinary Tract Infections: The Current Scenario and Future Prospects', *Pathogens.*, 12(4).
[108] Mancuso, G. *et al.* (2023) 'Urinary Tract Infections: The Current Scenario and Future Prospects.', *Pathogens (Basel, Switzerland)*, 12(4). doi: 10.3390/pathogens12040623.
[109] Martins, K. B. *et al.* (2019) 'In vitro Effects of Antimicrobial Agents on Planktonic and Biofilm Forms of Staphylococcus saprophyticus Isolated From Patients With Urinary Tract Infections.', *Frontiers in microbiology*, 10, p. 40. doi: 10.3389/fmicb.2019.00040.
[110] Mattoo, T. K. (2007) 'Medical management of vesicoureteral reflux--quiz within the article. Don't overlook placebos.', *Pediatric nephrology (Berlin, Germany)*, 22(8), pp. 1113–1120. doi: 10.1007/s00467-007-0485-3.
[111] mayoclinichealthsystem (2024) *5 tips to prevent a urinary tract infection*. Available at: 5 tips to prevent a urinary tract infection.
[112] McGuckin, M. (2012) *The patient survival guide: 8 simple solutions to prevent hospital and healthcare-associated infections.* New York, NY: Demos Medical Publishing.
[113] McKertich, K. and Hanegbi, U. (2021) 'Recurrent UTIs and cystitis symptoms in women', *Australian Journal for General Practitioners*, 50, pp. 199–205. Available at: https://www1.racgp.org.au/ajgp/2021/april/recurrent-utis-and-cystitis-symptoms-in-women.
[114] Meddings, J. and Saint, S. (2011) 'Disrupting the life cycle of the urinary catheter.', *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America*. United States, pp. 1291–1293. doi: 10.1093/cid/cir195.
[115] Medina-Polo, J., Naber, K. G. and Bjerklund Johansen, T. E. (2021) 'Healthcare-associated urinary tract infections in urology', in Naber, K. G. and Bjerklund Johansen, T. E. (eds) *Urogenital Infections and Inflammations*. Jose Medina-Polo, Hospital Universitario 12 de Octubre, Madrid, Department of Urology, Health Research Institute i+12, Avda Córdoba s/n, 28045, Madrid, Spain, Phone: 0034 913908000, E-mail: josemedinapolo@movistar.es: German Medical Science GMS Publishing House. doi: 10.5680/lhuii000066.
[116] Medina, M. and Castillo-Pino, E. (2019) 'An introduction to the epidemiology and burden of urinary tract infections.', *Therapeutic advances in urology*, 11, p. 1756287219832172. doi: 10.1177/1756287219832172.
[117] Merritt, J. L. (1981) 'Residual urine volume: correlate of urinary tract infection in patients with spinal

cord injury.', *Archives of physical medicine and rehabilitation*, 62(11), pp. 558–561.
[118] Miller, W. R., Munita, J. M. and Arias, C. A. (2014) 'Mechanisms of antibiotic resistance in enterococci.', *Expert review of anti-infective therapy*, 12(10), pp. 1221–1236. doi: 10.1586/14787210.2014.956092.
[119] Mlugu, E. M. *et al.* (2023) 'Prevalence of urinary tract infection and antimicrobial resistance patterns of uropathogenic with biofilm-forming capacity among outpatients in Morogoro, Tanzania: a cross-sectional study', *BMC Infectious Diseases*, 23(1), p. 660. doi: 10.1186/s12879-023-08641-x.
[120] Mohanty, S., Purohit, G., Rath, S., Seth, R. K., & Mohanty, R. R. (2021) 'Urinary tract infection due to Group B Streptococcus: A case series from Eastern India.', *Clinical Case Reports*, 9(10), p. e04885. doi: https://doi.org/10.1002/ccr3.4885.
[121] Mohd Khairul, I. O., Nurzam, S. C. H. and Hamat, R. A. (2022) 'Complicated urinary tract infection caused by Corynebacterium urealyticum - A pathogen that should not be forgotten.', *The Medical journal of Malaysia*, 77(1), pp. 110–112.
[122] Moore, A. *et al.* (2018) 'Recommendations on screening for asymptomatic bacteriuria in pregnancy.', *CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne*, 190(27), pp. E823–E830. doi: 10.1503/cmaj.171325.
[123] Mueller M, T. C. (2023) *Escherichia coli Infection. [Updated 2023 Jul 13]. In:* StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing.
[124] Ng Lai-King and Martin, I. E. (2005) 'The laboratory diagnosis of Neisseria gonorrhoeae.', *The Canadian Journal of Infectious Diseases & Medical Microbiology = Journal canadien des maladies infectieuses et de la microbiologie medicine*, 16(1), pp. 15–25. doi: 10.1155/2005/323082.
[125] Nicolle, L. E. (2005) 'Complicated urinary tract infection in adults.', *The Canadian Journal of Infectious Diseases & Medical Microbiology = Journal canadien des maladies infectieuses et de la microbiologie medicine*, 16(6), pp. 349–360. doi: 10.1155/2005/385768.
[126] Nicolle, L. E. (2014) 'Catheter-associated urinary tract infections.', *Antimicrobial resistance and infection control*, 3, p. 23. doi: 10.1186/2047-2994-3-23.
[127] Nitzan, O. *et al.* (2015) 'Urinary tract infections in patients with type 2 diabetes mellitus: review of prevalence, diagnosis, and management.', *Diabetes, metabolic syndrome and obesity : targets and therapy*, 8, pp. 129–136. doi: 10.2147/DMSO.S51792.
[128] Norsworthy, A. N. and Pearson, M. M. (2017) 'From Catheter to Kidney Stone: The Uropathogenic Lifestyle of Proteus mirabilis.', *Trends in microbiology*, 25(4), pp. 304–315. doi: 10.1016/j.tim.2016.11.015.
[129] Olson-Wood, M. G. *et al.* (2021) 'Inclusion Membrane Growth and Composition Are Altered by Overexpression of Specific Inclusion Membrane Proteins in Chlamydia trachomatis L2.', *Infection and immunity*, 89(7), p. e0009421. doi: 10.1128/IAI.00094-21.
[130] Ouslander, J. G., Greengold, B. and Chen, S. (1987) 'External catheter use and urinary tract infections among incontinent male nursing home patients.', *Journal of the American Geriatrics Society*, 35(12), pp. 1063–1070. doi: 10.1111/j.1532-5415.1987.tb04922.x.
[131] Paduch, D. (2007) 'Viral lower urinary tract infections', *Current urology reports*, 8, pp. 324–335. doi: 10.1007/s11934-007-0080-y.
[132] Pang, Z., Raudonis, R., Glick, B. R., Lin, T., & Cheng, Z. (2018) 'Antibiotic resistance in Pseudomonas aeruginosa: Mechanisms and alternative therapeutic strategies.', *Biotechnology Advances*, 37(1), pp. 177–192.
[133] Parveen, R. M. *et al.* (2011) 'Extended-spectrum β-lactamase producing Klebsiella pneumoniae from blood cultures in Puducherry, India.', *The Indian Journal of Medical Research*. India, pp. 392–395.
[134] Pass, R. F. (2008) 'CHAPTER 206 - Cytomegalovirus', in Long, S. S. B. T.-P. and P. of P. I. D. (Third E. (ed.). Edinburgh: W.B. Saunders, pp. 1029–1036. doi https://doi.org/10.1016/B978-0-7020-3468-8.50212-1.
[135] Patton, J. P., Nash, D. B. and Abrutyn, E. (1991) 'Urinary tract infection: economic considerations.', *The Medical clinics of North America*, 75(2), pp. 495–513. doi: 10.1016/s0025-7125(16)30466-7.
[136] Pendergast HJ, Leslie SW, R. D. (2024) *Chronic Prostatitis and Chronic Pelvic Pain Syndrome in Men. [Updated 2024 Jan 11].* In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-.
[137] Peterson JW. (1996) *Bacterial Pathogenesis.* 4th ed. Edited by Baron S. Galveston (TX): University of Texas Medical Branch at Galveston.
[138] Qin, S. *et al.* (2022) 'Pseudomonas aeruginosa: pathogenesis, virulence factors, antibiotic resistance, interaction with host, technology advances and emerging therapeutics.', *Signal transduction and targeted therapy*, 7(1), p. 199. doi: 10.1038/s41392-022-01056-1.
[139] Quillin, S. J. and Seifert, H. S. (2018) 'Neisseria gonorrhoeae host adaptation and pathogenesis', *Nature*

Reviews Microbiology, 16(4), pp. 226–240. doi: 10.1038/nrmicro.2017.169.
[140] Rasmussen, P. E., and Nielsen, F. R. (1988) 'Hydronephrosis during pregnancy: a literature survey.', *European Journal of Obstetrics, gynecology, and reproductive biology*, 27(3), pp. 249–259. doi: 10.1016/0028-2243(88)90130-x.
[141] Ratiner, Y. A. *et al.* (2003) 'Serology and genetics of the flagellar antigen of Escherichia coli O157:H7a,7c.', *Journal of Clinical Microbiology*, 41(3), pp. 1033–1040. doi: 10.1128/JCM.41.3.1033-1040.2003.
[142] Redgrove, K. A., & McLaughlin, E. A. (2014) 'The Role of the Immune Response in Chlamydia trachomatis Infection of the Male Genital Tract: A Double-Edged Sword.', *Frontiers in Immunology*, 5(107989). doi: https://doi.org/10.3389/fimmu.2014.00534.
[143] Reynolds, D. and Kollef, M. (2021) 'The Epidemiology and Pathogenesis and Treatment of Pseudomonas aeruginosa Infections: An Update.', *Drugs*, 81(18), pp. 2117–2131. doi: 10.1007/s40265-021-01635-6.
[144] Richard Goering, Hazel Dockrell, Mark Zuckerman, Ivan Roitt, P. L. C. (2013) *Mims' Medical Microbiology*. Elsevier Sunders. Available at: www.elsevier.com.
[145] Riley, L. W. (2014) 'Pandemic lineages of extraintestinal pathogenic Escherichia coli.', *Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases*, 20(5), pp. 380–390. doi: 10.1111/1469-0691.12646.
[146] Riwu, K. H. P. *et al.* (2022) 'A review: Virulence factors of Klebsiella pneumonia as emerging infection on the food chain.', *Veterinary World*, 15(9), pp. 2172–2179. doi 10.14202/vetworld.2022.2172-2179.
[147] Rosen, D. A. *et al.* (2007) 'Detection of intracellular bacterial communities in human urinary tract infection.', *PLoS Medicine*, 4(12), p. e329. doi: 10.1371/journal.pmed.0040329.
[148] Rowe, T. A. and Juthani-Mehta, M. (2013) 'Urinary tract infection in older adults.', *Aging Health*, 9(5). doi: 10.2217/ahe.13.38.
[149] Sabih, A. and Leslie, S. W. (2024) 'Complicated Urinary Tract Infections.', in. Treasure Island (FL).
[150] Sabih A, L. S. (2024a) *Complicated Urinary Tract Infections.* Updated ed. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing.
[151] Sabih A, L. S. (2024b) *Complicated Urinary Tract Infections. [Updated 2023 Nov 12].* In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing.
[152] Said MS, Tirthani E, L. E. (2024) *Enterococcus Infections. [Updated 2024 Feb 12].* In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan.
[153] Sathiananthamoorthy, S. *et al.* (2019) 'Reassessment of Routine Midstream Culture in Diagnosis of Urinary Tract Infection.', *Journal of Clinical Microbiology*, 57(3). doi: 10.1128/JCM.01452-18.
[154] Schaffer, J. N. and Pearson, M. M. (2015) 'Proteus mirabilis and Urinary Tract Infections.', *Microbiology spectrum*, 3(5). doi: 10.1128/microbiolspec.UTI-0017-2013.
[155] Scholes, D. *et al.* (2010) 'Family history and risk of recurrent cystitis and pyelonephritis in women.', *The Journal of Urology*, 184(2), pp. 564–569. doi: 10.1016/j.juro.2010.03.139.
[156] Schumann JA and Plasner S. (2023) *S. Trichomoniasis.* In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing;2024 Jan.
[157] Sedor, J. and Mulholland, S. G. (1999) 'HOSPITAL-ACQUIRED URINARY TRACT INFECTIONS ASSOCIATED WITH THE INDWELLING CATHETER', *Urologic Clinics of North America*, 26(4), pp. 821–828. doi: https://doi.org/10.1016/S0094-0143(05)70222-6.
[158] Seid, M. *et al.* (2023) 'Community-Acquired Urinary Tract Infection Among Sexually Active Women: Risk Factors, Bacterial Profile and Their Antimicrobial Susceptibility Patterns, Arba Minch, Southern Ethiopia.', *Infection and drug resistance*, 16, pp. 2297–2310. doi: 10.2147/IDR.S407092.
[159] Shackley, D. C. *et al.* (2017) 'Variation in the prevalence of urinary catheters: a profile of National Health Service patients in England.', *BMJ Open*, 7(6), p. e013842. doi: 10.1136/bmjopen-2016-013842.
[160] Sharma, S. *et al.* (2023) 'Microbial Biofilm: A Review on Formation, Infection, Antibiotic Resistance, Control Measures, and Innovative Treatment.', *Microorganisms*, 11(6). doi: 10.3390/microorganisms11061614.
[161] SHEPPARD, M. *et al.* (2023) 'Asymptomatic bacteriuria in pregnancy', *Australian and New Zealand Journal of Obstetrics and Gynaecology*, 63(5), pp. 696–701. doi: https://doi.org/10.1111/ajo.13693.
[162] Shukla S and Maraqa NF. (2024) *Congenital Rubella.* In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing.
[163] Sihra, N. *et al.* (2018) 'Nonantibiotic prevention and management of recurrent urinary tract infection', *Nature Reviews Urology*, 15(12), pp. 750–776. doi: 10.1038/s41585-018-0106-x.
[164] Simmering, J. E. *et al.* (2017) 'The Increase in Hospitalizations for Urinary Tract Infections and the Associated Costs in the United States, 1998-2011.', *Open forum infectious diseases*, 4(1), p. ofw281.

doi: 10.1093/ofid/ofw281.

[165] Sixt, B. *et al.* (2018) 'Chlamydia trachomatis fails to protect its growth niche against pro-apoptotic insults', *Cell Death & Differentiation*, 26, p. 1. doi: 10.1038/s41418-018-0224-2.

[166] Skrzat-Klapaczyńska, A. *et al.* (2018) 'Factors associated with urinary tract infections among HIV-1 infected patients.', *PloS one*, 13(1), p. e0190564. doi: 10.1371/journal.pone.0190564.

[167] de Sousa, T. *et al.* (2023) 'Study of Antimicrobial Resistance, Biofilm Formation, and Motility of Pseudomonas aeruginosa Derived from Urine Samples.', *Microorganisms*, 11(5). doi: 10.3390/microorganisms11051345.

[168] Su, H. *et al.* (1990) 'Chlamydia trachomatis-host cell interactions: role of the chlamydial major outer membrane protein as an adhesin.', *Infection and immunity*, 58(4), pp. 1017–1025. doi: 10.1128/iai.58.4.1017-1025.1990.

[169] Taglialegna, A. *et al.* (2020) 'The biofilm-associated surface protein Esp of Enterococcus faecalis forms amyloid-like fibers', *npj Biofilms and Microbiomes*, 6(1), p. 15. doi: 10.1038/s41522-020-0125-2.

[170] Taha, D.-E. *et al.* (2020) 'Antibiotic therapy in patients with high prostate-specific antigen: Is it worth considering? A systematic review.', *Arab Journal of Urology*, 18(1), pp. 1–8. doi: 10.1080/2090598X.2019.1677296.

[171] Tan, C. K. *et al.* (2011) 'Current Understanding of Streptococcal Urinary Tract Infection', in Nikibakhsh, A. (ed.) *Clinical Management of Complicated Urinary Tract Infection*. Rijeka: IntechOpen. doi: 10.5772/22012.

[172] Tan, C. W. and Chlebicki, M. P. (2016) 'Urinary tract infections in adults.', *Singapore Medical Journal*, 57(9), pp. 485–490. doi: 10.11622/smedj.2016153.

[173] Tariq, M. and Kim, D.-M. (2022) 'Hemorrhagic Fever with Renal Syndrome: Literature Review, Epidemiology, Clinical Picture and Pathogenesis.', *Infection & chemotherapy*, 54(1), pp. 1–19. doi: 10.3947/ic.2021.0148.

[174] Terlizzi, M. E., Gribaudo, G. and Maffei, M. E. (2017) 'UroPathogenic Escherichia coli (UPEC) Infections: Virulence Factors, Bladder Responses, Antibiotic, and Non-antibiotic Antimicrobial Strategies.', *Frontiers in microbiology*, 8, p. 1566. doi: 10.3389/fmicb.2017.01566.

[175] Thakore P, L. T. (no date) 'Urolithiasis. [Updated 2023 Jun 5].', in. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-.

[176] The Journal of the American Paraplegia Society (1992) *The prevention and management of urinary tract infections among people with spinal cord injuries. National Institute on Disability and Rehabilitation Research Consensus Statement. January 27-29, 1992*. United States. doi: 10.1080/01952307.1992.11735873.

[177] Thomson, N. *et al.* (2000) 'Biosynthesis of carbapenem antibiotic and prodigiosin pigment in Serratia is under quorum sensing control', *Molecular Microbiology*, 36, pp. 539–556. doi: 10.1046/j.1365-2958.2000.01872.x.

[178] Tullus, K. and Shaikh, N. (2020) 'Urinary tract infections in children.', *Lancet (London, England)*, 395(10237), pp. 1659–1668. doi: 10.1016/S0140-6736(20)30676-0.

[179] Ulett, G. C. *et al.* (2010) 'Group B Streptococcus (GBS) Urinary Tract Infection Involves Binding of GBS to Bladder Uroepithelium and Potent but GBS-Specific Induction of Interleukin 1α', *The Journal of Infectious Diseases*, 201(6), pp. 866–870. doi: 10.1086/650696.

[180] Vornhagen, J. *et al.* (2016) 'Bacterial Hyaluronidase Promotes Ascending GBS Infection and Preterm Birth.', *mBio*, 7(3). doi: 10.1128/mBio.00781-16.

[181] Wang, X., Wu, H., Fang, C., & Li, Z. . (2024) 'Insights into innate immune cell evasion by Chlamydia trachomatis.', *Frontiers in Immunology*, 15(1289644.). doi https://doi.org/10.3389/fimmu.2024.1289644.

[182] Wawrysiuk, S. *et al.* (2019) 'Prevention and treatment of uncomplicated lower urinary tract infections in the era of increasing antimicrobial resistance-non-antibiotic approaches: a systemic review.', *Archives of gynecology and obstetrics*, 300(4), pp. 821–828. doi: 10.1007/s00404-019-05256-z.

[183] Weaver, T. M., Hocking, J. M., Bailey, L. J., Wawrzyn, G. T., Howard, D. R., Sikkink, L. A., Ramirez-Alvarado, M., & Thompson, J. R. (2009) 'Structural and Functional Studies of Truncated Hemolysin A from Proteus mirabilis.', *Journal of Biological Chemistry*, 284(33), pp. 22297–22309. doi: https://doi.org/10.1074/jbc.M109.014431.

[184] Wolfe, A. J. *et al.* (2012) 'Evidence of uncultivated bacteria in the adult female bladder.', *Journal of Clinical Microbiology*, 50(4), pp. 1376–1383. doi: 10.1128/JCM.05852-11.

[185] Workowski, K. A. *et al.* (2021) 'Sexually Transmitted Infections Treatment Guidelines, 2021.', *MMWR. Recommendations and reports : Morbidity and mortality weekly report. Recommendations and reports*, 70(4), pp. 1–187. doi: 10.15585/mmwr.rr7004a1.

[186] Y Becker (1996) *Chlamydia*. Medical Mi. Edited by editor. C. 39. In: Baron S. Galveston (TX): University of Texas Medical Branch at Galveston.
[187] Young A, Toncar A, Leslie SW, et al. (2024) *Urethritis. [Updated 2024 Apr 26]*. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan.
[188] Young A, Toncar A, Leslie SW, et al. (no date) *Urethritis. [Updated 2024 Apr 26]*. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing.
[189] Zhou, Y. *et al.* (2023) 'Urinary Tract Infections Caused by Uropathogenic Escherichia coli: Mechanisms of Infection and Treatment Options.', *International Journal of Molecular Sciences*, 24(13). doi: 10.3390/ijms241310537.

