Chapter 3

Microbiology of Catheter Associated Urinary Tract Infection

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Additional information is available at the end of the chapter

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Abstract

Urinary tract infection (UTI) is common ailment worldwide with female predominance. Catheter associated urinary tract infection (CAUTI) is the most common healthcare related infection commonly used in urinary obstruction and incontinence in critically ill patients with prolonged indwelling catheterization means more than 30 days, which is almost invariable in all patients within 14 days of catheterization which increases morbidity and mortality and treatment expenses. Approximately 80% of nosocomial UTI is CAUTI. CAUTI may be asymptomatic and symptomatic. 2–4% cases may develop bacteraemia. Organisms responsible for CAUTI is similar to UTI as *Escherichia coli* the commonest than proteus, Pseudomonas, Klebsiella, Enterobacter, Enterococci, Candida, Serratia and rarely with *Delftia tsuruhatensis*, *Achromobacter xylosoxidans* and few others. CAUTI can be multibacterial. In CAUTI infective organisms form biofilm and propagate from there. *E. coli* is the most common isolate of CAUTI but *Enterobacter cloacae* exhibit highest biofilm production. CAUTI organisms are more antibiotic resistance than UTI. Even due to extensive use of antibiotics now Extended Spectrum Beta Lactamase (ESBL) producing CAUTI organisms are isolated from catheter biofilm.

Keywords: UTI, catheterization, CAUTI, biofilm

1. General information about CAUTI

UTI affects approximately 150 million people worldwide, which is most common infection with female predominance [1]. Around 15–25% hospitalized patients receiving indwelling urinary catheter develops CAUTI with prolonged catheterization and in among 40% nosocomial UTI,

80% is due to CAUTI [2]. CAUTI causes about 20% of episodes of health-care acquired bacteraemia in intensive care facilities and over 50% in long term care facilities [3]. The microbiology of biofilm on an indwelling catheter is dynamic with continuing turnover of organisms in the biofilm. Patients continue to acquire new organisms at a rate of about 3–7%/day. In long term catheterization that is by the end of 30 days CAUTI develops in 100% patients usually with 2 or more symptoms or clinical sign of haematuria, fever, suprapubic or loin pain, visible biofilm in character or catheter tube and acute confusion all state [4]. In CAUTI the incidence of infection is *Escherichia coli* in 24%, Candida in 24%, Enterococcus in 14% Pseudomonas in 10%, Klebsiella in 10% and remaining part with other organisms [5]. Bacteraemia occurs in 2–4% of CAUTI patients where case fatality is three times higher than nonbacteremic patients [6]. Adhesions in bacteria initiate attachment by recognizing host cell receptors on surfaces of host cell or catheter. Adhesins initiate adherence by overcoming the electrostatic repulsion observed between bacterial cell membranes and surfaces to allow intimate interactions to occur [7]. A biofilm is an aggregate of micro-organisms in which cells adhere to each other on a surface embedded within a self-produced matrix of extracellular polymeric substance [8]. In biofilm microorganisms growing in colonies within an extra-cellular mucopolysaccharide substance which they produce. Tamm-Horsfall protein and magnesium and calcium ions are incorporated into this material. Immediately after catheter insertion, biofilm starts to form and organisms adhere to a conditioning film of host proteins along the catheter surface. Both the inner and outer surfaces of catheter are involved. In CAUTI biofilms are initially formed by one organism but in prolonged Catheterization multiple bacteria's are present. In biofilm main mass is formed by extra cellular polymeric substance (EPS) within which organisms live. So there are three layers in biofilm, where deeper layer is abiotic, than environmental zone and on surface biotic zone [9]. Growth of bacteria in biofilms on the inner surface of catheters promotes encrustation and may protect bacteria from antimicrobial agents and the consequence is more drug resistance of biofilm organisms. When antibiotic treatment ends the biofilm can again shed bacteria, resulting recurrent acute infection. The patients may present as asymptomatic bacteriuria or symptomatic. In symptomatic bacteriuria patient present with fever, suprapubic or costovertebral angle tenderness, and systemic symptoms such as altered mentation, hypotension, or evidence of a systemic inflammatory response syndrome. In asymptomatic CAUTI diagnosis is made with presence of 10^5 cfu/mL of one bacterial species in a single catheter urine specimen [10]. In symptomatic CAUTI bacteriological criteria is present with clinical symptoms.

2. The collection of specimens

It is recommended that urine specimens be obtained through the catheter port using aseptic technique or, if a port is not present, puncturing the catheter tubing with a needle and syringe in patients with short term catheterization [11]. In long term indwelling catheterization, the ideal method of obtaining urine for culture is to replace the catheter and collect the specimen from the freshly placed catheter. In a symptomatic patient, this should be done immediately prior to initiating antimicrobial therapy. Culture specimens from the urine beg should not be obtained [10, 12]. Urine sample can be collected from suprapubic puncture also. Biofilm can be cultured from the catheter, for this swab is taken from inner side of catheter.

3. Microbiologic diagnosis of CAUTI

Catheter Associated Asymptomatic Bacteriuria (CA-ASB) is diagnosed when one or more organisms are present at quantitative counts $\geq 10^5$ cfu/mL from an appropriately collected urine specimen in a patient with no symptoms [13]. Lower quantitative counts may be isolated from urine specimens prior to $\geq 10^5$ cfu/mL being present, but these lower counts likely reflect the presence of organisms in biofilm forming along the catheter, rather than bladder bacteriuria [14]. Thus, it is recommended that the catheter be removed and a new catheter inserted, with specimen collection from the freshly placed catheter, before antimicrobial therapy is initiated for symptomatic infection [13]. In biofilm culture, most biofilm contains mixed bacterial communities meaning polymicrobial colonization.

Patients who remain catheterized without having antimicrobial therapy and who have colony counts $\geq 10^2$ cfu/mL (or even lower colony counts), the level of bacteriuria or candiduria uniformly increases to $>10^5$ cfu/mL within 24–48 h [14]. Given that colony counts in bladder urine as low as 10^2 cfu/mL are associated with symptomatic UTI in non-catheterized patients [15], untreated catheterized patients and those who have colony counts $\geq 10^2$ cfu/mL or even lower, the level of bacteriuria or candiduria uniformly increases to $>10^5$ cfu/mL within 24–48 h [10, 16]. Colony counts as low as 10^2 cfu/mL in bladder urine may be associated with symptomatic UTI in non-catheterized patients. Whereas low colony counts in catheter urine specimens are likely to be contaminated by periurethral flora, and the colony counts will increase rapidly if untreated. Low colony counts in catheter urine specimens are also reflective of significant bacteriuria in patients with intermittent catheterization [14].

4. Other laboratory tests

Pyuria is usually present in CA-UTI, as well as in CA-ASB. The sensitivity of pyuria for detecting infections due to enterococci or yeasts appears to be lower than that for gram-negative bacilli. Dipstick testing for nitrites and leukocyte esterase was also shown to be unhelpful in establishing a diagnosis in catheterized patients hospitalized in the ICU [17].

5. Microorganisms causing CAUTI

5.1. CAUTI with *E. coli*

5.1.1. Introduction

It is the most common cause of CAUTI in 24–60% patients [5, 18]. In CAUTI the source of this organism is usually patients own colonic flora. *E. coli* is large and diverse group of bacteria found in environment, foods and intestine of human and animal. Among many species of *E. coli* only a few causes disease in human being. It is beneficial in that it prevents the

growth and proliferation of other harmful species of bacteria. Even it plays an important role in current biological engineering.

5.1.2. Structure and pathogenesis

E. coli was discovered in 1885 by Theodor Escherich, German bacteriologist, is gram negative rod, lactose fermenter, composed of one circular chromosome which is common facultative anaerobes in colon and farces of human. Distribution is diverse and most of them are harmless belonging to genus Escherichia. Harmful species causes infection of urinary tract, gastrointestinal tract, respiratory system and rarely bacteraemia and septicemia. Phylogenetic analysis of *E. coli* showed majority of the strains responsible for UTI belongs to the phylogenetic group B2 and D, while in smaller percentage belong to A and B1 [19].

It has three antigens O-cell was antigen, H- flagella antigen and k- Capsular antigen. It has pili—a capsule, fimbriae, endotoxins and exotoxins also. Uropathogenic *E. coli* use P fimbriae (pyelonephritis-associated pili) to bind urinary tract endothelial cells. Vast majority of catheter-colonizing cells (up to 88%) express type 1 fimbriae and around 73% in *E. coli* causing CAUTI [20]. In UPEC fimbrial genes are ygiL, yadN, yfcV, and c2395 [21]. Pathogenesis of CAUTI initiated with UPEC colonization in periurethral and vaginal areas. Then it ascends to bladder lumen and grows as planktonic cells in urine. Sequentially adherence to bladder epithelium, then biofilm formation and invasion with replication and kidney colonization and finally bacteremia [22] (**Figure 1**).

5.1.3. Laboratory diagnosis

Diagnosis of *E. coli* infection is simple, by isolation and laboratory identification of bacterium from urine or biofilm. Laboratory diagnosis by culture of specimen—urine or catheter biofilm in blood agar, MacConkey's agar or eosin-methylene blue agar (which reveal lactose fermentation). Immunomagnetic separation and specific ELISA, latex agglutination tests, colony immunoblot assays, and other immunological-based detection methods are other ways for diagnosis of *E. coli*.

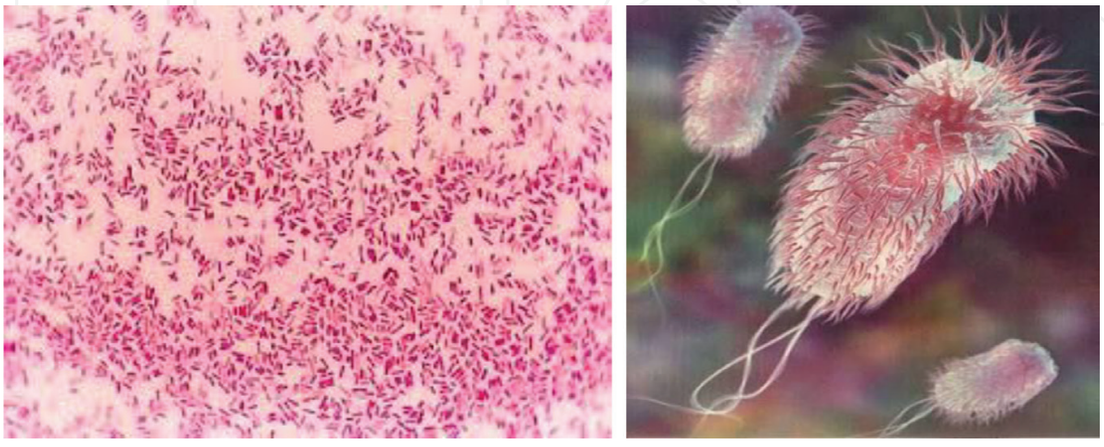

Figure 1. Gram stain picture and morphology of *E. coli*. Adapted from CCBC faculty web. BIOL 230 Lab Manual: gram stain of *E. coli* and infection landscapes: *Escherichia coli*. http://faculty.ccbcmd.edu/courses/bio141/labmanua/lab16/gramstain/gnrod.html.

5.2. Proteus in CAUTI

5.2.1. Introduction

Proteus species, member of the Enterobacteriaceae family of gram-negative bacilli are distinguishable from most other genera by their ability to swarm across an agar surface [23, 24]. Proteus species are most widely distributed in environment and as other enterobacteriaceae, this bacteria is part of intestinal flora of human being [25, 26]. Proteus also found in multiple environmental habitats, including long-term care facilities and hospitals. In hospital setting, it is not unusual for proteus species to colonize both the skin and mucosa of hospitalized patient and causing opportunistic nosocomial infections. It is one of the common causes of UTI in hospitalized patients undergoing urinary catheterization [26, 27].

UTIs are the most common manifestation of Proteus infection. Proteus infection accounts for 1–2% of UTIs in healthy women and 5% of hospital acquired UTIs. Catheters associated UTI have a prevalence of 20–45%. Proteus mirabilis causes 90% of proteus infection and proteus vulgaris and proteus penneri also isolated from long-term care facilities and hospital and from patients with underlying disease or specialized care. Most common age group is 20–50 years. More common in female group and the ratio between male female begins to decline after 50 years. UTI in men younger than 50 are usually caused by urologic abnormalities. Patients with recurrent infections, those with structural abnormalities of the urinary tract, those who have had urethral instrumentation or catheterization have an increase frequency of infection caused by proteus species [28].

5.2.2. Structure and pathogenesis

Proteus mirabilis produces an acidic capsular polysaccharide which was shown from glycose analysis, carboxyl reduction, methylation, periodate oxidation and the application high resolution nuclear magnetic resonance techniques. Proteus species possess an extracytoplasmic outer membrane, a common feature shared with other gram-negative bacteria. Infection depends upon the interacting organism and the host defense mechanism. Various component of the membrane interplay with the host to determine virulence. Virulence factors associated with adhesion, motility, biofilm formation, immunoavoidance, nutrient acquisition and as well as factors that cause damage to the host [29, 30] (**Figure 2**).

Certain virulence factors such as adhesin, motility and biofilm formation have been identified in Proteus species that has a positive correlation with risk of infection. After attachment of Proteus with urothelial cells, interleukin 6 and interleukin 8 secreted from the urothelial cells causes apoptosis and mucosal endothelial cell desquamation. Urease production of proteus also augments the risk of UTI. Urease production, together with the presence of bacterial motility and fimbriae or pili, as well as adhesins anchored directly within bacterial cell membrane may favor the upper urinary tract infection. Once firmly attached on the uroepithelium or catheter surface, bacteria begin to phenotypically change, producing exopolysaccharides that entrap and protect bacteria. These attached bacteria replicate and form microcolonies that eventually mature into biofilms [31, 32]. Once established, biofilms inherently protect uropathogens from antibiotic and the host immune response [33, 34]. Proteus mirabilis as with other uropathogens is capable of adapting to the urinary tract environment and acquiring nutrients. And this is accomplished by the production of degradative

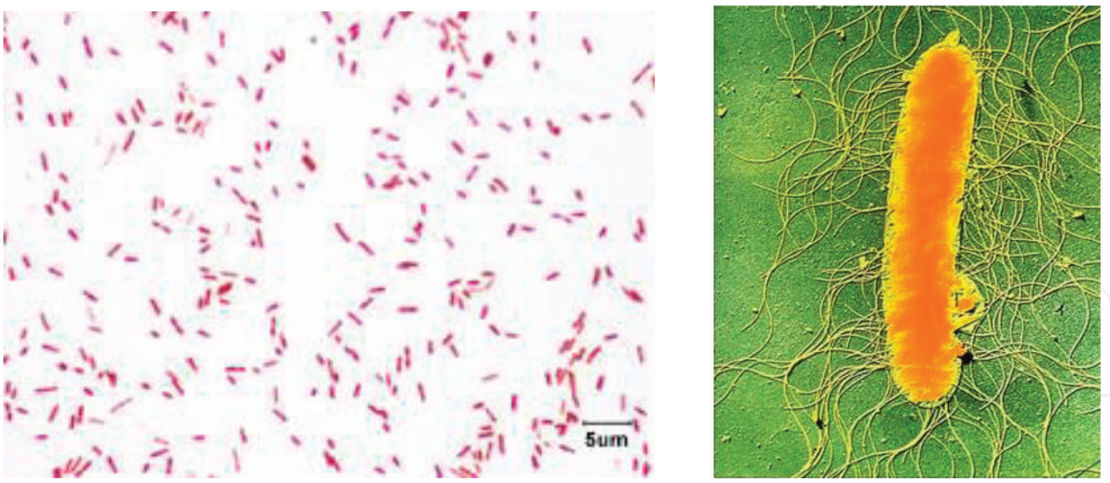

Figure 2. Gram stain picture and morphology of Proteus. Adapted from CCBC faculty web. BIOL 230 Lab Manual: gram stain of Proteus mirabilis and Proteus vulgaris bacteria (SEM) | Macro & Micro: Up Close and Personal | Pinterest | Microbiology, Bacteria shapes and Fungi. https://www.pinterest.com › pin.

enzymes such urease and proteases, toxins such as Haemolysin Hpm A and iron nutrient acquisition proteins.

5.2.3. Laboratory diagnosis

The infection with Proteus can be diagnosed by taking a urine sample for microscopy and culture which is sufficient in most of the cases except in few cases where advanced diagnostic tools are used. If the urine is alkaline, it is suggestive of infection with Proteus sp. The diagnosis of Proteus is made on swarming motility on media, unable to metabolized lactose and has a distinct fishy door. Ultrasound or CT scan to identify renal stone (Struvite stone) or to visualized kidneys or surrounding structures. It will allow to exclude other possible problems, mimicking symptoms of urinary tract infection [35, 36].

5.3. Pseudomonas in CAUTI

5.3.1. Introduction

Pseudomonas is a gram-negative bacteria belonging to the family Pseudomonadaceae and containing 191 validly described species [37]. Because of their widespread occurrence in water and plant seeds, the pseudomonas was observed in early history of microbiology. Pseudomonas is flagellated, motile, aerobic organism with Catalase and oxidase-positive. Pseudomonas may be the most common nuclear or of ice crystals in clouds, thereby being of utmost importance to the formation of snow and rain around the world [38]. All species of Pseudomonas are strict aerobes, and a significant number of organisms can produce exopolysaccharides associated with biofilm formation [39]. Pseudomonas is an opportunistic human pathogen that is especially adept at forming surface associated biofilms. Pseudomonas causes catheter associated urinary tract infection(CAUTIs) through biofilm formation on the surface of indwelling catheters, and biofilm mediated infection including ventilator associated pneumonia, infections related to mechanical heart valves, stents, grafts, sutures, and contract lens associated corneal infection [40].

Pseudomonas is third ranking causes nosocomial UTI about 12%, where *E. coli* remain on the top [41]. CAUTI is directly associated with duration of catheterization. Within 2–4 days of catheterization 15–25% patients develop bacteriuria [42].

5.3.2. Structure and pathogenesis

Pseudomonas aeruginosa is a gram-negative, rod shaped, asporogenous and monoflagellated, noncapsular bacterium but many strains have a mucoid slime layer. Pseudomonas has an incredible nutritional versatility. Pseudomonas can catabolize a wide range of organic molecule including organic compounds such as benzoate. This, then make Pseudomonas a very ubiquitous microorganism and Pseudomonas is the most abundant organism on earth [43] (**Figure 3**).

Pseudomonas is widely distributed in nature and is commonly present in moist environment of hospitals. It is pathogenic only when introduce into areas devoid of normal defense such as disruption of mucous membrane and skin, usage of intravenous or urinary catheters and neutropenia due to cancer or in cancer therapy. Its pathogenic activity depends on its antigenic structure, enzymes and toxins [44]. Among the enzymes Catalase, Pyocyanin, Proteases, elastase, haemolysin, Phospholipase C, exoenzyme S and T and endotoxin and endotoxin A play role in disease process and as well as immunosuppression. Pseudomonas can infect almost any organ or external site. Pseudomonas in invasive and toxigenic. It attached to and colonized the mucous membrane of skin. Pseudomonas can invade locally to produce systemic disease and septicemia. Pseudomonal UTs are usually hospital acquired and are associated with catheterization, instrumentation and surgery. These infections can involve the urinary tract through an ascending infection or through bacteriuria spread. These UTIs may be a source of bacteraemia or septicemia [45].

5.3.3. Laboratory diagnosis

Identification of bacterium with microscopy is simple method of identification of pseudomonas. Culture and antibiotic sensitivity pattern can be done in most laboratory media commonly on blood agar or eosin-methylthionine blue agar. Pseudomonas has inability to ferment lactose and has a positive oxidase reaction. Fluorescence under UV light is helpful in

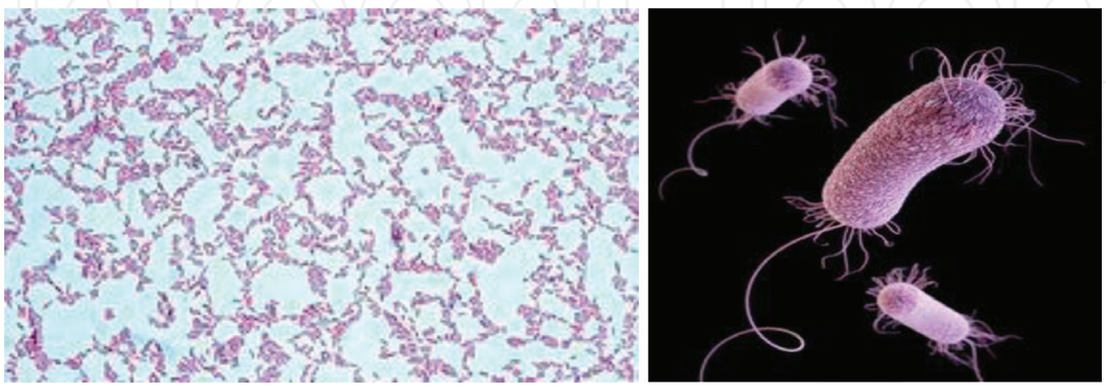

Figure 3. Gram stain picture and morphology of Pseudomonas aeroginosa. Adapted from Science News. A new antibiotic uses sneaky tactics to kill drug-resistant Pseudomonas aeruginosa illustration and Pseudomonas Aeruginosa Stock Photos & Pseudomonas Aeruginosa Stock Images—Alams. https://www.alamy.com › stock-photo.

early identification of colonies. Fluorescence is also used to suggest the presence of pseudomonas in wounds [46].

5.4. CAUTI with Klebsiella

5.4.1. Introduction

Urinary catheters are standard medical devices utilized in both hospital and nursing home settings are associated with a high frequency of catheter-associated urinary tract infections (CAUTI). The contribution of Klebsiella spp. in CAUTI is near about 7.7% [47].

5.4.2. Structure and pathogenesis

Klebsiella pneumoniae is a gram-negative pathogenic bacterium, is part of the Enterobacteriaceae family. It has got polysaccharide capsule attached to the bacterial outer membrane, and it ferments lactose. Klebsiella species are found ubiquitously in nature, including in plants, animals, and humans. They are the causative agent of several types of infections in humans. It has a large accessory genome of plasmids and chromosomal gene loci. This accessory genome divides *K. pneumoniae* strains into opportunistic, hyper virulent, and multidrug-resistant groups [48] (**Figure 4**).

The source of Klebsiella causing CAUTI can be endogenous typically via meatal, rectal, or vaginal colonization or exogenous, such as via equipment or contaminated hands of healthcare personnel. They typically migrate along the outer surface of the indwelling urethral catheter, until they enter the urethra.

Migration of the Klebsiella along the inner surface of the indwelling urethral catheter occurs much less frequently, compared with along the outer surface Internal (intraluminal) bacterial ascension occurs by Klebsiella tend to be introduced when opening the otherwise closed urinary drainage system, ascend from the urine collection bag into the bladder via reflux, biofilm formation occurs.

A critical step in progression to CAUTI by Klebsiella is to adhere to host surfaces, which is frequently achieved using pili (fimbriae) [49]. Pili are filamentous structures extending from

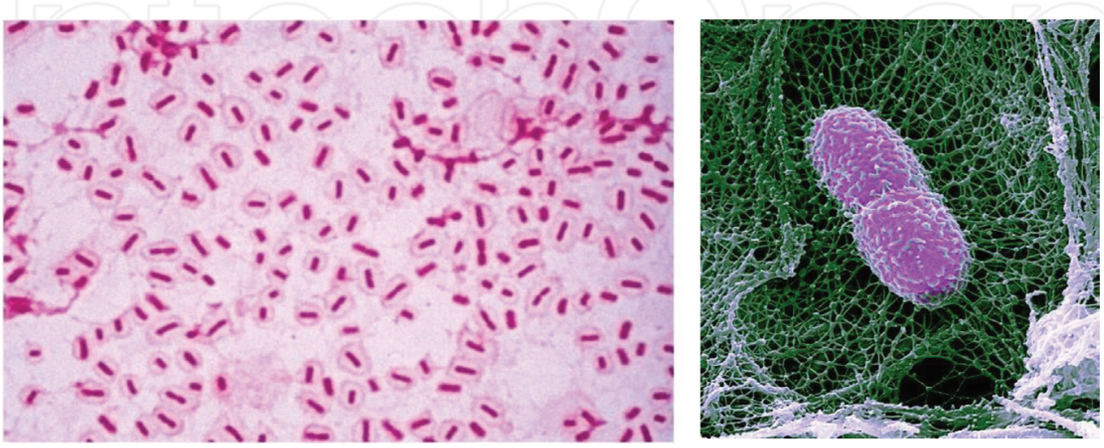

Figure 4. Gram stain picture and morphology of Klebsiella pneumonie. Adapted from studyblue.com. Microbio Lab Practical I—Microbiology 101 with Johnson at University of Vermont—StudyBlue. Study 368 Microbio Lab Practical I flashcards from Tess H. on StudyBlue and Klebsiella Pneumoniae Stock Photos and Pictures. Getty Images https://www.gettyimages.com › photos.

the surface of Klebsiella. They can be as long as 10 μm and between 1 and 11 nm in diameter. Among the two types of pili—type 1 (fim) pili and type 3 (mrk) pili, type 1 aids virulence by their ability to adhere with mucosal surfaces and type 3 pili strongly associated with biofilm production [50]. Both fim and mrk pili are considered part of the core genome [51]. It is thought that both types of pili play a role in colonization of urinary catheters, leading to CAUTI [52]. In addition to fim and mrk pili, a number of additional usher-type pili have been identified in Klebsiella with an average of ~8 pili clusters per strain. Based on varying gene frequencies, some of these appear to be part of the accessory genome. Immediately after catheterization Klebsiella starts biofilm production on the inner as well as outer surface of the catheter and on urothelium. Biofilm augments migration of Klebsiella into urethra and urinary bladder. Biofilm formation on the catheter surface by *Klebsiella pneumoniae* causes severe problem. Type 1 and type 3 fimbriae expressed by *K. pneumoniae* enhance biofilm formation on urinary catheters in a catheterized bladder model that mirrors the physicochemical conditions present in catheterized patients. These two fimbrial types does not is expressed when cells are grown planktonically. Interestingly, during biofilm formation on catheters, both fimbrial types are expressed, suggesting that they are both important in promoting biofilm formation on catheters [53]. The biofilm life cycle illustrated in three steps: initial attachment events with inert surfaces type 1 and type 3 fimbriae encoded by the mrk ABCDF gene cluster within *K. pneumoniae* promotes biofilm formation [54, 55]. Detachment events by clumps of Klebsiella or by a 'swarming' phenomenon within the interior of bacterial clusters, resulting in so-called 'seeding dispersal'.

Modifiable risk factor are prolonged catheterization, lack of adherence to aseptic catheter care, insertion of the indwelling urethral catheter in a location other than an operating room, presence of a urethral stent, feecal incontinence. Non-modifiable risk factor—renal disease (i.e., serum creatinine >2 mg/dL), diabetes mellitus, older age (i.e., age > 50 years old), female sex, malnutrition and severe underlying illness [53]. For infection several virulence factors such as surface factors (fimbriae, adhesins, and P and type 1 pili) and extracellular factors toxins, siderophores, enzymes, and polysaccharide coatings are necessary for initial adhesion with colonization of host mucosal surfaces for tissue invasion overcoming the host defense mechanisms, and causing chronic infections [55].

5.4.3. Laboratory diagnosis

Diagnosis of klebsiella infection is by isolation and laboratory identification of bacterium from urine or biofilm. Laboratory diagnosis can be done by culture of specimen—urine or catheter biofilm in blood agar, MacConkey's agar. Specific ELISA, latex agglutination tests, PCR and other immunological-based detection methods are sophisticated alternatives for diagnosis of klebsiella. Determination of a gene on capsule of Klebsiella is rapid and simple method for the determination of the K types of most *K. pneumoniae* clinical isolates [56].

5.5. CAUTI with Enterobacter

5.5.1. Introduction

Enterobacter species, particularly Enterobacter cloacae and *Enterobacter aerogenes*, are important nosocomial pathogens responsible for about 1.9–9% CAUTI, rarely causes bacteremia [57, 58]. *Enterobacter cloacae* exhibited the highest biofilm production (87.5%) among isolated pathogens [53].

5.5.2. Structure and pathogenesis

Enterobacter bacteria are motile, rod-shaped cells, facultative anaerobic, non-spore-forming, some of which are encapsulated belonging to the family Enterobacteriaceae. They are important opportunistic and multi-resistant bacterial pathogens. As facultative anaerobes, some Enterobacter bacteria ferment both glucose and lactose as a carbon source, presence of ornithine decarboxylase (ODC) activity and the lack of urease activity. In biofilms they secrete various cytotoxins (enterotoxins, hemolysins, pore-forming toxins. Though it is microflora in the intestine of humans, it is pathogens in plants and insects. Amp C β-lactamase production by *E. cloacae* is responsible for cephalosporin resistance. They possess peritrichous, amphitrichous, lophotrichous, polar flagella. *E. aerogenes* flagellar genes and its assembly system have been acquired in bloc from the Serratia genus [59] (**Figure 5**).

5.5.3. Laboratory diagnosis

The most important test to document Enterobacter infections is culture. Direct gram staining of the specimen is also useful. In the laboratory, growth of Enterobacter isolates is occurs in 24 h or less; Enterobacter species grow rapidly on selective (i.e., MacConkey) and nonselective (i.e., sheep blood) agars.

5.6. CAUTI with Enterococcus

5.6.1. Introduction

Enterococci are gram-positive facultative anaerobic cocci, two species are common commensal organisms in the intestines of humans: Enterococcus faecalis (90–95%) and Enterococcus faecium (5–10%) [60]. Though normally a gut commensal, these organisms are commonly responsible for nosocomial infection of urinary tract, biliary tract and blood, particularly in intensive care units (ICU) [61]. *E. coli* is usually the most frequent species isolated from

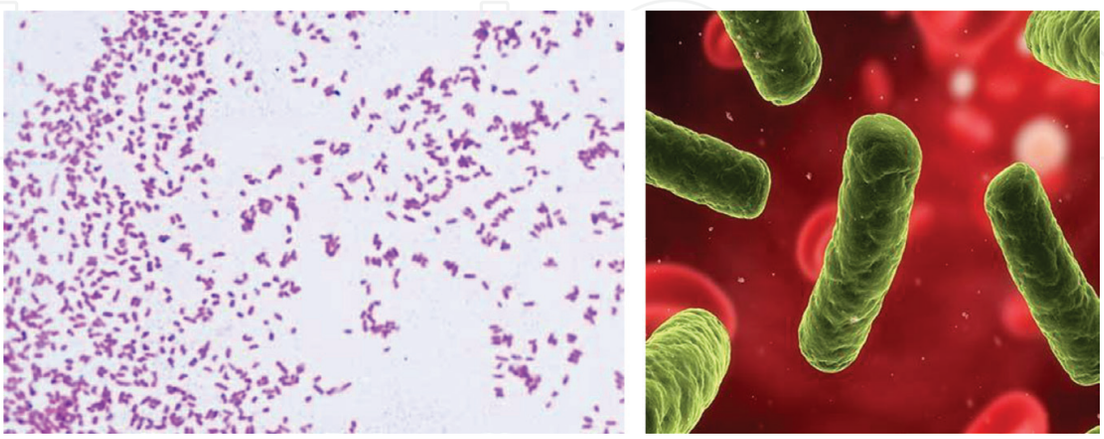

Figure 5. Gram stain picture and morphology of Enterobacter species. Adapted from Gram Stain Kit | Microorganism Stain | abcam.comAdwww.abcam.com/ and Science Prof Online. Gram-negative Bacteria Images: photos of *Escherichia coli*, Salmonella & Enterobacter and Enterobacter aerogenes | Gram-negative microorganism—HPV Decontamination | Hydrogen Peroxide Vapour—Bioquellhealthcare.bioquell.com › microbiology.

bacteremic catheter associated urinary tract infections (CAUTI). However, Enterococcus spp. (28.4%) and Candida spp. (19.7%) were also reported to be most common [62]. In another study, *E. coli* was found the commonest (36%) followed by Enterococcus spp. (25%), Klebsiella species (20%) and Pseudomonas spp. (5%) [63].

5.6.2. Structure and pathogenesis

The most important cause of bacteriuria is the formation of biofilm along the catheter surface [64]. Enterococcus is gram positive bacteria often found in pairs or short chains. Broadly, Enterococcus is in two groups—faecalis and non-faecalis (*E. gallinarum* and *E. casseliflavus*). Enterococcus faecalis formerly classified as part of the group D Streptococcus is a gram-positive, commensal bacterium inhabiting the gastrointestinal tracts of humans and other mammals, survive harsh environmental conditions including drying, high temperatures, and exposure to some antiseptics [65]. *E. faecalis* has the important characteristics of complex set of biochemical reactions, including fermentation of carbohydrates, hydrolysis of arginine, tolerance to tellurite, and motility and pigmentation. Presence of the catheter itself is essential for *E. faecalis* persistence in the bladder, *E. faecalis* depends on the catheter implant for persistence via an unknown mechanism that more than likely involves its ability to produce biofilms on the silicone tubing and immune-suppression [66].

E. faecalis produce a heteropolymeric extracellular hair-like fimbrial structure called the endocarditis- and biofilm-associated pilus-Ebp, having three components the organelle (EbpC), a minor subunit that forms the base of the structure (EbpB) and a tip-located adhesin (EbpA) [67]. EbpA is responsible for adhesion in urothelial and catheter surface for biofilm production (**Figure 6**).

5.6.3. Laboratory diagnosis

Urine sample and biofilm microscopy can identify this gram positive organism. Culture yields the growth of *E. faecalis* in appropriate media. Advanced diagnostic methods like immunological-based detection methods and PCR are rarely needed for diagnosis.

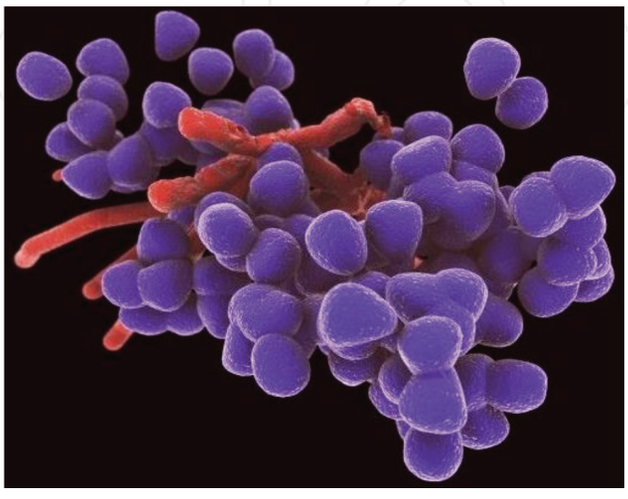

Figure 6. Morphology of Enterococcus. Adapted from Science Photo Library/Alamy Stock Photo Image ID: F6YBC3.

5.7. CAUTI with Candida

5.7.1. Introduction

One of the common causes of catheter associated urinary tract infection is fungal infection. Bacterial infections are accounted for 70.9% of catheter associated urinary infection. *E. coli* is the most commonly isolated organism (41.6%) whereas fungal infections are accounted for 16.6% and mixed fungal and bacterial infections accounted for 12.5% [68]. The National nosocomial infections surveillance (NNIS) data indicated that *C. albicans* caused 21% of catheter-associated urinary tract infections, in contrast to 13% of non-catheter-associated infections [69]. In one study 24% of the cases showing fungal yeast growth. Candida spp. was the commonest. Non-albicans Candida (86%) isolated more commonly than *Candida albicans* (14%) [70]. Candida are commensals, and to be pathogenic, interruption of normal host defenses is crucial which is facilitated in conditions like immunocompromised states as AIDS, diabetes mellitus, prolonged broad spectrum antibiotic use, indwelling devices, intravenous drug use and hyperalimentation fluids [71]. Diabetes mellitus has been reported as the most common risk factor for fungal infection [72, 73]. The duration of catheterization is also an important risk factor as the duration increases the incidence of fungal infection is increased [74].

5.7.2. Structure and pathogenesis

Candida albicans is an oval, budding yeast, which is a member of the normal flora of mucocutaneous membrane. Twenty species of Candida yeasts can cause in human infection but most common is *Candida albicans*. Sometimes it can gain predominance and can produce disease. Other candida species that can cause disease occasionally are *Candida parapsilosis*, *Candida tropicalis* and *Candida krusei* [75]. Although *Candida albicans* are common isolates in CAUTI, *Candida tropicalis* is increasingly reported in CAUTI [76]. The majority of *Candida albicans* infections are associated with biofilm formation on host or abiotic surfaces such as indwelling medical devices, which carry high morbidity and mortality [63, 77]. Several factors and activities contribute to the pathogenesis of this fungus which mediate adhesion to and invasion into host cells, which are in sequences are the secretion of hydrolases, the yeast-to-hypha transition, contact sensing and thigmotropism, biofilm formation, phenotypic switching and a range of fitness attributes [78] (**Figure 7**).

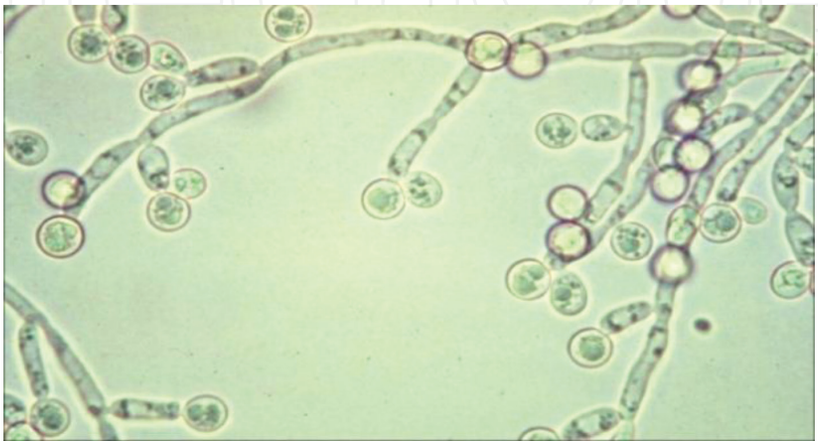

Figure 7. Morphology of Candida albicans. Adapted from biomedik8888, Aug 24, 2011. http://www.BioMedik.com.au3.

5.7.3. Laboratory diagnosis

Urine and materials removed from catheter are needed. Microscopic examinations of gram-stained specimen showed pseudohyphae and budding cells. Culture on Sabouraud's agar at room temperature and at 37°C showed typical colonies and budding pseudomycelia [79].

5.8. CAUTI with *Serratia marcescens*

It is facultative anaerobic bacilli gram-negative rod of Enterobacteriaceae family considered opportunistic human pathogen but not a component of human facial flora. It is capable of producing a pigment called prodigiosin, which ranges in color from dark red to pale pink. It is ubiquitously spent in nature and has preference for damp conditions. Though previously known as nonpathogenic, but since 1970s it is associated with multi drug resistant infection due to presence of R factor—a plasmid. A study in Japan showed 6.8% incidence of UTI with this organism [80]. It also causes bacteraemia rarely. Diagnosis is confirmed by culture of the urine specimen or catheter biofilm. Automated bacterial identification systems and Matrix-Assisted Laser Desorption Ionization-Time of Flight Mass Spectrometry (MALDI-TOF MS) is the other modality for diagnosis of serratia as well as other enterobacteriaceae [81].

5.9. CAUTI with *Delftia tsuruhatensis*

This non-fermentative gram-negative rod discovered as plant growth-promoting bacterium and potential biocontrol agent against plant pathogens. Infection with this uncommon organism in CAUTI occurs in combination with commonest bacteria *E. coli*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*. *D. tsuruhatensis* and *E. coli* coexist and tend to co-aggregate over time and also cooperate synergistically [82]. *D. tsuruhatensis* metabolized citric acid more rapidly leaving more uric acid available in the medium to be used by *E. coli* for dynamic growth of both organisms. Identification of this organism is not confirmatory with culture, so molecular methods are more reliable [83].

5.10. CAUTI with *Achromobacter xylosoxidans*

Achromobacter denitrificans is gram negative bacterium formerly known as *Alcaligenes denitrificans*. Infection with this organism predominantly observed in elderly patients with predisposing factors as urological abnormalities, malignancies and immune-suppression. Rarely it causes bacteraemia. This bacterium has high level of antibiotic resistance [84].

In polymicrobial biofilm, *Achromobacter xylosoxidans* cohabits with common organisms *E. coli*, *Pseudomonas aeruginosa* and *Klebsiella pneumoniae*. Diagnosis is by bacterial culture and molecular methods.

5.11. CAUTI with Staphylococci

Staphylococci (methicillin-sensitive *Staphylococcus aureus* [MSSA] and methicillin-resistant *S. aureus* [MRSA], *Staphylococcus saprophyticus*. These are the common gram positive bacteria usually responsible for skin and soft tissue infections but rarely cause CAUTI and bacteraemia [85].

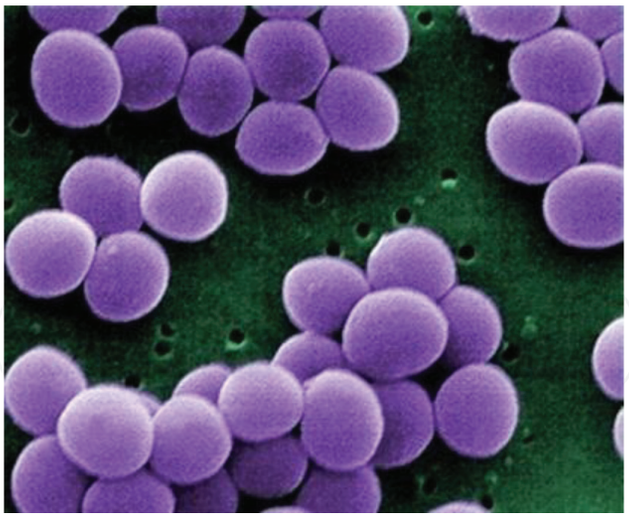

Figure 8. Morphology of Staphylococcus aureus. Adapted from abcam.comAdwww.abcam.com/ pharmacist-driven intervention improves care of patients with S aureus Bacteremia/Staph aureus. Nebraska Medicine https://asap.nebraskamed.com.

The incidence of Staphylococcal UTI as well as CAUTI is increasing and the organisms carry wide variety of multidrug-resistant genes on plasmids, which augment spread of resistance among other species [86].

Diagnosis is easy, gram stain of the sample, culture is sufficient. Advanced techniques rarely needed (**Figure 8**).

6. Conclusion

CAUTI is one of the most nosocomial Infection worldwide resulting from rational as well as sometimes irrational use of indwelling urinary catheter. Cause of CAUTI is formation of pathogenic biofilm commonly due to UPEC, Proteus, Klebsiella, Pseudomonas, Enterobacter rarely Candida and other uncommon opportunistic organisms. CAUTI has got high impact on morbidity and mortality as biofilm producing organisms are more antibiotic resistant. Antibiotic resistance is a global problem. Early detection of CAUTI is simple by examination of urine and catheter biofilm with microscopy as well as culture with antibiogram. It is easy and cost effective with early diagnosis and treatment for good clinical outcome. Advanced and sophisticated methods like Immunomagnetic separation, specific ELISA, colony immunoblot assays and PCR for diagnosis of CAUTI is seldom necessary.

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References

[1] Florece-Mireles AL, Waslker JN, Caparon M, Hultgren SJ. Urinary tract infections: Epidemiology, mechanisms of infection and treatment options. Nature Reviews Microbiology. 2015;**13**(5):269-264. DOI: 10.1038/nrmicro3432

[2] Esposito S, Noviello S, Leone S. Catheter-associated urinary tract infections: Epidemiology and prevention. Le Infezioni in Medicina. 2008;**16**(3):130-143

[3] Nicolle LE. Catheter associated urinary tract infections. Antimicrobial Resistance and Infection Control. 2014;**3**:23. DOI: 10.1186/2047-2994-3-23

[4] Parida S, Mishra SK. Urinary tract infections in the critical care unit: A brief review. Indian Journal of Critical Care Medicine. 2013;**17**(6):370-374. DOI: 10.4103/0972-5229.123451

[5] Weiner LM, Webb AK, Limbago B, et al. Antimicrobial-resistant pathogens associated with healthcare-associated infections: Summary of data reported to the national healthcare safety network at the centers for disease control and prevention, 2011-2014. Infection Control and Hospital Epidemiology. 2016;**37**(11):1288

[6] Walter E, Stamm MD. Catheter-associated urinary tract infections: Epidemiology, pathogenesis, and prevention. The American journal of Medicine. 1991;**91**(3, Supplement 2.19):S65-S71

[7] Jacobsen SM, Stickler DJ, Mobley HLT, Shirtliff ME. Complicated catheter associated urinary tract infections due to *Escherichia coli* and *Proteus mirabilis*. Clinical Microbiology Reviews. 2008;**21**(1):26-59. DOI: 10.1128/CMR.00019-07

[8] Tomar R, Paviaya R, Ghosh S, Murthy R, Pradhan S, Agrawal E. Biofilm production by uropathogens causing catheter associated urinary tract infection. International Journal of Medical Research and Review. 2017;**5**(07):710 Available online at: www.ijmrr.in

[9] Buhmann MT, Stiefel P, Maniura-Weber K, Ren Q. In vitro biofilm models for device-related infections. Trends in Biotechnology. 2016;**34**(12):945-948. DOI: 10.1016/j.tibtech.2016.05.016

[10] Hooton TM, Bradley SF, Cardenas DD, Colgan R, Geerlings SE, Rice JC, et al. Diagnosis, prevention and treatment of catheter-associated urinary tract infection in adults 2009 international clinical practice guidelines from the Infectious Diseases Society of America. Clinical Infectious Diseases. 2010;**50**:625-663

[11] Bergqvist D, Bronnestam R, Hedelin H, et al. The relevance of urinary sampling methods in patients with indwelling Foley catheters. British Journal of Urology. 1980;**52**:92-95

[12] Grahn D, Norman DC, White ML, et al. Validity of urinary catheter specimen for diagnosis of urinary tract infection in the elderly. Archives of Internal Medicine. 1985;**145**:1858-1860

[13] Stark RP, Maki DG. Bacteriuria in the catheterized patient. What quantitative level of bacteriuria is relevant? The New England Journal of Medicine. 1984;**311**:560-564

[14] Nicolle LE. Catheter-related urinary tract infection. Drugs & Aging. 2005;**22**:627-639

[15] Tambyah PA, Maki DG. The relationship between pyuria and infection in patients with indwelling urinary catheters: A prospective study of 761 patients. Archives of Internal Medicine. 2000;**160**:673-677

[16] Nicolle LE, Bradley S, Colgan R, et al. Infectious Diseases Society of America guidelines for the diagnosis and treatment of asymptomatic bacteriuria in adults. Clinical Infectious Diseases. 2005;**40**:643-654

[17] Schwartz DS, Barone JE. Correlation of urinalysis and dipstick results with catheter-associated urinary tract infections in surgical ICU patients. Intensive Care Medicine. 2006;**32**:1797-1801

[18] Majumder MI, Ahmed T, Hossain D, et al. Bacteriology and antibiotic sensitivity patterns of urine and biofilm in patients with indwelling urinary catheter in a tertiary hospital in Bangladesh. Journal of Bacteriology and Parasitology. 2014;**5**:3. DOI: 10.4172/2155-9597.1000191

[19] Lee JH, Subhadra B, Son YJ, et al. Phylogenetic group distributions, virulence factors and antimicrobial resistance properties of uropathogenic *Escherichia coli* strains isolated from patients with urinary tract infections in South Korea. Letters in Applied Microbiology. 2016;**62**(1):84-90. DOI: 10.1111/lam.12517 Epub 2015 Dec 9

[20] Reisner A, Maierl M, Jörger M, et al. Type 1 fimbriae contribute to catheter-associated urinary tract infections caused by *Escherichia coli*. Journal of Bacteriology. 2014;**196**(5): 931-939. DOI: 10.1128/JB.00985-13

[21] Spurbeck RR, Stapleton AE, Johnson JR, Walk ST, Hooton TM, Mobley HL. Fimbrial profiles predict virulence of uropathogenic *Escherichia coli* strains: Contribution of ygi and yad fimbriae. Infection and Immunity. 2011;**79**(12):4753-4763

[22] Terlizzi ME, Gribaudo G, Maffei ME. UroPathogenic Escherichia coli (UPEC) infections: Virulence factors, bladder responses, antibiotic, and non-antibiotic antimicrobial strategies. Frontiers in Microbiology. 15 Aug, 2017;**8**:1566. DOI: 10.3389/fmicb.2017.01566. eCollection 2017

[23] Penner JL. Genus XI Proteus. In: Krieg NR, Holt JG, editors. Bergey's Annual of Systemic Bacteriology. Vol. 1. Baltimore, M.D: Williams & Wilkins Co; 1984. pp. 491-494

[24] Penner JL, Hennessy J. Clinical isolates of *Proteus mirabilis* and *Proteus vulgaris*. Journal of Clinical Microbiology. 1980;**12**:304-309

[25] Luzzaro F, Brigante G, D'Andrea MM, Pini B, Giani T, Mantengoli E, et al. Spread of multidrug-resistant *Proteus mirabilis* isolates producing AmpC-type beta-lactamase: Epidemiology and clinical management. International Journal of Antimicrobial Agents. 2009;**33**(4):328-333

[26] Chow AW, Taylor PR, Yoshikawa TT, et al. A nosochomial outbreak of infections due to multiply resistant *Proteus mirabilis*: Role of intestinal colonization as a major reservoir. The Journal of Infectious Diseases; Jun 1979;**139**(6):621-627

[27] Wang JT, Chen PC, Chang SC, Shiau YR, Wang HY, Lai JF, et al. Antimicrobial susceptibilities of *Proteus mirabilis*: A longitudinal nationwide study from the Taiwan Surveillance of antimicrobial resistance (TSAR) program. BMC Infectious Diseases. 2014;**14**:486

[28] Lipsky BA. Urinary tract infection in men. Epidemiology, pathophysiology, diagnosis and treatment. Annals of Internal Medicine. 1989;**110**(2):138-150

[29] Beynon LM, Dumanski AJ, MacLean RJ, et al. Capsule structure of *Proteus mirabilis*. Journal of Bacteriology. 1992;**174**(7):2172-2177

[30] Jacobsen SM, Stickler DJ, Mobley THL, Shirtliff EM. Complicated cather-associated urinary tract infection due to *E. coli* and *Proteus mirabilis*. Clinical Microbiology Reviews. 2008;**21**(1):26-59

[31] Costerton JW, Lewandowski DE, Caldwell DR. Korberetal microbial bioflims. Annual Review of Microbiology. 1995;**49**:711-745

[32] Williams GJ, Stickler DJ. Effect of triclosan on the formation of crystalline biofilms by mixed communities of Urinary tract pathogens on urinary catheters. Journal of Medical Microbiology. 2008;**57**:1135-1140

[33] Kucheria R, Dasgupt P, Sacks SH, Khan MS, Sheerin NS. Urinary tract infection: New insight into a common problem. Postgraduate Medical Journal. 2005;**81**:83-86

[34] Kunin CM. Can we built a better urinary catheter? The New England Journal of Medicine. 1988;**319**:365-366

[35] Mobley HL, Belas R. S warming and pathogenicity of *Proteus mirabilis* in the urinary tract. Trends in Microbiology. 1995;**3**:280-284

[36] Mobley HL, Island MD, Hausinger RP. Molecular biology of microbial urease. Microbiological Reviews. 1995;**59**:451-480

[37] Madigan MT, Bender KS, Buckley DH, Sattkey WM, Stahl DA, editors. Brock Biology of Microbiology. 15th ed. London: Pearson; 2017

[38] Biello D. Do Microbes Makev Sniw? Scientific American. 2008;**2**:45-61

[39] Ryan KJ, Ray CG. Sherris Medical Microbiology. 6th ed. New York: McGRaw Hill; 2014

[40] Costerton JW, Stewart PS, Greenberg EP, et al. Bacterial biofilms: A common cause of persistent infection. Science; 21 May, 1999;**284**(5418):1318-1322

[41] Kunin CM. Infection of the urinary tract due to pseudomonas. In: Baltch AL, Smith RP, editors. Pseudomonas Infections and Treatment. New York: Marcel Dekker; 1994

[42] Warren JW. Catheter-associated urinary tract infections. International Journal of Antimicrobial Agents. 2001;**17**:299-303

[43] Costerton JW, Anwar H. *Pseudomonas aeruginosa*: The microbe and Pathogen. In: *Pseudomonas aeruginosa* Infections and Treatment. 1994. pp. 2-17

[44] Stewart PS, Costerton JW. Antibiotic resistance of bacteria on biofilms. Lancet; Jul 14, 2001;**358**(9276):135-138

[45] Flux CA, Costerton JW, Stewart PS, Stoodley P. Survival strategies of infectious biofilms. Trends in Microbiology. 2005;**13**:34-40

[46] Cole SJ, Angela R, Mona W, et al. Catheter-associated urinary tract infection by *Pseudomonas aeruginosa* is mediated by exopolysaccharide-dependent biofilms. Infection and Immunity. 2014;**82**(5):2048-2058

[47] Gould C, Umscheid C, Agarwal R, et al. Healthcare Infections Control Practices Advisory Committee (HICPAC). In: Guideline for Prevention of Catheter-associated Urinary Tract Infections. 2009 Available at: www.cdc.gov/hicpac/pdf/CAUTI/CAUTIguideline2009final.pdf

[48] Podschun and Ullmann. Klebsiella spp. as Nosocomial Pathogens: Epidemiology, Taxonomy, Typing Methods, and Pathogenicity Factors. 1998;**11**(4):589-603

[49] Ofek I, Doyle RJ. Bacterial Adhesion to Cells and Tissues. 1st edition. Principles of Bacterial Adhesion. US: Springer; 1994; Chapter-1. Pages 1-15. ISBN: 978-1-4684-6437-5. Online ISBN: 978-1-4684-6435-1. DOI: https://doi.org/10.1007/978-1-4684-6435-1

[50] Schroll et al. Role of type 1 and type 3 fimbriae in *Klebsiella pneumoniae* biofilm formation. BMC Microbiology. 2010;**10**:179

[51] Andrade BGN, de Veiga Ramos N, Marin MFA, Fonseca EL, Vicente ACP. The genome of a clinical *Klebsiella variicola* strain reveals virulence-associated traits and a pl9-like plasmid. FEMS Microbiology Letters. 2014;**360**:13-16. DOI: 10.1111/1574-6968.12583

[52] Murphy CN, Mortensen MS, Krogfelt KA, Clegg S. Role of *Klebsiella pneumoniae* type 1 and type 3 fimbriae in colonizing silicone tubes implanted into the bladders of mice as a model of catheter-associated urinary tract infections. Infection and Immunity. 2013; **81**:3009-3017. DOI: 10.1128/IAI.00348-13

[53] Clarke K. Catheter-Associated Urinary Tract Infections (CAUTIs). Austin Journal of Clinical Medicine. 2015;**2**(1):1022.1-1022.3

[54] Stahlhut SG, Struve C, Krogfelt KA, Reisner A. Biofilm formation of *Klebsiella pneumoniae* on urethral catheters requires either type 1 or type 3 fimbriae. Fems Immunology and Medical Microbiology. 2012;**65**(2):350-359. DOI: 10.1111/j.1574-695X.2012.00965.x

[55] Delcaru C, Alexandru I, Podgoreanu P, et al. Microbial biofilms in urinary tract infections and prostatitis: Etiology, pathogenicity, and combating strategies. Young LS, ed. Pathogens. 2016;**5**(4):65. DOI: 10.3390/pathogens5040065

[56] Brisse S, Passet V, Haugaard AB, et al. wzi gene sequencing, a rapid method for determination of capsular type for Klebsiella strains. Journal of Clinical Microbiology. 2013;**51**(12):4073-4078. DOI: 10.1128/JCM.01924-13

[57] Afzal S, Ashraf M, Bukhsh A, et al. Efficacy of anti-microbial agents with ascorbic acid in catheter associated urinary tract infection. Journal of Infectious Diseases & Preventive Medicine. 2017;**5**:3. ISSN: 2329-8731. DOI: 10.4172/2329-8731.100016

[58] Sabir N, Ikram A, Zaman G, et al. Bacterial biofilm-based catheter-associated urinary tract infections: Causative pathogens and antibiotic resistance. American Journal of Infection Control. 2017;**45**(10):1101-1105. DOI: 10.1016/j.ajic.2017.05.009 Epub 2017 Jun 16

[59] Bhani D, Bachhiwal R, Sharma R, Maheshwari RK. Microbial profile and antimicrobial susceptibility pattern of uropathogens isolated from Catheter Associated Urinary Tract Infection (CAUTI). International Journal of Current Microbiology and Applied Sciences. 2017;**6**(8):2446-2453 ISSN: 2319-7706

[60] Abdallah NMA, Elsayed SB, Yassin MM, et al. Biofilm forming bacteria isolated from urinary tract infection, relation to catheterization and susceptibility to antibiotics. International Journal for Biotechnology and Molecular Biology Research. 2011;**2**(10):172-178 Available online at: http://www.academicjournals.org/IJBMBR

[61] Davin-Regli A, Pagès JM. *Enterobacter aerogenes* and *Enterobacter cloacae*; versatile bacterial pathogens confronting antibiotic treatment. Frontiers in Microbiology. 18 May, 2015;**6**:392. DOI: 10.3389/fmicb.2015.00392. eCollection 2015

[62] Gilmore MS et al., editors. The Enterococci: Pathogenesis, Molecular Biology, and Antibiotic Resistance. Washington, D.C.: ASM Press; 2002

[63] Brooks GF, Carroll KC, Butel JS, Morse SA. Mietzner TA, editors. Jawetz, Melnick & Adelburg's Medical Microbiology. 26th ed. NewYork, London: Mc-Graw Hill; 2013

[64] Chang R, Greene MT, Chenoweth CE, Kuhn L, Shuman E, Rogers NAM, Saint S. Epidemiology of hospital-acquired urinary-tract related blood stream infection at a university hospital. Infection Control and Hospital Epidemiology. 2011;**32**:1127-1129

[65] Murray BE. The life and times of the Enterococcus. Clinical Microbiology Reviews. 1990;**3**(1):46

[66] Guiton PS, Hannan TJ, Ford B, Caparon MG, Hultgren SJ. *Enterococcus faecalis* overcomes foreign body-mediated inflammation to establish urinary tract infections. Morrison RP, ed. Infection and Immunity. 2013;**81**(1):329-339. DOI: 10.1128/IAI.00856-12

[67] Schembri MA, Lo AW, Ulett GC. Blocking the "MIDAS" touch of *Enterococcus faecalis*. Annals of Translational Medicine. 2015;**3**(Suppl 1):S3. DOI: 10.3978/j.issn.2305-5839.2015.03.32

[68] Warren JW. The catheter and urinary tract infection. The Medical Clinics of North America. 1991;**75**:481-493

[69] Warren JW, Tenney JH, Hoopes JM, Muncie HL, Anthony WC. A prospective microbiologic study of bacteriuria in patients with chronic indwelling urethral catheters. The Journal of Infectious Diseases. 1982;**146**:719-723

[70] Mohammad EJ. Catheter associated fungal urinary tract infection. The Iraqi Post Graduate Medical Journal. 2012;**11**(3):11

[71] Kojic EM, Darouiche RO. Candida infections of medical devices. Clinical Microbiology Reviews. 2004;**17**:255-267

[72] Sangamithra V, Sneka, Praveen S, Manonmoney. Incidence of catheter associated urinary tract infection in medical ICU in a tertiary care hospital. International Journal of Current Microbiology and Applied Sciences. 2017;**6**(4):662-669

[73] Kremery V, Barnes AJ. Non-albicans Candida spp. causing fungaemia: pathogenicity and antifungal resistance. The Journal of Hospital Infection. 2002;**50**:243-260

[74] Kauffman CA, Vazquez JD, Sobei HA, Gallis DSMK, Karchmer AW, Sugar AM, et al. Prospective multicenter surveillance study of funguria in hospitalized patients and the National Institute for Allergy and Infectious Diseases (NIAID) Mycoses Study Group. Clinical Infectious Diseases. 2000;**30**:14-18

[75] Wey SB, Mori M, Pfaller MA, Woolson RF, Wenzel RP. Risk factors for hospital-acquired candidemia. A matched case-control study. Archives of Internal Medicine. 1989;**149**: 2349-2353

[76] Hamory BH, Wenzel RP. Hospital associated candiduria: Predisposing factors and review of the literature. The Journal of Urology. 1978;**120**:444-448

[77] Mayer FL, Wilson D, Hube B. Candida albicans pathogenicity mechanisms. Virulence. 2013;**4**(2):119-128

[78] Deorukhkar SC, Saini S, Raytekar NA, Sebastian MD. Catheter associated urinary tract candida infections in intensive care unit patients. Journal of Clinical Microbiology and Biochemical Technology. 2016;**2**(1):015-017

[79] Tsui C, Kong EF, Jabra-Rizk MA. Pathogenesis of *Candida albicans* biofilm. Pathogens and Disease. 2016;**74**(4):ftw018. DOI: 10.1093/femspd/ftw018

[80] Ishikawa K, Matsumoto T, Yasuda M, Uehara S, Muratani T, et al. The nationwide study of bacterial pathogens associated with urinary tract infections conducted by the Japanese Society of Chemotherapy. Journal of Infection and Chemotherapy. 2011;**17**(1):126-138 Epub 2010 Dec 21

[81] Rodriguesa NMB, Bronzatoa GF, Santiago GS, et al. The Matrix-Assisted Laser Desorption Ionization-Time of Flight Mass Spectrometry (MALDI-TOF MS) identification versus biochemical tests: A study with enterobacteria from a dairy cattle environment Braz. Journal of Microbiology. 2017;**48**(1). DOI: 10.1016/j.bjm.2016.07.025

[82] Preiswerk B, Ullrich S, Speich R, Bloemberg GV, Hombach M. Human infection with Delftia tsuruhatensis isolated from a central venous catheter. Journal of Medical Microbiology. 2011;**60**:246-248. DOI: 10.1099/jmm.0.021238-0

[83] Azevedo AS, Almeida C, Gomes LC, Ferreira C, Mergulhão FJ, Melo LF, Azevedo NF. An in vitro model of catheter-associated urinary tract infections to investigate the role of uncommon bacteria on the *Escherichia coli* microbial consortium. Biochemical Engineering Journal. 2017;**118**:64-69

[84] Tena D, Praetorius AG, Balsalobre MP, Bisquert J. Urinary tract infection due to *Achromobacter xylosoxidans*. Report of 9 cases. Infectious Diseases. 2008;**40**(2):84-87. DOI: 10.1080/00365540701558714

[85] Romero-Vivas J, Rubio M, Fernandez C, Picazo JJ. Mortality associated with nosocomial bacteremia due to methicillin-resistant *Staphylococcus aureus*. Clinical Infectious Diseases. 1995;**21**(6):1417-1423. DOI: 10.1093/clinids/21.6.1417

[86] Looney AT, Redmond EJ, Davey NM, et al. Methicillin-resistant *Staphylococcus aureus* as a uropathogen in an Irish setting. Medicine (Baltimore). 2017;**96**(14):e4635. DOI: 10.1097/MD.0000000000004635

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