Infection and Biofilms

3

Arie S. Parnham and Vijay K. Sangar

Abstract

Prosthetics in general are susceptible to bacterial infection often with disastrous consequences, especially if not recognized and managed promptly. Consequently a good working knowledge of the underlying concepts of infections and biofilms is essential for clinicians involved in this area of urological surgery.

Keywords

Biofilm • Bacteria • Prostheses • Antibiotics • Urology • Infection • Sepsis

Biofilms

History

Although the term 'biofilm' was first published in 1975 in Microbial Ecology they were recognised much earlier [1]. The first description of a biofilm was Anthony van Leeuwnhoek, "the father of microbiology." He lived in Holland and worked as a linen salesman whose interest extended into producing microscopes using diamond shavings and also observing the natural world. In a report to the Royal Society of London regarding dental, plaques, he remarked "the number of these animalcules in the scurf of a man's teeth are so many that I believe that they exceed the number of men in a kingdom." Work by Koch in the 1800s allowed bacteria to be studied more closely, however the focus was on planktonic culture (single cells floating in a liquid medium). Although important progress was made on the more serious pathogens, as time progressed more and more scientists felt that this didn't represent the true nature of bacteria. This was later confirmed by Geesey in 1977 who confirmed that 99 % of bacteria are attached to surfaces as opposed to free floating (planktonic) [2].

In the 1940s H. Heukelekian and A. Heller wrote, "Surfaces enable bacteria to develop in substrates otherwise too dilute for growth.

A.S. Parnham, MBChB, FRCS (Urol) (✉)
Department of Andrology, University College London Hospital, London, UK
e-mail: arie_parnham@hotmail.com

V.K. Sangar, BSc, MBChB, MD, FRCS (Urol)
Department of Urology, The Christie Hospital NHS Foundation Trust, Wilmslow Road, Manchester M20 4BX, UK
e-mail: vijay.sangar@nhs.net

A. Muneer et al. (eds.), *Prosthetic Surgery in Urology*, DOI 10.1007/978-3-319-13859-6_3

Development takes place either as bacterial slime or colonial growth attached to surfaces" [3].

Claude Zobell in the mid-1900s later described his glass bottle experiments noting that bacteria introduced into said vessel rapidly disappeared from the water contained within and seemed to rapidly colonise the walls of the container creating a microenvironment of supportive nutrients [4].

The recognition of the importance of biofilms on healthcare and industry, and the related economic costs led to the formation of the Centre for Biofilm Engineering in Montana, USA in 1990. This type of centre was subsequently mirrored in several other countries.

Introduction to Biofilms

Although a number of definitions exist, a biofilm is essentially an assemblage of microbial cells that is irreversibly associated (not removed by gentle rinsing) with a surface and enclosed in a matrix of primarily polysaccharide material [5]. It is rare for a biofilm to contain one organism in nature and usually there are many different varieties.

There are a number of advantages for bacteria to live in a biofilm.

1. A biofilm has the ability to concentrate ions and organic compounds and in nutrient poor environments where single organisms would otherwise struggle, as demonstrated by Zobell and Grant [4].
2. Within a biofilm there are a wide variety of microenvironments that can cater for different organism requirements [6]
3. Biofilms in nature are composed of multiple different species of bacteria many of which will have complementary enzyme profiles for the breakdown of nutrients.
4. They augment the transfer of genetic material through transformation (the take up and incorporation of foreign DNA), conjugation (transfer of a plasmid of DNA facilitated by an F-pilli) and transduction (a virus or phage packaged with the DNA of one bacteria is absorbed by a receiving bacterium which incorporates the new DNA into its own) [7–9]. They can also facilitate the activation of certain genes that promote transformation by allowing greater accumulation of molecules that initiate this upregulation (a process known as Quorum sensing- a phenomenon in which bacteria can chemically sense the presence of other bacteria and when bacterial populations become high enough, new suites of genes may be expressed) [10]
5. They confer a degree of resistance to phagocytes and protozoa [11]
6. They confer a degree of antibiotic resistance. A number of mechanisms have been investigated and are thought to be responsible for the increased resistance to antimicrobial agents:
   (a) In a few cases biofilms can prevent penetration; this is not the case in the vast majority of circumstances.
   (b) Biofilms allow enzymes that degrade the antibiotic to become concentrated in the microenvironment.
   (c) Due to the variable microenvironments some bacteria are quiescent and, as such have a lower metabolic activity and are less susceptible.
   (d) Biofilms are known to alter the genetic expression conferring antimicrobial resistance e.g. expression of efflux pumps.
   (e) Persister cells produce toxins that prevent critical metabolic activities. Consequently bacteria have fewer critical targets for antibiotics and disinfectants to work against. They can also produce an antitoxin that allows resumption of activity once the threat has dissipated [12]

Formation of Biofilms

Through detailed studies of biofilms we now understand that their creation is a very complex process. As a bacterium approaches a surface within a fluid, Van der Waal forces attract them. However, the closer they are to a surface the net negative electrostatic charge of bacteria and the interacting surface, results in a counteracting repulsive force. The incorporation of flagellae and pilli helps overcome this. Attachment of the bacterium is further augmented by a hydrodynamic boundary layer created by the sur-

face interaction with the suspensory fluid, creating a low turbulence and relatively calm zone. A rough surface promotes adherence compared to a smooth surface, as the surface area is increased and shear forces are diminished [13]. Once bacteria come in contact with a surface they will produce a 'conditioning film' that will build over the ensuing hours. The surface that the bacterium comes in contact with will influence the biofilm structure and properties, and no surface is immune to this process.

The attachment of bacterium to a surface occurs in two stages: reversible attachment and irreversible attachment.

As the name suggests reversible attachment is unstable and microbes under a microscope can be seen as twitching as their flagella anchors them, but the microbe body is free to be influenced by the environment. It is possible for some bacteria to move across the surface they adhere to by contracting their pilus. Eventually the bacteria become encased in a polymeric matrix, they themselves create, essentially fixing them to the surface – irreversible attachment. The time it takes for this to occur can be in the realm of minutes but is clearly organism dependent. Other species are then recruited both randomly and in some cases specifically, as well as non-living debris that can provide structural and nutritional support. An example of a developing biofilm can be seen in Fig. 3.1.

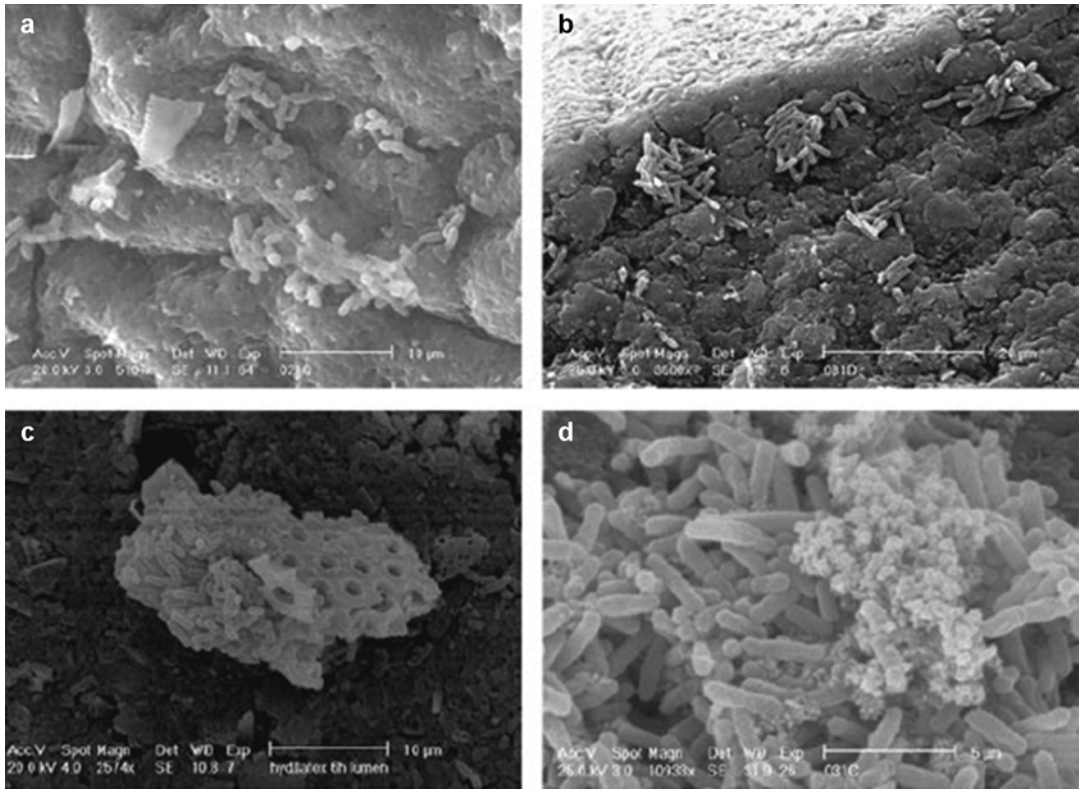

Fig. 3.1 Electron micrographs illustrating the colonization of a hydrogel-coated latex catheter by Proteus mirabilis in a laboratory model of the bladder. (**a**) This image shows bacteria trapped in crevices in the surface of the eyeholes 2 h after incubation in the model. (**b**) Microcolonies of *P. mirabilis* develop at the eyehole 4 h after incubation. (**c**) Bacteria attach to a diatom skeleton embedded in the luminal surface of the catheter 6 h after incubation in the model. (**d**) Biofilm develops at the eyehole 6 h after incubation in the model. Aggregates typical of apatite can be seen forming in the biofilm as the urine becomes alkaline (From Stickler [14]; with permission from Nature Publishing Group)

Table 3.1 Variables important in cell attachment and biofilm formation [5]

Properties of the substratum	Properties of the bulk fluid	Properties of the cell
Texture or roughness	Flow velocity	Cell surface hydrophobicity
Conditioning film hydrophobicity	pH	Fimbriae
	Temperature	Flagella
	Cations	Extracellular polymeric substances
	Presence of antimicrobial agents	

The flow of the surrounding medium can influence the structure of the biofilm; with fast flowing habitats often creating dense strongly adhered mushroom shapes whilst flat weakly attached biofilms occur in slow flow rates. Table 3.1 summarizes the important variables in cell attachment and biofilm formation.

Although biofilms confer to their 'residents' a number of advantages there are a number of circumstances in which bacteria may detach and disperse. These include passive forces including abrasion, erosion and fluid shear; or biological reasons such as nutrient limitation.

Bacteria and Biofilms in Urology

The management of biofilms is extremely important in the placement and success of prostheses in urological surgery.

Urinary Catheters

Approximately 20–30 % of patients catheterised in hospital will develop bacteriuria, with the risk increasing by 5 % each day such that by 20 days most patients, if tested, will exhibit bacteriuria [15–17]. Catheter-associated urinary tract infection (CAUTI) occurs in 2–6 % of patients [18] and is the most common hospital acquired infection, It is associated with an increased risk of mortality of as high as 30 % when associated with a bacteraemia [19, 20]. In 2012 it was estimated that there were 54,500 catheter related urinary tract infections in the United States alone [21].

A CAUTI is defined as a UTI where an indwelling urinary catheter was in place for >2 calendar days on the date of event, with day of device placement being day 1, and an indwelling urinary catheter was in place on the date of event or the day before. If an indwelling urinary catheter was in place for > 2 calendar days and then removed, the date of event for the UTI must be the day of discontinuation or the next day for the UTI to be catheter-associated [22].

CAUTIs are commonly a result of endogenous bacteria from the perineum [23]. However, a proportion (34 %) are a consequence of direct inoculation i.e. lapses in aseptic technique [23]. In some rare circumstances i.e. with Staphylococcus aureus it can be haematogenous [24].

Biofilms form both on the outer surface and inner drainage channel of a catheter within 3 days [25, 26]. The outer surface biofilm is generally populated by bacteria from the gastrointestinal tract, whilst drainage channel bacteria usually originate from cross-contamination due to a non-closed system, i.e., from a health worker's hands [27]. The presence of *Proteus mirabilis* within a biofilm generates urease, creating ammonia from urea, leading to an increase in urinary pH and subsequent crystallisation of magnesium ammonium phosphate (struvite) and calcium phosphate (hydroxyapatite), thereby causing stone formation.

The most common organisms involved depends on the duration of catheterisation as well as the location of the patient. CAUTI within 1 month of catheter placement is most commonly caused by Escherichia coli followed by Enterococcus species, Pseudomonas aeruginosa and yeast species [23]. In cases where a catheter has been in situ for longer than a month it is likely that there will be more than one microorganism cultured including enterobacteriae, gram negative and positive bacteria and yeast such as

Candida albicans. Further, these are more likely to be multiresitant [28, 29]. CAUTI in the intensive care setting are more likely to be Candida species [24].

Most patients with an indwelling catheter will have pyuria or bacteriuria whether or not they have a symptomatic urinary tact infection and do not routinely require treatment. Inappropriate use of antibiotics poses a significant risk for the development of multi-resistant organisms. Therefore the use of urine culture in the diagnosis CAUTI as an independent test is not reliable. Symptoms are therefore the most important aspect in deciding which patients have a CAUTI and require treatment [30]. In cases of CAUTI with long term catheters i.e. more than 2 weeks, the catheter should be removed and urine sent immediately from a new catheter (long-term if judged necessary or from a single intermittent self catheterisation) and empiric antibiotics initiated as per local guidelines based on epidemiological data and/or previous urinary cultures [31, 32]. Data from a randomised controlled trial suggests a shorter time to resolution and lower relapse rates with this approach rather than leaving the catheter in situ [33]. Once sensitivities return the antibiotic should be selected with the narrowest spectrum of appropriate cover [31, 32]. Duration of cover is variable dependent on the clinical situation and should be guided as per local, regional and national guidelines [31, 32].

Ureteric Stents

Although ureteric stents lie completely within the body they are not immune to the formation of biofilms or infection and rates of colonisation have been quoted as between 42 and 90% [34, 35]. However, despite this high rate few progress to develop symptomatic urinary tract infection.

The risk of bacteriuria and colonisation is directly related to the length of time the stent stays in situ, female gender and the presence of systemic disease such as diabetes mellitus, chronic renal failure and diabetic nephropathy [36].

When treating patients with a suspected urinary tract infection, with ureteric stents in situ, it is worth noting that the sensitivity of a urine culture to the presence and characterisation of colonisation is low and therefore a negative culture does not rule out a colonised stent [34]. Further the bacteria are often more resistant as previously described [34].

Both the American Urological Association and the European Association of Urology recommend prophylactic antibiotics prior to the insertion of ureteral stents however no RCTs exist to guide decision making [37]. However, there is RCT and meta-analysis data from transurethral resections of the prostate and transurethral resections of bladder tumour, favour prophylaxis to reduce sepsis episodes and bacteriuria [38–40].

Penile Prostheses

One complication related to penile prostheses which requires removal of the device. The most common bacterium causing medical device and penile implant infections is Staphylococcus epidermidis [41, 42]. Chapter 19 (“Complications of Penile Prosthesis Surgery”) covers the management of such complications but overviews of the steps that currently are employed to reduce the risk of infection are outlined in the next section.

Pre-operative and Perioperative Preparation

Pre-operative assessment is crucial in patients undergoing implant insertion. Patients undergoing revision surgery, impaired host defences, diabetes mellitus, spinal cord injury and penile fibrosis are all at a higher risk of infection and as such should be optimised where possible and appropriately counselled.

Parenteral antibiotics are recommended 1 h prior to incision and continuing for 24 h (American Urological Association [AUA] best practice statement 2008), although the guidance acknowledges that there are no randomised controlled trials regarding antimicrobial prophylaxis for insertion of penile prosthesis and is based on meta-analyses of mesh hernia repair and orthopaedic surgery [37]. The choice of antibiotic varies but the AUA recommend an Aminoglycoside

and a 1st or 2nd generation Cephalosporin or Vancomycin [37].

A Cochrane review in 2006 found no difference in surgical site infections (SSIs) among patients who have had hair removed prior to surgery and those who have not, however if it is necessary to remove hair then clipping resulted in fewer SSIs than shaving using a razor [43]. There was insufficient evidence regarding depilatory cream compared with shaving using a razor and there was no difference in SSIs when patients were shaved or clipped 1 day before surgery or on the day of surgery [43].

Many implanters have adopted a 10 minute timed surgical scrub of the patient although there is little in the literature to recommend this. However, the choice of scrub used appears to make a difference with Chlorhexidine appearing to be more efficacious [44].

The theatre should ideally have a laminar flow system and traffic in and out of theatre should be limited.

Device

Currently the main three-piece penile prosthesis manufacturers are American Medical Systems (AMS, Minnetonka, MN now part of Boston Scientific Mens Health), and Coloplast Corporation (Humlebaek, Denmark). Both companies have taken different approaches to reducing the risk of infection and biofilm formation.

In 2001 AMS introduced Inhibizone™ to their implants, a combination of the antibiotics minocycline and rifampicin impregnated into all the components of the prosthesis, which elute maximally for 3 days and continue to elute to a lesser extent over a 14- to 21-day period [45, 46].

In 2002 Coloplast Corporation released a device coated in polyvinylpyrrolidone (PVP), a hydrophilic polymer that covers the whole device including the reservoir. The PVP-coated implant allows the surgeon to select their own antibiotic combinations at the time of surgery by simply immersing it in a bath of the antibiotic(s). In addition the coating prevents bacterial adherence.

A systematic review in 2012 of 9910 implants found that the infection rates for non-coated versus coated penile implants were 2.32 % and 0.89 % respectively ($P = <0.01$) firmly establishing their role [47].

Surgical Technique

Contamination of the implant with Staphylococcus epidermidis is most likely from the patient's own skin. Consequently a "no touch" technique has been shown in a large single surgeon series using historical controls, to reduce infection rates to 0.48 % [48]. This technique requires gloves and instruments to be changed and an additional sterile drape to be placed once the incisions in the corpora are made.

Artificial Urinary Sphincters

Many issues surrounding the use of artificial urinary sphincters mirror those of penile implants. The most commonly employed artificial sphincter is the AMS 800® produced by American Medical Systems (AMS, Minnetonka, MN). Like its penile implant equivalent the sphincter is coated with Inhibizone™. It should follow that with the convincing data from penile implants, there should be an improvement in infection rates with Inhibizone use in sphincters but there is a paucity of data pertaining to its clinical benefits in this setting. In a retrospective review of 426 consecutive patients (213 without and 213 with Inhibizone™) implanted by a single surgeon, the rates of infection were identical 3.3 %, $P = 0.99$ [49]. Further, in a subgroup of complex patients there was no statistically significant difference between the coated and non-coated devices (2 of 38 patients or 5 % vs. 3 of 50 or 6 %, $P = 0.42$) [49]. However a lower incidence of infection in patients with diabetes was noted in the coated group vs non-coated, although this was not statistically significant (0 of 42 or 0 % vs. 4 of 40 or 10 %, $P = 0.052$) [49].

Conclusions

Careful consideration of biofilms when placing prostheses is of upmost importance to the serious implanter and ultimately the patient. A clearer understanding of how biofilms and

bacteria work and the mechanisms by which they survive and proliferate has lead to a number of important changes in surgery which have resulted in fewer complications and ultimately better patient outcomes.

References

1. Mack WN, Mack JP, Ackerson AO. Microbial film development in a trickling filter. Microb Ecol. 1975;2(3):215–26.
2. Geesey GG, Richardson WT, Yeomans HG, Irvin RT, Costerton JW. Microscopic examination of natural sessile bacterial populations from an alpine stream. Can J Microbiol. 1977;23(12):1733–6.
3. Heukelekian H, Heller A. Relation between food concentration and surface for bacterial growth. J Bacteriol. 1940;40(4):547–58.
4. Zobell CE, Grant CW. Bacterial utilization of low concentrations of organic matter. J Bacteriol. 1943;45(6):555–64.
5. Donlan RM. Biofilms: microbial life on surfaces. Emerg Infect Dis. 2002;8(9):881–90.
6. Stewart PS, Franklin MJ. Physiological heterogeneity in biofilms. Nat Rev Microbiol. 2008;6(3):199–210.
7. Griffith F. The significance of pneumococcal types. J Hyg. 1928;27(2):113–59.
8. Babic A, Lindner AB, Vulic M, Stewart EJ, Radman M. Direct visualization of horizontal gene transfer. Science. 2008;319(5869):1533–6.
9. Whitchurch CB, Tolker-Nielsen T, Ragas PC, Mattick JS. Extracellular DNA required for bacterial biofilm formation. Science. 2002;295(5559):1487.
10. Li YH, Lau PC, Lee JH, Ellen RP, Cvitkovitch DG. Natural genetic transformation of Streptococcus mutans growing in biofilms. J Bacteriol. 2001; 183(3):897–908.
11. Costerton JW, Stewart PS, Greenberg EP. Bacterial biofilms: a common cause of persistent infections. Science. 1999;284(5418):1318–22.
12. Lewis K. Persister cells: molecular mechanisms related to antibiotic tolerance. Handb Exp Pharmacol. 2012;211:121–33.
13. Characklis WG, McFeters GA, Marshall KC. Physiological ecology in biofilm systems. In: Biofilms. New York: Wiley; 1990. p. 341–94.
14. Stickler DJ. Bacterial biofilms in patients with indwelling urinary catheters. Nat Clin Pract Urol. 2008;5:598–608. doi:10.1038/ncpuro1231.
15. Garibaldi RA, Burke JP, Britt MR, Miller MA, Smith CB. Meatal colonization and catheter-associated bacteriuria. N Engl J Med. 1980;303(6):316–8.
16. Garibaldi RA, Mooney BR, Epstein BJ, Britt MR. An evaluation of daily bacteriologic monitoring to identify preventable episodes of catheter-associated urinary tract infection. Infect Control IC. 1982;3(6):466–70.
17. Warren JW, Tenney JH, Hoopes JM, Muncie HL, Anthony WC. A prospective microbiologic study of bacteriuria in patients with chronic indwelling urethral catheters. J Infect Dis. 1982;146(6):719–23.
18. Stamm WE. Urinary tract infections. In: Bennett JV, Brachman PS, editors. Hospital infection. 4th ed. Philadelphia: Lippincott-Raven; 1998. p. 477–85.
19. Platt R, Polk BF, Murdock B, Rosner B. Mortality associated with nosocomial urinary-tract infection. N Engl J Med. 1982;307(11):637–42.
20. Saint S. Clinical and economic consequences of nosocomial catheter-related bacteriuria. Am J Infect Control. 2000;28(1):68–75.
21. Data and statistics of healthcare associated infections. 2014 [01/08/2014]. Available from: http://www.cdc.gov/HAI/surveillance/index.html.
22. 2016 NHSN Patient Safety Component Manual. [02/04/2016]. Available from: http://www.cdc.gov/nhsn/.
23. Tambyah PA, Halvorson KT, Maki DG. A prospective study of pathogenesis of catheter-associated urinary tract infections. Mayo Clin Proc. 1999;74(2):131–6.
24. Chenoweth CE, Gould CV, Saint S. Diagnosis, management, and prevention of catheter-associated urinary tract infections. Infect Dis Clin North Am. 2014;28(1):105–19.
25. Donlan RM, Costerton JW. Biofilms: survival mechanisms of clinically relevant microorganisms. Clin Microbiol Rev. 2002;15(2):167–93.
26. Sabbuba N, Hughes G, Stickler DJ. The migration of Proteus mirabilis and other urinary tract pathogens over Foley catheters. BJU Int. 2002;89(1):55–60.
27. Warren JW. Catheter-associated urinary tract infections. Int J Antimicrob Agents. 2001;17(4):299–303.
28. Sievert DM, Ricks P, Edwards JR, Schneider A, Patel J, Srinivasan A, 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, 2009-2010. Infect Control Hosp Epidemiol Off J Soc Hosp Epidemiol Am. 2013;34(1):1–14.
29. Dalhoff A. Global fluoroquinolone resistance epidemiology and implications for clinical use. Interdiscip Perspect Infect Dis. 2012;2012:976273.
30. Grabe M, Bartoletti R, Bjerklund Johansen TE, Cai T, Cek M, Koves B, Naber KG, Pickard RS, Tenke P, Wagenlehner F, Wullt B. Guidelines on urological infections. 2015. 12 Apr 2015. Available from: http://uroweb.org/guideline/urological-infections/.
31. 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. Clin Infect Dis Off Publ Infect Dis Soc Am. 2010;50(5):625–63.
32. Naber KG, et al. Urogenital infections, in International Consultations on Urological Diseases. 2010. 12 Apr

2015. Available from: http://www.icud.info/PDFs/ICUD%20Urogenital%20Infections.pdf.
33. Raz R, Schiller D, Nicolle LE. Chronic indwelling catheter replacement before antimicrobial therapy for symptomatic urinary tract infection. J Urol. 2000;164(4):1254–8.
34. Kehinde EO, Rotimi VO, Al-Hunayan A, Abdul-Halim H, Boland F, Al-Awadi KA. Bacteriology of urinary tract infection associated with indwelling J ureteral stents. J Endourol Endourol Soc. 2004;18(9):891–6.
35. Reid G, Denstedt JD, Kang YS, Lam D, Nause C. Microbial adhesion and biofilm formation on ureteral stents in vitro and in vivo. J Urol. 1992; 148(5):1592–4.
36. Kehinde EO, Rotimi VO, Al-Awadi KA, Abdul-Halim H, Boland F, Al-Hunayan A, et al. Factors predisposing to urinary tract infection after J ureteral stent insertion. J Urol. 2002;167(3):1334–7.
37. Wolf JS, Bennett C, Dmochowski RR, Hollenbeck BK, Pearle MS, Schaeffer AJ. Best practice policy statement on urological surgery antimicrobial prophylaxis. 2008. 10 Apr 2015. Available from: https://www.auanet.org/education/guidelines/antimicrobial-prophylaxis.cfm.
38. Qiang W, Jianchen W, MacDonald R, Monga M, Wilt TJ. Antibiotic prophylaxis for transurethral prostatic resection in men with preoperative urine containing less than 100,000 bacteria per ml: a systematic review. J Urol. 2005;173(4):1175–81.
39. MacDermott JP, Ewing RE, Somerville JF, Gray BK. Cephradine prophylaxis in transurethral procedures for carcinoma of the bladder. Br J Urol. 1988;62(2):136–9.
40. Wagenlehner FM, Wagenlehner C, Schinzel S, Naber KG, Working Group "Urological Infections" of German Society of Urology. Prospective, randomized, multicentric, open, comparative study on the efficacy of a prophylactic single dose of 500 mg levofloxacin versus 1920 mg trimethoprim/sulfamethoxazole versus a control group in patients undergoing TUR of the prostate. Eur Urol. 2005; 47(4):549–56.
41. Henry GD, Wilson SK, Delk 2nd JR, Carson CC, Silverstein A, Cleves MA, et al. Penile prosthesis cultures during revision surgery: a multicenter study. J Urol. 2004;172(1):153–6.
42. McCann MT, Gilmore BF, Gorman SP. Staphylococcus epidermidis device-related infections: pathogenesis and clinical management. J Pharm Pharmacol. 2008;60(12):1551–71.
43. Tanner J, Woodings D, Moncaster K. Preoperative hair removal to reduce surgical site infection. Cochrane Database Syst Rev. 2006;(2):CD004122.
44. Yeung LL, Grewal S, Bullock A, Lai HH, Brandes SB. A comparison of chlorhexidine-alcohol versus povidone-iodine for eliminating skin flora before genitourinary prosthetic surgery: a randomized controlled trial. J Urol. 2013;189(1):136–40.
45. Mansouri MD, Boone TB, Darouiche RO. Comparative assessment of antimicrobial activities of antibiotic-treated penile prostheses. Eur Urol. 2009; 56(6):1039–45.
46. Wilson SK, Costerton JW. Biofilm and penile prosthesis infections in the era of coated implants: a review. J Sex Med. 2012;9(1):44–53.
47. Mandava SH, Serefoglu EC, Freier MT, Wilson SK, Hellstrom WJ. Infection retardant coated inflatable penile prostheses decrease the incidence of infection: a systematic review and meta-analysis. J Urol. 2012;188(5):1855–60.
48. Eid JF, Wilson SK, Cleves M, Salem EA. Coated implants and "no touch" surgical technique decreases risk of infection in inflatable penile prosthesis implantation to 0.46%. Urology. 2012;79(6):1310–5.
49. de Cogain MR, Elliott DS. The impact of an antibiotic coating on the artificial urinary sphincter infection rate. J Urol. 2013;190(1):113–7.