AUA White Paper on

THE PREVENTION AND TREATMENT OF THE MORE COMMON COMPLICATIONS RELATED TO PROSTATE BIOPSY UPDATE

2016 TASK FORCE:

Michael A. Liss, MD, MAS
Behfar Ehdaie, MD, MPH
Stacy Loeb, MD, MSc
Maxwell V. Meng, MD
Jay D. Raman, MD
Vanessa Spears, RN, BSN, MHA, CURN
Sean P. Stroup, MD

ORIGINAL TASK FORCE MEMBERS 2012:

Chris M. Gonzalez, MD, MBA
Timothy Averch, MD
Lee Ann Boyd, MSN, ARNP, CUNP
J. Quentin Clemens, MD, MSCI
Robert Dowling, MD
Howard B. Goldman, MD
Danil V. Makarov, MD, MHS
Vic Senese, RN
Mary Anne Wasner, BSN, CURN

AUA 2016 STAFF:

Jennifer Bertsch
Emma Hitt, PhD, ELS (Medical Writer)
Heddy Hubbard, PhD, MPH, RN, FAAN
Suzanne Pope, MBA
Victoria Wilder (Medical Librarian)

AUA 2012 STAFF:

Kirsten Aquino (Consultant)
Jennifer Bertsch
Lu Lu Lee, PhD
Emma Nichols, PhD (Medical Writer)
Stephanie Stinchcomb, CPC, CCS-P, ACS-UR

American Urological Association
Education & Research, Inc.

PURPOSE OF THIS REVIEW

1. Identify the prevalence of common complications of prostate biopsy to facilitate up-to-date informed consent and to guide shared decision-making process.

2. Determine prevention strategies for the most common complications from prostate biopsy, especially in response to the rise in infectious complications.

3. Recognize early signs of complications and implement appropriate strategies to minimize patient morbidity and mortality.

UPDATES FROM 2012

-   Focus on prevention and early treatment of complications

-   Expanded discussion on infection and prostate biopsy

-   Discussion on informed consent

-   Expanded topics such as erectile dysfunction and needle tract seeding

-   Expanded discussion on bleeding complications

RECOMMENDATIONS

Informed Consent

A proper informed consent should be discussed regarding the risks and benefits of prostate biopsy after shared decision making to proceed. The typical risks of prostate biopsy and their frequency are listed.

Infection				5-7%
	Hospitalization			1-3%
Bleeding				
	Hematuria			50%
		Needs intervention		<1%
	Rectal Bleeding			30%
		Needs intervention		2.5%
	Hematospermia			50%
		Prolonged (>4 weeks)		30%
Other				
	LUTS	Transient	(~1 month)	6-25%
	Urinary Retention			0.2 -2.6%
	ED	Transient	(~1 month)	Less than 1%

Complication Prevention

1. A risk assessment should be performed on all patients to identify known risk factors for harboring fluoroquinolone resistance, especially healthcare workers or those with recent travel, antibiotics, or hospitalizations.

2. Immunocompromised patients may need special attention and assistance from infectious disease specialists.

3. The AUA Best Practice Policy Statement on Urologic Surgery Antimicrobial Prophylaxis suggests a fluoroquinolone for less than 24 hours.

4. Check local antibiograms for current local levels of fluoroquinolone resistance.

5. Check your current equipment and cleaning practices. Adhere to guidelines regarding cleaning equipment, checking probes, and changing lubricant containers often.

6. Consider stopping anticoagulation if possible, though this is unlikely to significantly impact bleeding risk.

7. Confirm medications prior to prostate biopsy.

Prompt Treatment of Infectious Complications

8. Review reasons to return to the emergency room (ER) at the completion of the biopsy

9. Fever and/or chills should prompt the patient to return for evaluation

10. Empiric intravenous treatment with carbapenems, amikacin, or second- and third-generation cephalosporins can be considered until culture sensitivities are known.

11. Do not use oral Bactrim if bacteremia is suspected.

INTRODUCTION

Prostate cancer is the most common non-skin malignancy among men in the United States with nearly 250,000 new diagnoses each year.[1] Due to the United States Preventive Services Task Force recommendations in 2012, prostate biopsies may be decreasing. Published reports from Canada and the US have noted a nearly 20 percent reduction in prostate biopsies.[2,3] The decrease in diagnostic biopsies may be offset by the increased emphasis on active surveillance for the management of low-grade prostate cancer where repeat prostate biopsy is an integral component, but could also increase cumulative infection risk due to repeated fluoroquinolone exposure for prophylaxis. Transrectal ultrasound (TRUS)-guided prostate needle biopsy (PNB) is the most common method of prostate cancer diagnosis and is the focus of this document. Complications related to prostate biopsy are infrequent, but can range from minor to life-threatening. This

document provides an updated critical review of the literature addressing the incidence, etiology, risk factors, prevention, and treatment of prostate biopsy-related complications.

INDICATIONS AND TECHNIQUES FOR BIOPSY

Available evidence for prostate biopsy indications may be reviewed within the AUA Best Practice Statement on PSA Testing for the Pretreatment Staging and Post-treatment Management of Prostate Cancer,[4] and specifics of the biopsy approach and tissue handling can be obtained in the AUA/Optimal Techniques of Prostate Biopsy and Specimen Handling white paper.[5]

COMPLICATIONS FOLLOWING PROSTATE BIOPSY

I. INFECTION

One of the most common complications from prostate biopsy is infection, including urinary tract infection (UTI), prostatitis, epididymitis, orchitis, bacteremia, and sepsis. Occasionally, these complications are severe enough to lead to hospitalization, prolonged antibiotic therapy, and secondary adverse sequelae. Therefore, understanding the causes and implementing strategies for prevention and prompt treatment are imperative.

Etiology

In the era of fluoroquinolone prophylaxis, the most common cause of infection after transrectal prostate biopsy is fluoroquinolone-resistant *Escherichia coli*.[6,7] Overall resistance to fluoroquinolones is rising, likely due to their global increased use. Bacterial chromosomal mutations and the acquisition of plasmids mediate antibiotic resistance. Mechanisms of resistance include the creation of pores to change cell membrane permeability, efflux pumps, and mutations in DNA gyrase.[8] These mutations occur largely after bacteria are exposed to antimicrobials at or below minimum inhibitory concentration, even when such antimicrobials are

dosed appropriately.[9,10] The use of fluoroquinolones in livestock and veterinary practice may also contribute to resistance.[11] Bacteria causing infection are found in the rectum prior to biopsy and are seeded into the prostate, bladder, and/or bloodstream by the hollow core biopsy needle traversing the rectum into the prostate/bladder.[12] Cultures obtained from the rectum immediately prior to biopsy have demonstrated a fluoroquinolone-resistant colonization rate of 10 to 22 percent.[13,14] There is a four-fold increased risk of infection in men colonized with fluoroquinolone-resistant organisms.[13,14]

Epidemiology

Infectious complications from transrectal prostate biopsy have increased in recent years.[15,16] Reported rates of infectious complications range from 0.1 to 7.0 percent and sepsis rates range from 0.3 to 3.1 percent depending on antibiotic prophylaxis regimens and background antibiotic resistance in various geographic locations.[17-20] The overall risk of hospitalization after prostate biopsy was 1.9 percent in a Canadian study of 75,000 patients undergoing prostate biopsy;[21] over 70 percent of those hospitalizations were related to infection, and the incidence increased four-fold over the 10-year study period. Another follow-up study of over 17,000 Medicare patients from 1991 to 2007 noted a 1.1 percent risk of hospitalization after prostate biopsy.[16] Considering hospitalization after transrectal prostate biopsy has been estimated at $5,800 per event, infection can have a substantial impact on costs of care.[22,23]

Risk Factors

The most common and consistent risk factor for post-prostate biopsy infections is exposure to antimicrobials within six months prior to biopsy[14,24,25], which may promulgate the presence of

resistant organisms. Nearly one in five men is colonized with fluoroquinolone-resistant *E. coli* strains in their fecal flora, which is a significant risk factor for post-biopsy infection.[13,14] The introduction of bacteria is necessary but not sufficient to cause disease, implying that in most patients host defenses clear these organisms before they can cause adverse sequelae. Resistant organisms can be found in hospitals and long-term care facilities. Therefore, hospital employees, physicians, and their family members are at risk for prostate biopsy-related infectious complications.[25,26] Recent international travel to areas where fluoroquinolone resistance is endemic and the use of antimicrobials to prevent traveler's diarrhea also increase risk of post-biopsy infection.[27] One study noted a 2.7-fold relative risk for infection after prostate biopsy among those who had recently returned from abroad.[24] Prior prostate biopsy may be another risk factor for infectious complications, though Loeb et al. did not show increased risk for later biopsy sessions comparing 13,883 men who underwent a single prostate biopsy and 3,640 who had multiple biopsies in the SEER database from 1991 to 2007.[28] Ehdaie et al. performed a retrospective analysis noting a 3.5 percent rate of severe infection (14/591) in men on active surveillance (AS) and that the odds of severe infection increased by 1.3 times for every subsequent biopsy (OR 1.33, 95 percent CI 1.01-1.74, $P = .04$).[29] Whether or not the repeat biopsy session carries a higher risk, the more biopsies one undergoes, the cumulative risk of complications is greater. Finally, a study of nearly 5,000 prostate biopsies did not detect an association between complication rates and the number of biopsy cores,[30] while other studies have shown increased infections with number of cores.[31]

Table 1: Risk Factors for Prostate Biopsy Infection
Medical History
Diabetes
Significant comorbidities (Charlson Score >1)
Immunosuppression (steroids, chemotherapy, HIV)
Urologic History
History of urinary tract infection (UTI) or prostatitis
Previous prostate biopsy infection
Greater cumulative number of biopsies
Exposures to Antibiotic Resistance
Antibiotics in last six months

Recent international travel
    (Endemic resistant locations: India and Southeast Asia)
    (Use of antibiotics to prevent traveler's diarrhea)

Healthcare worker
Colonization with Resistant Bacteria
Colonized with fluoroquinolone-resistant *E. coli* via rectal culture

Preventative Risk Assessment

The first step for prevention is a preoperative assessment of risk factors for resistant bacteria, such as past medical, antibiotic, occupational, and travel histories (Table 1).[24,32,33] Due to the community-acquired colonization of fluoroquinolone-resistant organisms, a clinical history is beneficial but may miss at-risk individuals in the general population. An alternative and more direct way to assess the risk of resistant bacteria is to sample the rectal flora.[34] The utility of pre-biopsy urine cultures to screen for asymptomatic bacteriuria is controversial, and it may be most useful in men with a history of UTI or urinary retention.[35] However, men with lower urinary tract symptoms should be cultured and treated for infection prior to undergoing prostate biopsy. Repeat culture should be performed prior to prostate biopsy.

Selection of Antimicrobial Prophylaxis

Antimicrobial prophylaxis reduces the risk of bacteriuria, bacteremia, and clinical infections after prostate biopsy.[36,37] Fluoroquinolones and first-, second-, and third-generation cephalosporins are recommended for prostate biopsy unless rectal swab culture is performed; in that case, culture-directed antimicrobials can be administered.[38] Gentamicin (aminoglycoside) and ceftriaxone (third-generation cephalosporin) are the most commonly studied and utilized.[39,40] Of note, gentamicin should be dosed according to patient's weight, and the traditional dose of ceftriaxone is 1 g. Both are given intramuscularly at least one hour prior to the TRUS-guided PNB for one dose only. The recommended duration of antimicrobial prophylaxis is 24 hours, and a single dose of antibiotics is sufficient.[41-43] A three-day or longer fluoroquinolone prophylaxis regimen should be avoided as it has shown no benefit to the patient and may promote resistance. Many physicians are now using multiple antibiotics for transrectal prostate biopsy prophylaxis.[44]

Although multiple studies have shown reduction of prostate biopsy infection using additional broad-spectrum antibiotics, this may yield short-term gains with severe long-term consequences and worsening of the overall antibiotic resistance crisis. If one were to add additional antibiotics, we recommend reviewing the local susceptibility profiles (antibiograms), as there are geographic differences in antimicrobial resistance.[45] Unfortunately antibiograms based on hospitalized patients may not represent ambulatory men who present for prostate biopsy. Therefore, alternative approaches are needed to improve patient selection.

One alternative approach is to use rectal swab cultures to assess rectal flora prior to prostate biopsy.[6,15] Approximately 10 to 22 percent of rectal swab cultures are positive for fluoroquinolone-resistant organisms.[46] Infectious complications are rare among patients treated with targeted prophylaxis;[23,47] however, the rate of fluoroquinolone resistance on rectal swabs is higher than the rate of clinical infection, suggesting that other factors mediate the development of infectious complications.[34,48] Rectal cultures are performed by inserting a cotton swab 1 to 2 cm into the anus and spinning the swab 360 degrees at least twice. Visual confirmation of stool on the swab confirms an adequate sample. Some studies have suggested that the culture can obtained from swabbing the gloved finger after digital rectal examination; however, this may reduce the amount of stool obtained and affect the quality of the specimen, though no comparisons have been examined regarding yield. A concern about rectal swab cultures is the need to perform this several days before biopsy for results to guide prophylaxis. A small study found 93 percent agreement between rectal swabs done a median of two weeks prior to and those at the time of biopsy.[49] Concerns exist regarding the necessity, logistics, and cost-effectiveness of performing rectal swab cultures in all patients, but a selected approach for men with known risk factors may have increased benefits (See Table 1 for risk factors).[34] No prospective studies

have evaluated the effectiveness of rectal swab culture-based prophylaxis in preselected at-risk populations.

Currently, there are no guidelines regarding a cut-point in the level of resistance at which fluoroquinolone antibiotics would be deemed ineffective. For example, the Infectious Disease Society of America (IDSA) encourages alternative antibiotic therapy when a particular local antibiotic resistance reaches levels of greater than 20 percent pertaining to women with pyelonephritis.[50] We extrapolate these findings to provide guidance in interpreting the provider's local antibiograms. As such, if a provider finds a rise in infectious complications they should refer to their local antibiograms. If fluoroquinolones are above a 20 percent resistance rate for at least *E. coli*, consider alternative antibiotics that have less local resistance and are within the AUA Best Practice Policy Statement on Urologic Surgery Antimicrobial Prophylaxis. If no appropriate or familiar alternatives are available, one could consider rectal culture with targeted prophylaxis prior to biopsy and/or contacting an infectious disease specialist for an alternative prophylaxis regimen to augment a fluoroquinolone. Alternative antibiotics outside the scope of the AUA Best Practice Policy Statement on Urologic Surgery Antimicrobial Prophylaxis that have been reported in the literature include oral fosfomycin and intramuscular or intravenous amikacin, which seem to have low co-resistance to fluoroquinolones but are relatively untested in clinical trials for prostate biopsy prophylaxis.[51-54]

Rectal Preparation

Rectal preparation prior to prostate biopsy may have several advantages, including emptying the rectal vault and the potential to reduce bacterial load. Visualization of the prostate may be improved without gross stool in the rectal vault, which can be accomplished by enema or a

suppository. As a practical point, a rectal exam performed immediately prior to the prostate biopsy will confirm the rectal vault is empty. If not, the patient could be directed to have a bowel movement prior to proceeding although enemas prior to prostate biopsy remain controversial. A Cochrane Review found that enemas plus antibiotics are associated with less bacteremia but no difference in bacteriuria or fever.[36] Some reports have suggested povidone-iodine rectal preparation decreases the rate of infectious complications,[55-58] while other studies have not.[17,59,60] Advantages of rectal povidone-iodine preparation are low cost, ease of use, and general protection against a range of microorganisms, including fluoroquinolone-resistant *E. coli*. There are limited data on pre-procedural restriction to a clear liquid diet for 24 hours before biopsy.[61]

Procedural Factors to Prevent Infection

Adherence to standard principles of infection control and proper sterilization of equipment are essential. Infectious complications have been linked to contaminated ultrasound gel from a refillable container, placement of tissue samples on non-sterile foam pads, and improper processing of the ultrasound transducer.[62,63] Any outbreak of biopsy-related infections should trigger a prompt evaluation. Further, the US Food and Drug Administration issued a notification with instructions for reprocessing of reusable transducer probes used for TRUS-guided PNB.[64]

One technical modification is disinfection of the biopsy needle with formalin (10 percent) between each sampling,[65] which is inexpensive and easily performed. Although experimental data found no growth of fluoroquinolone-resistant *E. coli* following formalin disinfection, the reduction in clinical infectious complications was not statistically significant.[66] Similarly, washing the needle between biopsies with povidone-iodine did not lead to a significant

reduction.[67] Other options are also under investigation, such as the use of a needle coated with a sustained-release chlorhexidine varnish, which reduces bacterial transmission in an agar prostate model.[68]

Another way to reduce infection is to avoid the rectum altogether by performing prostate biopsy via the perineum. The transperineal approach is associated with generally low rates of infectious complications,[69-71] although it is unclear whether the risk of overall complications is significantly different from transrectal biopsy.[69,72-74] Furthermore, transperineal biopsy is more painful and is typically performed in the operating room with general anesthesia, presenting a different set of logistical issues, potential risks, and cost. While higher rates of perineal hematoma have been described from this approach,[31] studies of transrectal and transperineal PNB found no differences in hematuria or hematospermia between the techniques.[72,74]

Treatment and Response to Biopsy-related Infection

Although most post-procedure infections are limited to febrile cystitis and prostatitis, severe sequelae may occur resulting in bacteremia and sepsis. There is a concern that the subsequent infections may be more severe in nature than previously observed cystitis. Many men require hospitalization and intensive care.

Despite antimicrobial coverage, there still remains a potential for introduction of rectal bacteria into the bloodstream (bacteremia) followed by sepsis. Sepsis is a clinical syndrome characterized by a systemic inflammatory reaction to an infectious process.[75] The symptoms of sepsis are nonspecific, and may include fever, hypothermia, tachypnea, tachycardia, altered mental status,

and hypotension (Table 2). Any patient who presents with a fever following a prostate biopsy should be assessed for the presence of sepsis. Septic shock refers to acute circulatory failure (hypotension) that persists despite adequate fluid resuscitation.

Table 2. Signs and Symptoms of Sepsis.[75]
General
Fever (>38.3°C)
Hypothermia (<36°C)
Tachycardia >90/min
Tachypnea
Hypotension (SBP<90 mmHg)
Altered mental status
Significant edema or positive fluid balance
Oliguria
Ileus
Altered mental status/lethargy
Laboratory
Normal WBC with >10% immature forms
Creatinine increase >0.5 mg/dL
INR >1.5 or aPTT >60 secs
Thrombocytopenia (platelet count <100,000/mm^3)
Hyperglycemia (plasma glucose >120 mg/dL) in the absence of diabetes
Hyperlactatemia (>1 mmol/L)

In a patient series of 1,000 biopsies, 25 men presented to the emergency department with nearly

half (n=12) of post-biopsy complications requiring hospital admission due to urosepsis or febrile

urinary tract infection.[76] In this study, 67 percent of patients had urine cultures positive for *E.

coli* resistant to both ciprofloxacin and co-trimoxazole. Specifically referring to hospitalization

for prostate biopsy infection, a population-based study of over 75,000 men in Ontario, Canada

noted an increased rate of hospital admissions from 1996 (1 percent) to 2005 (4.1 percent). The

infection-related hospitalizations have brought awareness to the rise in prostate biopsy

infections.[21] In a more recent study within the SEER-Medicare database, hospitalization within

30 days after transrectal prostate biopsy was significantly higher than a randomly selected

control group (6.9 vs 2.7 percent) who did not undergo biopsy, due primarily to infectious

complications.[16] Comparable rates of hospital admission were found in a large cohort of men

undergoing transperineal prostate biopsy (1.2 percent), with the majority (56 percent) due to

febrile urinary traction infection.[77] Response to these severe infections includes both prevention

and prompt recognition/treatment.

A recent study of 5,355 patients was conducted at Southern California Kaiser Permanente

utilizing targeted prophylaxis as a prevention strategy. Urologists chose between physician's

judgments for empiric antibiotic selection or rectal culture-based targeted prophylaxis. The rate

of post-biopsy sepsis was not significantly different between the two groups: 0.44 percent

(8/1,802) in the targeted prophylaxis group and 0.56 percent (20/3,553) in the empirical

prophylaxis group (P = .568). However, the empiric group often received more than one

antibiotic; so the targeted prophylaxis group achieved this low rate of sepsis utilizing 25 percent

fewer antibiotics by using only one culture-directed antibiotic.[78] The statewide Michigan

Urological Surgery Improvement Collaborative (MUSIC) was able to reduce post-prostate biopsy infection-related hospitalization by 53 percent via culture directed antibiotics or augmented prophylactic regimens, to rates of 0.56 percent.[79] Cultures were positive for *E. coli* in >90 percent and rates of fluoroquinolone resistance were comparable in both pre- and post-implementation groups (78 percent and 63 percent, respectively). Thus, the increasing prevalence of resistant organisms, primarily *E. coli*, likely accounts for current trends in post-biopsy infectious complications. Patients with *E. coli* bacteremia due to prostate biopsy were more likely to require ICU admission than non-biopsy-related, community-acquired bacteremia and had greater resistance to gentamicin (43 percent), trimethoprim-sulfamethoxazole (60 percent), ciprofloxacin (62 percent), and all three (19 percent).[80] Thus, empiric treatment in this setting may be different from community-onset bacteremia. The specific ST131 clone accounted for >40 percent of post-biopsy isolates and may be a significant emerging pathogen with frequent fluoroquinolone resistance.

The timely application of appropriate antibiotics directed at the causative pathogen is critical in the treatment of patients with bacteremia and sepsis. In addition to fluoroquinolone resistance, organisms producing extended-spectrum-beta-lactamase (ESBL) are of clinical relevance. A retrospective review of nearly 200 patients with ESBL-producing *Enterobacteriaceae* bacteremia found that over half were caused by *E. coli* and that inadequate initial therapy was a significant predictor of mortality.[81] Inadequate initial therapy for febrile illness after prostate biopsy includes the continued use of oral fluoroquinolone alone or with the addition of trimethoprim-sulfamethoxazole.

The management of those with severe infection (e.g., bacteremia, sepsis) after prostate biopsy should consist of aggressive resuscitation and initial broad-spectrum antibiotic coverage (third-generation cephalosporin and aminoglycoside) after urine and blood cultures. Selection of initial antibiotics upon hospitalization must take into account fluoroquinolone-resistant and ESBL-producing *E. coli* (i.e., meropenem in these cases). In addition, prior antibiotic exposure and travel history should be considered. Results from blood and urine cultures and clinical improvement then dictate narrowing the antibiotic regimen to target the causative pathogen. The duration of therapy is typically 7 to 14 days with conversion to an appropriate oral medication, depending on the clinical response.

Reprocessing of Equipment

Prostate biopsy needle guides have long, narrow lumens that are easily contaminated by blood and feces during procedures. Because these lumens contact the biopsy needles that penetrate sterile tissues, manufacturers, the US FDA, and the US Centers for Disease Control and Prevention (CDC) recommend cleaning followed by heat sterilization for all reusable prostate biopsy needle guides. However, due to the lack of comparative effectiveness data between steam sterilization and high-level disinfection, high-level disinfection is an acceptable practice. The manufacturer recommendations for sterilization and high-level disinfection methods for specific devices should be reviewed and followed.[82] In addition, more information has been provided from American Institute of Ultrasound in Medicine official position statement: *Guidelines for Cleaning and Preparing External- and Internal-Use Ultrasound Probes Between Patients*.[83]

While vancomycin-resistant *Enterococc*i (VRE), methicillin-resistant *Staphylococcus aureus*

(MRSA), and *Klebsiella pneumonia* carbapenemase (KPC) are rare, one must by hypervigilant regarding current trends in the community and maintain high sterilization standards. Specific to transrectal biopsy is the survival of the *Pseudomonas*, which has been troublesome in the past. *Pseudomonas* organisms in the internal lumen of the needle guide are completely inactivated when equipment is properly disassembled, cleaned, and high-level disinfected.[84] In 2006, the CDC received a report of *Pseudomonas aeruginosa* infections related to reusable needle guides being improperly cleaned and sterilized, prompting the FDA to issue a public health notification regarding reprocessing of reusable prostate biopsy needle guides.[85] Reusable ultrasound transducer assembly parts should be disassembled for cleaning after each use with a brush properly sized for the lumen of the device being cleaned. All heat-sensitive parts should be cleaned, dried, and placed into high-level liquid disinfectant. Sterile water should be used to rinse the transducer of residual germicide. The use of organic solvents such as isopropyl alcohol can damage transducers and should not be used in cleaning or disinfection. The device should be thoroughly dried before reuse or storage. Single-use needle guides, single-use biopsy needles, and single-use combination biopsy gun/needles should be properly disposed of immediately after the biopsy.

Reports of rare bacteria causing infection sparked investigation into ultrasound gels stored with ultrasound equipment, such as infections with *P. aeruginosa*, *Burkholderia cepacia*, and *Achromobacter xylosoxidans*.[62,86,87] Specific guidelines for refilling and using ultrasound gel bottles are lacking. To prevent cross-infection among multiple patients, the dispenser tip of the bottle should not come in direct contact with patients, staff, the transducer, or the environment. The use of sterile packets of ultrasound gel for prostate biopsy should be considered. Prevention

measures include staff training and competency testing on hand washing as well as safe use and reprocessing of equipment. Infection control rounds/audits should be conducted annually to ensure compliance with reprocessing standards and policies. For specific cleaning/reprocessing instructions see appendix A.[85]

Infection Summary

If a provider is noticing more infection-related complications in transrectal prostate biopsy, we have provided an algorithm to assist in assessment of their site and practices to reduce infection rates (Figure 1). While simply adding more antibiotics will reduce infections in the short term, this accelerates antibiotic resistance in the long term. We urge all providers to practice antibiotic stewardship and use as few antibiotics as possible, while reducing infections.

II. BLEEDING

Bleeding complications, including hematuria, rectal bleeding, and hematospermia (or hemoejaculate), are common negative sequelae of TRUS-guided PNB, but the majority are mild and transient.

Hematuria

Hematuria following TRUS-guided PNB is relatively common with reported rates between 5 to 90 percent.[21,46,74] Although most men experience self-limiting hematuria, reports of gross hematuria and urinary clot retention with need for urethral catheterization and hospital admission can occur in up to 0.4 percent of patients post-biopsy.[76] Nonetheless, hematuria is rarely

problematic for patients.[88] Larger prostate volume as well as increased transition zone size,[89] but not the number of biopsy cores,[90,91] are reproducibly associated with hematuria.

Rectal bleeding

The rectal mucosa receives a rich vascular supply from the inferior and middle rectal arteries, and patients with hemorrhoids demonstrate congestion in the sub-mucosal venous plexus. Collectively, such underlying factors can contribute to rectal bleeding although it is typically minor without need for therapeutic intervention.[92] Rates of rectal bleeding vary between 1.3 and 58.6 percent of biopsies and are impacted by number of biopsy cores and anticoagulation.[46,89-91] One study using a self-reported scale found that 36.8 percent of TRUS-guided PNB patients had blood in the rectum, but only 2.5 percent considered it a moderate or major problem.[88]

Hematospermia (Hemoejaculate)

Hematospermia occurs following TRUS-guided PNB with reported rates ranging from 1.1 to 93 percent.[46,92,93] In the ERSPC trial, hematospermia was observed in approximately half of patients, with associated risk factors being age, prostate volume, and prior transurethral resection of the prostate.[89] Although a minor complication, it can cause anxiety.[88] Unlike other bleeding complications of TRUS-guided PNB, hematospermia can persist for a greater duration. Manoharan and colleagues highlighted an 84 percent rate after one week with gradual decline to 66 percent at two weeks and 32 percent still present at four weeks.[93]

Anticoagulation

Chronic anticoagulation in patients undergoing TRUS-guided PNB remains controversial due to heterogeneity in agents used and indications for prophylaxis. In a study of 3,218 men, hematuria increased 1.36-fold with low-dose aspirin use; however, there were no statistical differences in rectal bleeding or hematospermia.[18] Additionally, a meta-analysis of 3,145 cases in nine studies also noted no increase in bleeding complications when comparing antiplatelet discontinuation vs not ($P = .73$).[94] Therefore, continuation of antiplatelet agents appears to be relatively safe with no significant difference in minor bleeding events. The data regarding warfarin or clopidogrel use at TRUS-guided PNB are too limited to draw definitive conclusions, although most studies recommendation cessation five to seven days prior to elective biopsy.[46,95] Warfarin treatment warrants increased attention due to interactions with commonly used prophylactic antibiotics for TRUS-guided PNB including quinolones, cephalosporins, and macrolide families.[96]

Management of Significant Bleeding

Significant or massive rectal bleeding following TRUS-guided PNB is uncommon but can be potentially life-threatening. In a study of 2,049 patients undergoing TRUS-guided PNB with carefully annotated complications, 6 (0.3 percent) developed rectal bleeding requiring intervention while 1 (0.05 percent) had hematuria necessitating a blood transfusion.[97] Initial management for rectal bleeding includes compression on rectal bleeding points by finger, intrarectal tampon, Foley balloon, ultrasound probe, or anoscope. If these initial maneuvers are unsuccessful the patient should be admitted, and continued conservative treatments that could be implemented include bed rest, fluids, administration of blood products, endoscopic epinephrine injection, use of hemostatic agents, or direct vessel ligation.[98,99] If excessive rectal bleeding is encountered, consultation with general surgery, interventional radiology, and/or gastroenterology

may be necessary. Large-volume hematuria requiring intervention is similarly uncommon, and these rare occurrences can be initially managed with urethral catheter insertion, clot irrigation, and external traction for a compressive effect. Refractory cases may require cystoscopy and coagulation.

III.   URINARY OBSTRUCTION/RETENTION

Urinary retention is an uncommon complication that occurs early after transrectal prostate biopsy and may lead to hospitalization and subsequent intervention for management. The overall rate of hospitalization due to any complication within 30 days after prostate biopsy is 4.8 to 6.9 percent,[16,76,100] and urinary retention requiring intervention occurs at a rate of 0.2 percent to 2.6 percent.[46,59,76,89] Retention may occur due to a combination of factors including mechanical obstruction from procedure-related tissue trauma and dynamic obstruction related to constipation induced by narcotic pain medication or acute prostatitis.[101] The increasing rate of urinary retention with more biopsy cores, specifically in transperineal procedures incorporating >24 cores, supports this theory.[77] Observational studies evaluating longitudinal changes in lower urinary tract symptoms (LUTS) using patient-reported outcomes suggest transient worsening of symptoms, including rates of dysuria ranging from 6 to 25 percent.[102-104]

Pain associated with prostate biopsy can distract from common signs of urinary retention. The most common symptom associated with urinary retention is pain localized to the rectum, suprapubic region, or glans penis.[105] Therefore, post-biopsy instructions should recommend that men void prior to discharge and a low threshold should exist for measuring post-void residual.

Patient characteristics and reported baseline LUTS can predict patients at high risk for urinary retention after prostate biopsy. The risk of urinary retention is increased in individuals with an enlarged prostate gland (>50 g) and severe LUTS determined by the International Prostate Symptom Score (IPSS >19).[88,89] Specifically, an increasing ratio of transition zone to total prostate volume is associated with risk of urinary retention after biopsy.[89,93]

The treatment of acute urinary retention requires immediate bladder catheterization. In most cases, the retention is self-limiting and catheterization is recommended for approximately five to seven days.[96] A Cochrane review of five randomized controlled trials demonstrated a significant benefit of alpha-blockers compared to placebo in contributing to successful voiding after catheter removal.[31] Therefore, initiating an alpha-blocker at the time of catheterization is recommended.

Identifying patients at increased risk of urinary retention can prevent most episodes of acute urinary retention. In a prospective randomized study, men who were administered an alpha-blocker the day before prostate biopsy and continued treatment for seven days experienced improved flow rates and less acute urinary retention than men who underwent prostate biopsy without alpha-blocker treatment.[72]

IV.   ERECTILE DYSFUNCTION

Erectile dysfunction (ED), a significant quality of life concern for men, may be a complication of TRUS-guided PNB.[103] Several hypotheses exist about the cause, including peri-procedural anxiety, pain, apprehension about biopsy results, needle injury to the cavernosal nerves, cancer effects, or local tissue edema from the nerve block and hemorrhage; however, a cause-effect relationship remains unproven and the exact mechanism is still unknown.[103,106,107]
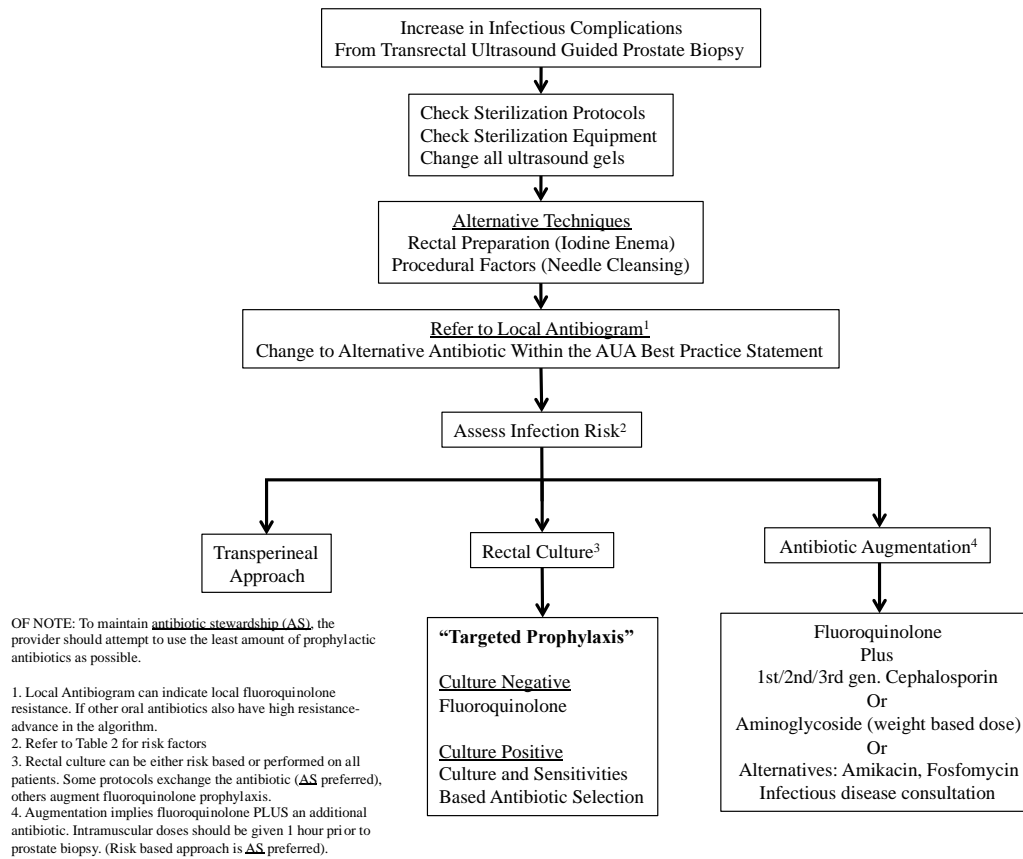
Fifteen percent of previously potent patients reported ED following biopsy using the IIEF-5 at days 7 and 30 in one study,[103] while others have found conflicting results.[107] ED is likely more common early after prostate biopsy but generally improves over time.[108-114] While periprostatic nerve block reduces mean pain scores, it has not been shown to change the overall effect on erections.[112,114] Literature was not available to indicate whether PNB approach (transperineal vs transrectal), biopsy location (apex vs base vs medial vs lateral), or MRI-directed biopsies were associated with an increased or decreased risk of ED. The number of cores taken during a biopsy session or over multiple biopsy sessions does not seem to affect rates of ED.[109] Repeat biopsy sessions (>3) have been associated with decreased SHIM scores in men on AS, but others note that scores are likely to return to baseline by one year.[108,111,113] In one study of 220 men undergoing a TRUS-guided PNB, 61.4 percent reported some degree of pre-biopsy erectile dysfunction.[106] Using a paired t-test, the authors noted the most significant decrease in IIEF-5 scores at one week (18.3 vs 15.4), while IIEF-5 scores at four and twelve weeks after the biopsy (18.4 vs 15.5; 18 vs 16.4) also remained lower but less clinically significant. Men >60 years and those ultimately diagnosed with prostate cancer also reported significantly lower IIEF-5 scores at one, four, and twelve weeks after TRUS-guided PNB, while those under 60 years of age only had the transient one week reduction in IIEF scores. These findings highlight the importance of counseling patients about the possibility of short-term changes in erectile function after TRUS-guided PNB. However, long-term ED is likely unrelated to the biopsy procedure itself, but rather associated with other factors such as advancing age, anxiety, comorbidities, or prostate cancer diagnosis and treatment.

V. NEEDLE-TRACT SEEDING

Tumor seeding along the needle tract appears to be extremely rare. Concerns exist as the number of TRUS-guided PNBs has increased due to widespread PSA testing, advancing patient age, and use of AS protocols. Likewise, the number of cores routinely taken has increased from 6 to 10 to 12 or more, particularly with saturation and combined systematic/targeted approaches. A comprehensive literature review identified 26 papers and a total of 40 patients with needle-tract seeding after transrectal PNB since 1953.[115] Given that several million biopsies have been reported since that time, this complication is exceedingly rare. Transperineal prostate biopsy accounted for 31 (78 percent) cases, while 9 cases were after transrectal biopsy. Most needle-tract seeding cases from these case reports involved poorly differentiated neoplasms, with the majority presenting as a hard nodule. There was no correlation between the type or gauge of needle used and the risk of needle-tract seeding. Tumor seeding did not appear to adversely affect cancer progression or outcomes after treatment. Most AS series of men with low- or very low-risk prostate cancer suggest that repeated TRUS-guided PNBs do not influence the risk of cancer progression or treatment outcomes.[116] Additionally, many men have negative follow up biopsies during AS suggesting against a significant seeding effect of the previous biopsies.

Figure 1: Infection Prevention Strategy

```
┌─────────────────────────────────────────────┐
│     Increase in Infectious Complications      │
│ From Transrectal Ultrasound Guided Prostate   │
│                  Biopsy                        │
└─────────────────────────────────────────────┘
                      │
                      ▼
┌─────────────────────────────────────────────┐
│        Check Sterilization Protocols          │
│        Check Sterilization Equipment          │
│        Change all ultrasound gels             │
└─────────────────────────────────────────────┘
                      │
                      ▼
┌─────────────────────────────────────────────┐
│            Alternative Techniques             │
│       Rectal Preparation (Iodine Enema)       │
│     Procedural Factors (Needle Cleansing)     │
└─────────────────────────────────────────────┘
                      │
                      ▼
┌─────────────────────────────────────────────┐
│        Refer to Local Antibiogram[1]          │
│ Change to Alternative Antibiotic Within the   │
│        AUA Best Practice Statement            │
└─────────────────────────────────────────────┘
                      │
                      ▼
┌─────────────────────────────────────────────┐
│          Assess Infection Risk[2]             │
└─────────────────────────────────────────────┘
```

Transperineal Approach	Rectal Culture[3]	Antibiotic Augmentation[4]
	"Targeted Prophylaxis" Culture Negative Fluoroquinolone Culture Positive Culture and Sensitivities Based Antibiotic Selection	Fluoroquinolone Plus 1st/2nd/3rd gen. Cephalosporin Or Aminoglycoside (weight based dose) Or Alternatives: Amikacin, Fosfomycin Infectious disease consultation

OF NOTE: To maintain antibiotic stewardship (AS), the provider should attempt to use the least amount of prophylactic antibiotics as possible.

1. Local Antibiogram can indicate local fluoroquinolone resistance. If other oral antibiotics also have high resistance-advance in the algorithm.
2. Refer to Table 2 for risk factors
3. Rectal culture can be either risk based or performed on all patients. Some protocols exchange the antibiotic (AS preferred), others augment fluoroquinolone prophylaxis.
4. Augmentation implies fluoroquinolone PLUS an additional antibiotic. Intramuscular doses should be given 1 hour prior to prostate biopsy. (Risk based approach is AS preferred).

REFERENCE LIST

1. Siegel, R. L., Miller, K. D., and Jemal, A. **Cancer statistics, 2015**. *CA Cancer J Clin*. 2015; 65: 5

2. Gaylis, F. D., Choi, J., and Kader, A. K. **Trends in metastatic breast and prostate cancer**. *N Engl J Med*. 2016; 374**:** 594

3. Bhindi, B., Mamdani, M., Kulkarni, G. S., Finelli, A., Hamilton, R. J., Trachtenberg, J. et al. **Impact of the U.S. Preventive Services Task Force recommendations against prostate specific antigen screening on prostate biopsy and cancer detection rates.** *J Urol*. 2015; 193**:** 1519

4. Carroll, P. R., Albertsen, P.C., Greene, K. L., et al. **PSA testing for the pretreatment staging and posttreatment management of prostate cancer: 2013 revision of 2009 Best Practice Statement**. American Urological Association Web site. Published 2013. http://www.auanet.org/education/guidelines/prostate-specific-antigen.cfm. Accessed 12-7-2015

5. Taneja, S. S., Bjurlin, M. A., Carter, B. H., Cookson, M. S., Gomella, L. G., Penson, D. F, Schellhammer, P., Schlossberg, S., and Troyer, D. **AUA/Optimal techniques of prostate biopsy and specimen handling**. American Urological Association Web site. Published 2014. https://www.auanet.org/common/pdf/education/clinical-guidance/Prostate-Biopsy-WhitePaper-Updated2015.pdf. Accessed 12-7-2015

6. Feliciano, J., Teper, E., Ferrandino, M., et al. **The incidence of fluoroquinolone resistant infections after prostate biopsy--are fluoroquinolones still effective prophylaxis?** *J Urol*. 2008; 179: 952

7. Lange, D., Zappavigna, C., Hamidizadeh, R., Goldenberg, S. L., Paterson, R. F., and Chew, B. H. **Bacterial sepsis after prostate biopsy--a new perspective**. *Urology*. 2009; 74: 1200

8. Machuca, J., Briales, A., Labrador, G., et al. **Interplay between plasmid-mediated and chromosomal-mediated fluoroquinolone resistance and bacterial fitness in *Escherichia coli***. *J Antimicrob Chemother*. 2014; 69: 3203

9. Redgrave, L. S., Sutton, S. B., Webber, M. A., and Piddock, L. J. **Fluoroquinolone resistance: mechanisms, impact on bacteria, and role in evolutionary success**. *Trends Microbiol*. 2014; 22**:** 438

10. Ball, P. **Bacterial resistance to fluoroquinolones: lessons to be learned**. *Infection*. 1994; 22 Suppl 2: S140

11. Bearden, D. T. and Danziger, L. H. **Mechanism of action of and resistance to quinolones**. *Pharmacotherapy*. 2001; 21: 224S

12. Liss, M. A., Johnson, J. R., Porter, S. B., et al. **Clinical and microbiological determinants of infection after transrectal prostate biopsy**. *Clin Infect Dis*. 2015; 60: 979

13. Roberts, M. J., Williamson, D. A., Hadway, P., Doi, S. A., Gardiner, R. A., and Paterson, D. L. **Baseline prevalence of antimicrobial resistance and subsequent infection following prostate biopsy using empirical or altered prophylaxis: A bias-adjusted meta-analysis**. *Int J Antimicrob Agents*. 2014; 43: 301

14. Liss, M. A., Taylor, S. A., Batura, D., et al. **Fluoroquinolone resistant rectal colonization predicts risk of infectious complications after transrectal prostate biopsy**. *J Urol*. 2014; 192: 1673

15. Wagenlehner, F. M., van, O. E., Tenke, P., et al. **Infective complications after prostate biopsy: outcome of the Global Prevalence Study of Infections in Urology (GPIU) 2010 and 2011, a prospective multinational multicentre prostate biopsy study**. *Eur Urol*. 2013; 63: 521

16. Loeb, S., Carter, H. B., Berndt, S. I., Ricker, W., and Schaeffer, E. M. **Complications after prostate biopsy: data from SEER-Medicare**. *J Urol*. 2011; 186: 1830

17. Abughosh, Z., Margolick, J., Goldenberg, S. L., et al. **A prospective randomized trial of povidone-iodine prophylactic cleansing of the rectum before transrectal ultrasound guided prostate biopsy**. *J Urol*. 2013; 189: 1326

18. Carmignani, L., Picozzi, S., Bozzini, G., et al. **Transrectal ultrasound-guided prostate biopsies in patients taking aspirin for cardiovascular disease: A meta-analysis**. *Transfus Apher Sci*. 2011; 45: 275

19. Dumford, D., III, Suwantarat, N., Bhasker, V., et al. **Outbreak of fluoroquinolone-resistant *Escherichia coli* infections after transrectal ultrasound-guided biopsy of the prostate**. *Infect Control Hosp Epidemiol*. 2013; 34: 269

20. Mosharafa, A. A., Torky, M. H., El Said, W. M., and Meshref, A. **Rising incidence of acute prostatitis following prostate biopsy: fluoroquinolone resistance and exposure is a significant risk factor**. *Urology*. 2011; 78: 511

21. Nam, R. K., Saskin, R., Lee, Y., et al. **Increasing hospital admission rates for urological complications after transrectal ultrasound guided prostate biopsy**. *J Urol*. 2010; 83: 963

22. Adibi, M., Pearle, M. S., and Lotan, Y. **Cost-effectiveness of standard vs intensive antibiotic regimens for transrectal ultrasonography (TRUS)-guided prostate biopsy prophylaxis**. *BJU Int*. 2012; 110: E86

23. Taylor, A. K., Zembower, T. R., Nadler, R. B., et al. **Targeted antimicrobial prophylaxis using rectal swab cultures in men undergoing transrectal ultrasound guided prostate biopsy is associated with reduced incidence of postoperative infectious complications and cost of care**. *J Urol*. 2012; 187: 1275

24. Patel, U., Dasgupta, P., Amoroso, P., Challacombe, B., Pilcher, J., and Kirby, R. **Infection after transrectal ultrasonography-guided prostate biopsy: increased relative risks after recent international travel or antibiotic use**. *BJU Int*. 2012; 109: 1781

25. Kamdar, C., Mooppan, U. M., Gulmi, F. A., and Kim, H. **Multi-drug-resistant bacteremia after transrectal ultrasound guided prostate biopsies in hospital employees and their relatives**. *Urology*. 2008; 72: 34

26. Carlson, W. H., Bell, D. G., Lawen, J. G., and Rendon, R. A. **Multi-drug resistant *E. coli* urosepsis in physicians following transrectal ultrasound guided prostate biopsies--three cases including one death**. *Can J Urol*; 2010; 17: 5135

27. Williamson, D. A., Freeman, J. T., Roberts, S. A., et al. **Rectal colonization with New Delhi metallo-beta-lactamase-1-producing *Escherichia coli* prior to transrectal ultrasound (TRUS)-guided prostate biopsy**. *J Antimicrob Chemother*. 2013; 68: 2957

28. Loeb, S., Carter, H. B., Berndt, S. I., Ricker, W., Schaeffer, E. M. **Is repeat prostate biopsy associated with a greater risk of hospitalization? Data from SEER-Medicare**. *J Urol*. 2013; 189**:** 867

29. Ehdaie, B., Vertosick, E., Spaliviero, M., Giallo-Uvino, A., Taur, Y., O'Sullivan, M. et al. **The impact of repeat biopsies on infectious complications in men with prostate cancer on active surveillance**. *J Urol*. 2014; 191**:** 660

30. Berger, A. P., Gozzi, C., Steiner, H., et al. **Complication rate of transrectal ultrasound guided prostate biopsy: a comparison among 3 protocols with 6, 10 and 15 cores**. *J Urol*. 2004; 171: 1478

31. Losa, A., Gadda, G. M., Lazzeri, M., Lughezzani, G., Cardone, G., Freschi, M. et al. **Complications and quality of life after template-assisted transperineal prostate biopsy in patients eligible for focal therapy**. *Urology*. 2013; 81**:** 1291

32. Wagenlehner, F. M., Pilatz, A., Waliszewski, P., Weidner, W., and Johansen, T. E. **Reducing infection rates after prostate biopsy**. *Nat Rev Urol*. 2014; 11: 80

33. Roberts, M. J., Parambi, A., Barrett, L., et al. **Multifocal abscesses due to multiresistant** *Escherichia coli* **after transrectal ultrasound-guided prostate biopsy**. *Med J Aust*. 2013; 198: 282

34. Liss, M. A., Chang, A., Santos, R., et al. **Prevalence and significance of fluoroquinolone resistant** *Escherichia coli* **in patients undergoing transrectal ultrasound guided prostate needle biopsy**. *J Urol*. 2011; 185: 1283

35. Bruyere, F., d'Arcier, B. F., Boutin, J. M., and Haillot, O. **Is urine culture routinely necessary before prostate biopsy?** *Prostate Cancer Prostatic Dis*. 2010; 13: 260

36. Zani, E. L., Clark, O. A., and Rodrigues, N. N., Jr. **Antibiotic prophylaxis for transrectal prostate biopsy**. *Cochrane Database Syst Rev*. 2011; CD006576

37. Yang, M., Zhao, X., Wu, Z., Xiao, N., and Lu, C. **Meta-analysis of antibiotic prophylaxis use in transrectal prostatic biopsy**. *Zhong Nan Da Xue Xue Bao Yi Xue Ban*. 2009; 34: 115

38. Wolf, J. S., Bennet, C. J., Dmochowski, R. R., Hollenbeck, B. K., Pearle, M. S., and Schaeffer, A. J. **Best practice statement on urologic surgery antimicrobial prophylaxis**. American Urological Society Web site. Published 2014. https://www.auanet.org/education/guidelines/antimicrobial-prophylaxis.cfm. Accessed 9-26-2015

39. Luong, B., Danforth, T., Visnjevac, O., Suraf, M., Duff, M., and Chevli, K. K. **Reduction in hospital admissions with the addition of prophylactic intramuscular ceftriaxone before transrectal ultrasonography-guided prostate biopsies**. *Urology*. 2015; 85**:** 511

40. Adibi, M., Hornberger, B., Bhat, D., Raj, G., Roehrborn, C. G., Lotan, Y. **Reduction in hospital admission rates due to post-prostate biopsy infections after augmenting standard antibiotic prophylaxis**. *J Urol*. 2013; 189**:** 535

41. Briffaux, R., Coloby, P., Bruyere, F., et al. **One preoperative dose randomized against 3-day antibiotic prophylaxis for transrectal ultrasonography-guided prostate biopsy**. *BJU Int*. 2009; 103: 1069

42. Cam, K., Kayikci, A., Akman, Y., and Erol, A. **Prospective assessment of the efficacy of single dose versus traditional 3-day antimicrobial prophylaxis in 12-core transrectal prostate biopsy**. *Int J Urol*. 2008; 15: 997

43. Lindstedt, S., Lindstrom, U., Ljunggren, E., Wullt, B., and Grabe, M. **Single-dose antibiotic prophylaxis in core prostate biopsy: Impact of timing and identification of risk factors**. *Eur Urol*. 2006; 50: 832

44. Hillelsohn, J. H., Duty, B., Blute, M. L., Jr., et al. **Variability of transrectal ultrasound-guided prostate biopsy prophylactic measures**. Can J Urol. 2012; 19**:** 6573

45. Gopal, R. G. and Batura, D. **Emergency hospital admissions attributable to infective complications of prostate biopsy despite appropriate prophylaxis: need for additional infection prevention strategies?** *Int Urol Nephrol*. 2014; 46: 309

46. Loeb, S., Vellekoop, A., Ahmed, H. U., et al. **Systematic review of complications of prostate biopsy**. *Eur Urol*. 2013; 64: 876

47. Duplessis, C. A., Bavaro, M., Simons, M. P., et al. **Rectal cultures before transrectal ultrasound-guided prostate biopsy reduce post-prostatic biopsy infection rates**. *Urology*. 2012; 79: 556

48. Siriboon, S., Tiengrim, S., Taweemongkongsup, T., Thamlikitkul, V., and Chayakulkeeree, M. **Prevalence of antibiotic resistance in fecal flora of patients undergoing transrectal ultrasound-guided prostate biopsy in Thailand**. *Urol Int*. 2012; 88: 187

49. Liss, M. A., Nakamura, K. K., Meuleners, R., Kolla, S. B., Dash, A., and Peterson, E. M. **Screening rectal culture to identify fluoroquinolone-resistant organisms before transrectal prostate biopsy: do the culture results between office visit and biopsy correlate?** *Urology*. 2013; 82: 67

50. Gupta, K., Hooton, T. M., Naber, K. G., Wullt, B., Colgan, R., Miller, L. G. et al. **International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: A 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases**. *Clin Infect Dis*. 2011; 52**:** e103

51. Lista, F., Redondo, C., Meilan, E., Garcia-Tello, A., Ramon de, F. F., Angulo, J. C. **Efficacy and safety of fosfomycin-trometamol in the prophylaxis for transrectal prostate biopsy. Prospective randomized comparison with ciprofloxacin**. *Actas Urol Esp*. 2014; 38**:** 391

52. Rhodes, N. J., Gardiner, B. J., Neely, M. N., Grayson, M. L., Ellis, A. G., Lawrentschuk, N. et al. **Optimal timing of oral fosfomycin administration for pre-prostate biopsy prophylaxis**. *J Antimicrob Chemother*. 2015; 70**:** 2068

53. Kehinde, E. O., Al-Maghrebi, M., Sheikh, M., Anim, J. T. **Combined ciprofloxacin and amikacin prophylaxis in the prevention of septicemia after transrectal ultrasound guided biopsy of the prostate**. *J Urol*. 2013; 189**:** 911

54. Batura, D., Rao, G. G., Bo, N. P., Charlett, A. **Adding amikacin to fluoroquinolone-based antimicrobial prophylaxis reduces prostate biopsy infection rates**. *BJU Int*. 2011; 107**:** 760

55. Gil-Vernet Sedo, J. M. and Alvarez-Vijande, G. R. **Effect of intrarectal povidone-iodine in the incidence of infectious complications after transrectal prostatic biopsy**. *Arch Esp Urol*. 2012; 65: 463

56. Gyorfi, J. R., Otteni, C., Brown, K., et al. **Peri-procedural povidone-iodine rectal preparation reduces microorganism counts and infectious complications following ultrasound-guided needle biopsy of the prostate.** *World J Urol*. 2014; 32: 905

57. Jeon, S. S., Woo, S. H., Hyun, J. H., Choi, H. Y., and Chai, S. E. **Bisacodyl rectal preparation can decrease infectious complications of transrectal ultrasound-guided prostate biopsy.** *Urology*. 2003; 62: 461

58. Park, D. S., Oh, J. J., Lee, J. H., Jang, W. K., Hong, Y. K., and Hong, S. K. **Simple use of the suppository type povidone-iodine can prevent infectious complications in transrectal ultrasound-guided prostate biopsy**. *Adv Urol*. 2009; 750598

59. Zaytoun, O. M., Anil, T., Moussa, A. S., Jianbo, L., Fareed, K., and Jones, J. S. **Morbidity of prostate biopsy after simplified versus complex preparation protocols: assessment of risk factors**. *Urology*. 2011; 77: 910

60. Carey, J. M. and Korman, H. J. **Transrectal ultrasound guided biopsy of the prostate. Do enemas decrease clinically significant complications?** *J Urol*. 2001; 166: 82

61. Ruddick, F., Sanders, P., Bicknell, S. G., and Crofts, P. **Sepsis rates after ultrasound-guided prostate biopsy using a bowel preparation protocol in a community hospital**. *J Ultrasound Med*. 2011; 30: 213

62. Olshtain-Pops, K., Block, C., Temper, V., et al. **An outbreak of *Achromobacter xylosoxidans* associated with ultrasound gel used during transrectal ultrasound guided prostate biopsy**. *J Urol*. 2011; 185: 144

63. Nielsen, T. K., Pinholt, M., Norgaard, N., and Mikines, K. J. **Inoculation of *Sphingobacterium multivorum* in the prostate by prostate biopsy.** *Scand J Urol*. 2014; 48: 116

64. Sabler, I. M., Lazarovitch, T., Haifler, M., et al. **Sterility of reusable transrectal ultrasound transducer assemblies for prostate biopsy reprocessed according to food and drug administration guidelines--bacteriologic outcomes in a clinical setup**. *Urology*. 2011; 77: 17

65. Singh, I. and Garg, G. **Re: formalin disinfection of biopsy needle minimizes the risk of sepsis following prostate biopsy: M. M. Issa, U. A. Al-Qassab, J. Hall, C. W. M. Ritenour, J. A. Petros and J. W. Sullivan J Urol 2013;190:1769-1775.** *J Urol*. 2014; 191: 1473

66. Issa, M. M., Al-Qassab, U. A., Hall, J., Ritenour, C. W., Petros, J. A., and Sullivan, J. W. **Formalin disinfection of biopsy needle minimizes the risk of sepsis following prostate biopsy**. 2013; *J Urol*. 2013; 190: 1769

67. Koc, G., Un, S., Filiz, D. N., Akbay, K., and Yilmaz, Y. **Does washing the biopsy needle with povidone-iodine have an effect on infection rates after transrectal prostate needle biopsy?** *Urol Int*. 2010; 85: 147

68. Lorber, G., Duvdevani, M., Friedman, M., et al. **Sustained-release antibacterial varnish-coated biopsy needle for reduction of infection rates following prostate biopsy-in vitro model**. *J Endourol*. 2013; 27: 277

69. Grummet, J. P., Weerakoon, M., Huang, S., et al. **Sepsis and 'superbugs': should we favour the transperineal over the transrectal approach for prostate biopsy?** *BJU Int*. 2014; 114: 384

70. Kobayashi, S., Maki, T., Kobayashi, T., et al. **[Significance of the antimicrobial drug used to prevent febrile infection following prostate needle biopsy]**. *Hinyokika Kiyo*. 2014; 60: 227

71. Symons, J. L., Huo, A., Yuen, C. L., et al. **Outcomes of transperineal template-guided prostate biopsy in 409 patients**. *BJU Int*. 2013; 112: 585

72. Hara, R., Jo, Y., Fujii, T., et al. **Optimal approach for prostate cancer detection as initial biopsy: prospective randomized study comparing transperineal versus transrectal systematic 12-core biopsy**. *Urology*. 2008; 71: 191

73. Miller, J., Perumalla, C., and Heap, G. **Complications of transrectal versus transperineal prostate biopsy.** *ANZ J Surg*. 2005; 75: 48

74. Shen, P. F., Zhu, Y. C., Wei, W. R., et al. **The results of transperineal versus transrectal prostate biopsy: a systematic review and meta-analysis**. *Asian J Androl*. 2012; 14: 310

75. Levy, M. M., Fink, M. P., Marshall, J. C., Abraham, E., Angus, D., Cook, D. et al. **2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference**. *Crit Care Med*. 2003; 31**:** 1250

76. Pinkhasov, G. I., Lin, Y. K., Palmerola, R., et al. **Complications following prostate needle biopsy requiring hospital admission or emergency department visits - experience from 1000 consecutive cases**. *BJU Int*. 2012; 110: 369

77. Pepe, P. and Aragona, F. **Morbidity after transperineal prostate biopsy in 3000 patients undergoing 12 vs 18 vs more than 24 needle cores**. *Urology*. 2013; 81: 1142,

78. Liss, M. A., Kim, W., Moskowitz, D., Szabo, R. J. **Comparative effectiveness of targeted vs empirical antibiotic prophylaxis to prevent sepsis from transrectal prostate biopsy: a retrospective analysis**. *J Urol*. 2015; 194**:** 397

79. Womble, P. R., Linsell, S. M., Gao, Y., et al. **A statewide intervention to reduce hospitalizations after prostate biopsy.** *J Urol*. 2015; 194: 403

80. Williamson, D. A., Roberts, S. A., Paterson, D. L., et al. *Escherichia coli* **bloodstream infection after transrectal ultrasound-guided prostate biopsy: implications of fluoroquinolone-resistant sequence type 131 as a major causative pathogen**. *Clin Infect Dis*. 2012; 54: 1406

81. Tumbarello, M., Sanguinetti, M., Montuori, E., **Predictors of mortality in patients with bloodstream infections caused by extended-spectrum-beta-lactamase-producing** *Enterobacteriaceae***: importance of inadequate initial antimicrobial treatment**. *Antimicrob Agents Chemother*. 2007; 51: 1987

82. Centers for Disease Control and Prevention (CDC). *Pseudomonas aeruginosa* **infections associated with transrectal ultrasound-guided prostate biopsies--Georgia, 2005**. *MMWR Morb Mortal Wkly Rep*. 2006; 55: 776

83. American Institute of Ultrasound in Medicine. **Guidelines for cleaning and preparing external- and internal-use ultrasound probes between patients**. American Institute of Ultrasound in Medicine Web site. Updated 4-2-2014. http://www.aium.org/officialstatements/57. Accessed 3-7-2016

84. Rutala, W. A., Gergen, M. F., and Weber, D. J. **Disinfection of a probe used in ultrasound-guided prostate biopsy.** *Infect Control Hosp Epidemiol*. 2007; 28: 916

85. U.S. Food and Drug Administration. **FDA Public Health Notification: Reprocessing of reusable ultrasound transducer assemblies used for biopsy procedures**. U.S. Food and Drug Administration Web site. Updated 6-22-2006. http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/PublicHealthNotifications/ucm062086.htm. Accessed 9-27-2015

86. Gillespie, J. L., Arnold, K. E., Noble-Wang, J., Jensen, B., Arduino, M., Hageman, J. et al. **Outbreak of** *Pseudomonas aeruginosa* **infections after transrectal ultrasound-guided prostate biopsy**. *Urology*. 2007; 69**:** 912

87. Organ, M., Grantmyre, J., Hutchinson, J. *Burkholderia cepacia* **infection of the prostate caused by inoculation of contaminated ultrasound gel during transrectal biopsy of the prostate**. *Can Urol Assoc J*. 2010; 4**:** E58

88. Rosario, D. J., Lane, J. A., Metcalfe, C., et al. **Short term outcomes of prostate biopsy in men tested for cancer by prostate specific antigen: prospective evaluation within ProtecT study**. *BMJ*. 2012; 344: d7894

89. Raaijmakers, R., Kirkels, W. J., Roobol, M. J., Wildhagen, M. F., and Schrder, F. H. **Complication rates and risk factors of 5802 transrectal ultrasound-guided sextant biopsies of the prostate within a population-based screening program**. *Urology*. 2002; 60: 826

90. Ghani, K. R., Dundas, D., and Patel, U. **Bleeding after transrectal ultrasonography-guided prostate biopsy: a study of 7-day morbidity after a six-, eight- and 12-core biopsy protocol**. *BJU Int*. 2004; 94: 1014

91. McCormack, M., Duclos, A., Latour, M., et al. **Effect of needle size on cancer detection, pain, bleeding and infection in TRUS-guided prostate biopsies: A prospective trial**. *Can Urol Assoc J*. 2012; 6: 97

92. Satyanarayana, R. and Parekh, D. **Prevention and treatment of biopsy-related complications**. *Curr Urol Rep*. 2014; 15: 381

93. Manoharan, M., Ayyathurai, R., Nieder, A. M., and Soloway, M. S. **Hemospermia following transrectal ultrasound-guided prostate biopsy: a prospective study**. *Prostate Cancer Prostatic Dis*. 2007; 10: 283

94. Wang, J., Zhang, C., Tan, G., Chen, W., Yang, B., and Tan, D. **Risk of bleeding complications after preoperative antiplatelet withdrawal versus continuing antiplatelet drugs during transurethral resection of the prostate and prostate puncture biopsy: a systematic review and meta-analysis**. *Urol Int*. 2012; 89: 433

95. Baillargeon, J., Holmes, H. M., Lin, Y. L., Raji, M. A., Sharma, G., Kuo, Y. F. **Concurrent use of warfarin and antibiotics and the risk of bleeding in older adults**. *Am J Med*. 2012; 125**:** 183

96. Ramachandran, N., MacKinnon, A., Allen, C., Dundas, D., and Patel, U. **Biopsy of the prostate guided by transrectal ultrasound: relation between warfarin use and incidence of bleeding complications**. *Clin Radiol*. 2005; 60: 1130

97. Efesoy, O., Bozlu, M., Cayan, S., Akbay, E. **Complications of transrectal ultrasound-guided 12-core prostate biopsy: a single center experience with 2049 patients**. *Turk J Urol*. 2013; 39**:** 6

98. Katsinelos, P., Kountouras, J., Dimitriadis, G., et al. **Endoclipping treatment of life-threatening rectal bleeding after prostate biopsy.** *World J Gastroenterol*. 2009; 15: 1130

99. Braun, K. P., May, M., Helke, C., Hoschke, B., and Ernst, H. **Endoscopic therapy of a massive rectal bleeding after prostate biopsy**. *Int Urol Nephrol*. 2007; 39: 1125

100. Ganeswaran, D., Sweeney, C., Yousif, F., Lang, S., Goodman, C., and Nabi, G. **Population-based linkage of health records to detect urological complications and hospitalisation following transrectal ultrasound-guided biopsies in men suspected of prostate cancer.** *World J Urol*. 2014; 32: 309

101. Thomas, K., Chow, K., and Kirby, R. S. **Acute urinary retention: a review of the aetiology and management.** *Prostate Cancer Prostatic Dis*. 2004; 7: 32

102. Ecke, T. H., Gunia, S., Bartel, P., Hallmann, S., Koch, S., and Ruttloff, J. **Complications and risk factors of transrectal ultrasound guided needle biopsies of the prostate evaluated by questionnaire**. *Urol Oncol*. 2008; 26: 474

103.	Zisman, A., Leibovici, D., Kleinmann, J., Cooper, A., Siegel, Y., and Lindner, A. **The impact of prostate biopsy on patient well-being: a prospective study of voiding impairment**. *J Urol*. 2001; 166: 2242

104.	Mkinen, T., Auvinen, A., Hakama, M., Stenman, U. H., and Tammela, T. L. **Acceptability and complications of prostate biopsy in population-based PSA screening versus routine clinical practice: a prospective, controlled study**. *Urology*. 2002; 60: 846

105.	Halliwell, O. T., Lane, C., and Dewbury, K. C. **Transrectal ultrasound-guided biopsy of the prostate: should warfarin be stopped before the procedure? Incidence of bleeding in a further 50 patients.** *Clin Radiol*. 2006; 61: 1068

106.	Murray, K. S., Bailey, J., Zuk, K., Lopez-Corona, E., and Thrasher, J. B. **A prospective study of erectile function after transrectal ultrasonography-guided prostate biopsy**. *BJU Int*. 2015; 116: 190

107.	Chrisofos, M., Papatsoris, A. G., Dellis, A., Varkarakis, I. M., Skolarikos, A., and Deliveliotis, C. **Can prostate biopsies affect erectile function?** *Andrologia*. 2006; 38: 79

108.	Pham, K. N., Johnston, R. B., Jeldres, C., Lewinshtein, D. J., and Porter, C. R. **The impact of multiple prostate needle biopsies on long-term erectile dysfunction.** *Urol Pract*. 2014; 2: 85

109.	Akbal, C., Turker, P., Tavukcu, H. H., Simsek, F., and Turkeri, L. **Erectile function in prostate cancer-free patients who underwent prostate saturation biopsy**. *Eur Urol*. 2008; 53: 540

110.	Tuncel, A., Kirilmaz, U., Nalcacioglu, V., Aslan, Y., Polat, F., and Atan, A. **The impact of transrectal prostate needle biopsy on sexuality in men and their female partners.** *Urology*. 2008; 71: 1128

111.	Hilton, J. F., Blaschko, S. D., Whitson, J. M., Cowan, J. E., and Carroll, P. R. **The impact of serial prostate biopsies on sexual function in men on active surveillance for prostate cancer**. *J Urol*. 2012; 188: 1252

112.	Aktoz, T., Kaplan, M., Turan, U., Memis, D., Atakan, I. H., and Inci, O. **'Multimodal' approach to management of prostate biopsy pain and effects on sexual function: efficacy of levobupivacaine adjuvant to diclofenac sodium - a prospective randomized trial.** *Andrologia*. 2010; 42: 35

113.	Fujita, K., Landis, P., McNeil, B. K., and Pavlovich, C. P. **Serial prostate biopsies are associated with an increased risk of erectile dysfunction in men with prostate cancer on active surveillance**. *J Urol*. 2009; 182: 2664

114.	Klein, T., Palisaar, R. J., Holz, A., Brock, M., Noldus, J., and Hinkel, A. **The impact of prostate biopsy and periprostatic nerve block on erectile and voiding function: a prospective study**. *J Urol*. 2010; 184: 1447

115.	Volanis, D., Neal, D. E., Warren, A. Y., and Gnanapragasam, V. J. **Incidence of needle-tract seeding following prostate biopsy for suspected cancer: a review of the literature.** *BJU Int*. 2015; 115: 698

116.	Kopp, R. P., Stroup, S. P., Schroeck, F. R., et al. **Are repeat prostate biopsies safe? A cohort analysis from the SEARCH database.** *J Urol*. 2012; 187: 2056