Best Practice Statement on Urologic Procedures and Antimicrobial Prophylaxis

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Purpose: The primary rationale for antimicrobial prophylaxis (AP) is to decrease the incidence of surgical site infection (SSI) and other preventable periprocedural infections, with the secondary goal of reducing antibiotic overuse. This Best Practice Statement (BPS) updates the prior American Urological Association (AUA) BPS and creates a comprehensive and user-friendly reference for clinicians caring for adult patients who are undergoing urologic procedures.

Materials and Methods: Recommendations are based on a review of English language peer-reviewed literature from 2006 through October 2018 and were made by consensus by a multidisciplinary panel. The search parameters included timing, re-dosing, and duration of AP across urologic procedures where there was the possibility of SSI. Excluded from the search were the management of infections outside the genitourinary (GU) tract and pediatric procedures.

Results: Single-dose AP is recommended for most urologic cases and antimicrobials should only be used when medically necessary, for the shortest duration possible, and not beyond case completion. Surgeons are the most accurate discerners of an SSI, and should use standard definitions to make better calculations of patient risk. The risk classification developed is dependent on the likelihood of developing SSI, and not the associated consequences of SSI.

Conclusions: The AUA developed a multi-disciplinary BPS to guide clinicians on the proper usage of AP across urologic procedures and wound classifications. It is recommended that the lowest dose of antimicrobials be administered to decrease the risk of infection and to minimize the risk of drug-resistant organisms.

Key Words: antibiotic prophylaxis, urologic surgical procedures, surgical wound infection, postoperative complications

Abbreviations and Acronyms

AP = antimicrobial prophylaxis
ASB = asymptomatic bacteriuria
AUA = American Urological Association
BPS = Best Practice Statement
GU = genitourinary
MDR = multidrug resistant
SSI = surgical site infection
UDS = urodynamic study
UTI = urinary tract infection
WHO = World Health Organization

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THE primary rationale for AP is to decrease the incidence of SSI and other preventable periprocedural infections, with the secondary goal of reducing antibiotic overuse. Tremendous variability in clinical practice persists, with known variation from hospital to hospital and provider to provider. The absence of strong evidence to support such variations, rapidly changing paradigms in periprocedural prophylaxis, and absent standardization practices for common clinical scenarios necessitate further update of the AUA BPS on Urologic Surgery Antimicrobial Prophylaxis (published in 2008, reviewed in 2011 and archived in 2019).[1] While a complex topic, this BPS is intended to be a comprehensive and user-friendly reference for the clinicians and providers caring for patients undergoing urologic procedures (table 1 in supplementary unabridged BPS, https://www.jurology.com).

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PRE- AND PERIPROCEDURAL PROPHYLAXIS

Systemic antimicrobial usage is the primary driver of antimicrobial resistance both in the index patient and the community. Limiting AP to cases when it is medically indicated will reduce the risks of antimicrobial overuse, which include patient-associated adverse events,[2–4] the development of multidrug resistant (MDR) organisms,[5] and the impact of MDR on recovery from common community-acquired infections.[5] Cases that may safely be performed without AP should rely on good sterile techniques and best surgical practices rather than AP, such as bathing the skin with soap or an antiseptic agent prior to surgery; preparing non-mucosal skin surfaces with chlorhexidine and alcohol in the operating room; and removing hair prior to surgery, although data do not show that hair removal decreases the risk of infection.[6] If hair removal is to be performed, clipping hair may be associated with lower infection compared to using razors.[6]

Simple outpatient diagnostic tests, which do not normally break either the mucosal or skin barrier, likely do not require AP in the healthy individual.[7] The least amount of antimicrobials needed to safely decrease the risk of infection to the patient should be used to minimize antimicrobial-related adverse effects and decrease the risk of drug-resistant organisms. The selection of the microbial should be directed towards likely organisms according to surgical site, and is best influenced by how well the agent penetrates the tissues/compartment of interest and is at minimum inhibitory concentrations or above at the time of procedure. Because AP is only effective when these tissue concentrations are maintained throughout the surgery, surgical AP may require re-dosing, weight-adjustment, or renal adjustment to ensure desired antimicrobial tissue levels.

Recent guidelines recommend that in addition to using a single dose of preoperative AP, there should be no postoperative continuation of antimicrobials, without exception for surgical procedure type.[8] There is no high-level evidence to support the use of multiple doses of antimicrobials in the absence of preoperative symptomatic infection. Furthermore, there is moderate-quality evidence from multiple randomized controlled trials that do not show a benefit of prolonging AP beyond the case completion;[9] and the use of prolonged AP (>48 hours post-incision) has been significantly associated with an increased risk of acquiring antibiotic-resistance, while conferring no decrease in SSI.[10] In the absence of high-quality research to suggest a benefit to continued AP beyond wound closure, this BPS recommends that AP be limited to the duration of the procedure itself with no subsequent dosing after wound closure, even in the presence of a drain.

AP should target the likely local organisms; take into account the anatomic site; the patient's biome, infection history, and living environment;[11] the type, duration, and invasiveness of procedure being performed; and institutional and regional variations[12] in antimicrobial sensitivities, all of which may impact prophylaxis and will guide the course of AP accordingly (tables 1 and 2 in supplementary unabridged BPS, https://www.jurology.com). Patient specific factors and local antimicrobial susceptibilities, as reflected in local antibiograms, should also influence choice of agent. Due to emerging MDR, these recommendations will remain in flux; clinicians are urged to consult their local antibiograms and local infectious disease experts where needed.

All antimicrobials have the potential to cause adverse reactions and should be chosen with consideration for the patient's medical risks and allergies. Testing for true allergy is appropriate with penicillin and other β-lactams considering it is likely to be required for current and future care. The use of these classes of drugs in the setting of a true Type I hypersensitivity reaction is contraindicated due to the risks of anaphylaxis and death.[13]

CLASS I/CLEAN PROCEDURES

In Class I/clean procedures (i.e. uninfected incisions with no inflammation and/or without entrance into the gastrointestinal GU tracts) single-dose AP coverage for usual skin flora may not be necessary (tables 3 and 4 in supplementary unabridged BPS, https://www.jurology.com). Recent studies of Class I/clean outpatient urologic procedures[14] including minimally invasive surgery for renal and adrenal tumors,[15] arteriovenous fistula, and graft creation,[16] as well as some Class II/clean contaminated procedures, such as ureteroscopy,[17] have not demonstrated a significant benefit of AP. However, groin, and presumably perineal incisions, may confer an increased risk of SSI, and a single-dose AP may be considered for these cases.[18] For prosthetic device implantation, AP coverage for skin flora, specifically coagulase negative staphylococci and also gram-negative bacilli, including *Pseudomonas* species, has been recommended.[19]

CLASS II/CLEAN-CONTAMINATED PROCEDURES

Single-dose periprocedural AP is currently recommended for patients undergoing specific Class II/clean-contaminated GU procedures, such as those entering into pulmonary, gastrointestinal or GU tract under controlled conditions and without other

contamination (tables 3 and 4 in supplementary unabridged BPS, https://www.jurology.com). For urologists, these include any opening into the GU tract, nephrectomy, cystectomy, endoscopic, and vaginal cases. Single-dose AP is also recommended prior to all procedures for the treatment of benign prostatic hyperplasia, transurethral bladder tumor resections, vaginal procedures (excluding mucosal biopsy), stone intervention for ureteroscopic stone removal, percutaneous nephrolithotomy, and open and laparoscopic/robotic stone surgery. These more invasive procedures entail higher SSI risk.

AP is not recommended for simple outpatient cystoscopy and/or urodynamic studies (UDS) in healthy adults in the absence of infectious signs and symptoms, or those without a concomitant urologic infection. No significant differences in post-cystoscopy urinary tract infections (UTI) were seen with or without AP[20] with moderate evidence allowing the establishment of a baseline rate of UTI of 3% in placebo-controlled cystoscopic trials.

Prophylactic antimicrobials are not indicated prior to UDS for patients without an associated UTI risk. However, a single dose of AP of trimethoprim-sulfamethoxazole is recommended for individuals undergoing UDS who have neurogenic lower urinary tract dysfunction, those who are immunosuppressed (as in the transplant population), those who have known or suspected abnormalities of the urinary tract with recent GU instrumentation, and those who have received recent antimicrobials given that they are at an increased risk for UTI. Alternatives include first- or second-generation cephalosporins, amoxicillin/clavulanate, or an aminoglycoside ± ampicillin. When indicated, a single oral dose given within an hour prior to the procedure, although dependent upon the agent's oral pharmacokinetics, is sufficient and was the route chosen in nearly all reviewed studies.

CLASS III/CONTAMINATED PROCEDURES

Single-dose AP agents are recommended for patients undergoing Class III/contaminated procedures, such as those including infectious stones and the use of large bowel segments, given that the risk reduction of a periprocedural infectious complication is considerable (tables 3 and 4 in supplementary unabridged BPS, https://www.jurology.com). Consistent with the larger body of the literature, one study demonstrated a risk reduction from 39% to 13% with appropriately selected AP.[21] In these contaminated cases, the surrounding tissue is exposed to pathogens routinely. Transrectal prostate biopsy is a high-risk Class III/contaminated procedure and requires antimicrobial prophylaxis.

For surgical procedures including the colorectum, the bacterial flora is extensive, and the predominant organisms are anaerobic. Hence, for patients undergoing colorectal surgical procedures, coverage for both aerobic and anaerobic organisms is required. Anaerobic coverage is critical in SSI reduction; the use of a single-agent first-generation cephalosporin, for example, without additional anaerobic coverage for a colorectal case increases the risk of a SSI from 12 to 39%.[22] Preoperative mechanical bowel preparation and oral antibiotics for colorectal procedures is recommended (based on moderate-quality evidence from 1990 through 2015) by the WHO,[23] consistent with most urologic practices using colorectal segments and associated with reduced complication rates.

CLASS IV PROCEDURES

Class IV wounds are by definition infected. AP guidelines may help choose the most appropriate empiric antimicrobial agent(s) for the most common offending pathogens until cultures inform targeted therapy (tables 3 and 4 in supplementary unabridged BPS, https://www.jurology.com). Wound classification, therefore, is best considered a flexible designation throughout the case. If contamination occurs, then the wound class changes and the AP agent(s) should be reconsidered.

URINE CULTURES

Prior to any urologic procedure, evaluation of a patient's urinary tract symptoms suggestive of a UTI should include a simple dipstick, laboratory performed microscopy, and/or formal culture, with assessed risks requiring higher levels of antimicrobial specificity and sensitivity. While a urine dipstick positive for nitrites may be presumptive evidence of an infection, as high bacterial colony counts will convert urinary nitrate to nitrite, the sensitivity of urinary nitrates is also poor, particularly where there is intense urinary frequency. Urine microscopy is more sensitive. Signs of skin contamination, such as presence of epithelial cells, suggest that a repeat instructed specimen or a catheterized specimen be obtained. Instrumentation in the setting of an infection is associated with an increased risk of post-procedural UTI/SSI, and these risks are further increased by patient and procedural characteristics.

Positive microscopy findings should be confirmed with a culture for antimicrobial sensitivities in the perioperative setting where the risk of an SSI is high and targeted antimicrobial treatment may be required. Urine culture should not be performed without an accompanying urine microscopy due to common sample contamination as well as bacterial

colonization.[24] The results should be used to direct if further testing is warranted and should be obtained prior to the selection of the AP for the procedure, thereby allowing for assessment of the likely infectious organism and its potential virulence.

Urgent and semi-urgent urologic procedures required in the setting of an active UTI should have current urine microscopy available, as well as microbiologic cultures with antimicrobial sensitivities, prior to proceeding if the clinical presentation allows. Antimicrobial usage is not prophylactic in this setting and requires active assessment of the most probable organisms, their sensitivities, and the antimicrobial's ability to penetrate the infected site.

Elective procedures should be deferred in the presence of symptoms consistent with an active infection until an antimicrobial course is complete and associated symptoms have improved. In particular, instrumentation of the GU tract in the setting of an active infection should be delayed, if possible and clinically appropriate, until the results of cultures and sensitivities are available. However, operative delay is often unsafe and places these patients at higher risk for periprocedural infectious complications.

ASYMPTOMATIC BACTERIURIA AND/OR FUNGURIA

Asymptomatic bacteriuria (ASB) and/or funguria may not require AP prior to low-risk urologic surgical procedures in otherwise low-risk patients or in non-urologic cases where entry into the GU system has not occurred. Funguria in asymptomatic females is often the result of contamination and carefully obtained catheterized urines may determine if funguria is indeed present. However, single-dose treatment of ASB is recommended in pregnant females since they are a high-risk population. The identification of ASB, which normally occurs in 3% to 5% of women, has been associated with a 40% risk of pyelonephritis during pregnancy, and has led to treatment of ASB in this cohort.[25] ASB need not be managed any differently prior to intermediate- or higher-risk procedures as single-dose AP, the standard practice prior to GU procedures where a mucosal barrier will be broken, should be administered regardless of the presence of ASB.

CATHETERS

AP may be considered at the time of clinical procedures such as trials of voiding and removal of catheter or drain tubing, stent or nephrostomy tube, especially when other patient and procedural risk factors are present. Placement of a drain is associated with an increased risk of SSI,[26] but should be utilized when surgically appropriate. Drain placement itself may not be directly causative, as the increased risk of an SSI is likely associated with those cases necessitating a drain. Reduction of SSI may occur if drains are brought through a separate stab wound.

Studies suggest that AP at the time of catheter removal has been common urologic practice,[27] and a recent systematic review suggested that patients indeed might benefit from AP at the time of catheter removal[28] as there was a significantly lower prevalence in symptomatic UTIs after AP given at the time of catheter removal.

STONES

While noninvasive procedures such as shock wave lithotripsy do not require antimicrobial prophylaxis if the pre-procedural urine microscopy is negative for infection, AP should be administered using a single dose prior to stone intervention for ureteroscopic stone removal, percutaneous nephrolithotomy, and open and laparoscopic/robotic stone surgery.[29,30] The AP agent chosen should be based on prior urine culture results and/or the local antibiogram.

ANTIFUNGAL PROPHYLAXIS

Antifungal treatment, rather than single-dose prophylaxis, is recommended for patients with symptomatic fungal UTIs at the time of exchange of any permanent drainage tube or stent once fungicidal levels are present. In the absence of neutropenia or other high-risk patient characteristics, nephrostomy exchanges and ureteral stenting procedures alone do not require antifungal prophylaxis for asymptomatic funguria. Antifungal prophylaxis should be given to patients with asymptomatic funguria who are undergoing specific intermediate- and high-risk GU procedures, including resective, enucleative, or ablative outlet procedures; transurethral resection of bladder tumor; ureteroscopy; percutaneous nephrolithotomy; all endoscopic procedures; procedures in which high pressure irrigants are used; when surgical entry into the urinary tract is planned and in neutropenic patients with a urinary tract obstruction, or in those who are undergoing urologic surgery. Patients undergoing treatment of fungal balls (mycetoma) require organism speciation with antifungal sensitivities, antifungal therapy at the time of the procedure, and continued antifungal treatment for an as yet undetermined length of therapy, although the majority opinion is five to seven days.

FUTURE STUDIES

As the risk of AP increases for the patient and his or her community, the benefits for many current AP practices remain understudied in high-quality randomized controlled trials. Many more of these

trials are needed, specifically comparing single-dose AP for Class I skin incisions versus no antibiotics and comparing single-dose AP versus multiple-doses for higher-risk patients and procedures. Similarly, the multiple periprocedural interventions aimed at risk reduction for low- and moderate-risk procedures, including drain or catheter care and subsequent removal, could be compared with those same procedures without AP. Surveillance data to more accurately define the at-risk populations and GU procedures are only possible when surgeons accurately record patient comorbidities, classify the wounds accurately, and report all SSI and bacteremic events to central repositories.

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EDITORIAL COMMENT

This is a well written review of antimicrobial prophylaxis, which is used often in urology, with a minimum number of well-designed studies to support recommendations. However, best practice guidance is well delineated and reasonable. The tenet that prophylaxis should be limited as to

whether to initiate and for how long is appropriately emphasized.

The use of local antibiograms would seem reasonable but hospital-based lab data available to the clinician usually include many nosocomial strains and the data will overstate resistance for outpatient acquired bacteria. Since many urological procedures are performed in an outpatient setting, antimicrobial resistance will not be as problematic and the clinician can frequently use drugs that would not be effective in the inpatient setting.

The Infectious Disease Society of America recently published updated guidelines on ASB and state that ASB should only be treated in pregnancy and before urological procedures that could impact the integrity of the urothelial mucosa.[1] Thus if a patient with ASB is to undergo simple cystoscopy for hematuria evaluation, the ASB does not have to be treated. However, if a bladder tumor is to be resected then the ASB should be treated, not just prophylaxis therapy, before the procedure.

Most patients with indwelling catheters will have ASB after 5 to 7 days. If the urinary tract is functioning well, then catheter removal does not require prophylaxis. If there is impaired urinary tract function that compromises drainage, therapy based on a catheter aspirate culture should be considered.

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