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Guidelines

Japanese guidelines for prevention of perioperative infections in urological field

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Abstract: For urologists, it is very important to master surgical indications and surgical techniques. On the other hand, the knowledge of the prevention of perioperative infections and the improvement of surgical techniques should always be considered. Although the prevention of perioperative infections in each surgical field is a very important issue, the evidence and the number of guidelines are limited. Among them, the preparation of guidelines has progressed, especially in gastrointestinal surgery. The Center for Disease Control and Prevention (CDC) proposed guidelines for the prevention of surgical site infections, which have been used worldwide. In urology, the original guidelines were different from those of general surgery, due to many endourological procedures and urine exposure in the surgical field. The Japanese Society of UTI Cooperative Study Group has thus framed these guidelines supported by The Japanese Urological Association. The guidelines consist of the following nine techniques: open surgeries, laparoscopic surgeries, transurethral resection of bladder tumor, ureterorenoscope and transurethral lithotripsy, transurethral resection of the prostate, prostate biopsy, cystourethroscope, pediatric surgeries in the urological field, and extracorporeal shock wave lithotripsy and febrile neutropenia. These are the first guidelines for the prevention of perioperative infections in the urological field in Japan. Although most of these guidelines were made using reliable evidence, there are parts without enough evidence. Therefore, if new reliable data is reported, it will be necessary for these guidelines to be revised in the future.

Key words: Open surgery, Laparoscopic surgery, TUR, Prostate biopsy, Cystourethroscope, ESWL.

I. General remarks

Urological practice mainly consists of surgical procedures, since the field of urology is a division of surgery. Therefore, it is very important to master surgical indications and surgical techniques. On the other hand, the knowledge of the prevention of perioperative infections and the improvement of surgical techniques should always be considered. Although the prevention of perioperative infections in each surgical field is a very important issue, these evidences are limited and the number of guidelines is limited. Among them, the preparation of guidelines has progressed, especially in gastrointestinal surgery. The Center for Disease Control and Prevention (CDC) proposed guidelines for the prevention of surgical site infections),[1] which have been used worldwide. In urology, the original guidelines were different from those of general surgery, due to many endourological procedures and urine exposure in the surgical field. We have thus framed these guidelines supported by The Japanese Urological Association.

I-I Definition and classification of perioperative infections

A perioperative infection is defined as an infection that occurs within one month after an operation. These infections are divided into two groups: surgical site infections (SSIs) and remote infections (RIs). Since the incidence of perioperative infections and the infection site depends on the specific procedure, surgical site, and the possibility of bacterial contamination, surgeries are classified depending on the possibility of bacterial contamination.

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In general surgery, surgical wounds are classified into four groups: clean (Class I), clean-contaminated (Class II), contaminated (Class III), and dirty and infected (Class IV) (Table 1). Clean operations have uninfected operative wounds without any preoperative infection in the respiratory tract, gastrointestinal tract, or urinary tract. Clean-contaminated operations are defined as operations without any surgical procedures directly to the respiratory tract, gastrointestinal tract or urinary tract, or operations with surgical procedures to those organs which are well controlled. Contaminated operations have open, fresh or accidental wounds. Dirty and infected operations are surgical procedures in highly contaminated sites, such as bacterial infective sites and old traumatic wounds.

However, not all urological surgeries can be classified into these categories because of their peculiarities. Using these categories to classify urological surgeries, radical nephrectomy, open adrenalectomy, and intrascrotal surgeries are categorized as clean operations. Radical prostatectomy, pyeloplasty, and partial cystectomy are categorized as clean-contaminated operations. Ileal bladder should be categorized as a contaminated operation. The removal of a perinephric abscess and repairs for an opened traumatic urinary tract should be categorized as a dirty and infected operation. We do not have a consensus as to how to classify endoscopic surgeries into these categories. Among the laparoscopic urological surgeries, laparoscopic adrenalectomy is thought to be a clean operation; however, laparoscopic radical prostatectomy and laparoscopic pyeloplasty are thought to be clean-contaminated operations. In addition, transurethral surgeries, which are the most popular in the urological field, are also thought to be clean-contaminated operations when the patients have either no urinary tract infections (UTIs) or well-controlled preoperative UTIs. They should, however, be classified as contaminated operations when the preoperative UTIs are not well controlled. Percutaneous nephrolithotripsy (PNL) and transurethral

Table 1 Surgical wound classification[1]

Wound classification		Definition
Class I	Clean	Uninfected operative wound in which no inflammation is encountered and respiratory, alimentary, genital or uninfected urinary tract is not entered.
Class II	Clean-contaminated	Operative wound in which the respiratory, alimentary, genital or urinary tract are entered under controlled conditions and without unusual contamination.
Class III	Contaminated	Open, fresh or accidental wounds.
Class IV	Dirty and Infected	Old traumatic wounds with retained devitalized tissue and those that involve existing clinical infection or perforated viscera.

Table 2 Classification of urological surgeries according to the Center for Disease Control and Prevention (CDC) wound classification[1]

Wound classification		Urological surgeries
Class I	Clean	Radical nephrectomy, Open adrenalectomy, etc.
Class II	Clean-contaminated	Radical prostatectomy, Partial cystectomy, TUR-P, TUR-Bt, PNL, TUL, etc.
Class III	Contaminated	Bowel utilizing urinary diversion, Operations for infectious stone, etc.
Class IV	Dirty and Infected	Open trauma of urinary tract, Operations for infected kidney, etc.

PNL, percutaneous nephrolithotripsy; TUL, transurethral ureterolithotripsy; TUR-Bt, transurethral resection of bladder tumor; TUR-P, transurethral resection of the prostate.

ureterolithotripsy (TUL) for infectious urinary stones are thought to be contaminated operations (Table 2).

The CDC classified SSIs into three groups: superficial incisional SSI, deep incisional SSI, and organ/space SSI. Although it remains controversial as to whether UTIs after transurethral surgeries should be classified in the urological field, we have herein classified them as SSIs.

I-II The CDC guidelines for the prevention of SSIs

Although the CDC guidelines are not included in our guidelines, it is necessary to understand the CDC guidelines because they have served as a reference for creating these guidelines, especially for open urological surgeries.

(1) Risk factors for perioperative infections

Risk factors for perioperative infections are divided into two groups: patient factors and environmental factors in the operation room or elsewhere.

Patient risk factors are advanced age, malnutrition, diabetes, smoking, obesity, infections in non-surgical sites, immunocompromised status, and long preoperative hospital stay. Environmental risk factors are inappropriate skin preparation, preoperative hair removal, prolonged operation time, inappropriate antimicrobial prophylaxis (AMP), poor controlled operating room ventilation system, inadequate sterilization of surgical instruments, foreign body use in operation, inappropriate drain use, and immature surgical techniques.

(2) Preoperative hair removal

Careful attention should be paid to the preoperative hair removal. The CDC recommends that preoperative hair removal should be avoided, but hair should be removed immediately before the operation preferably with electric clippers, if necessary. Preoperative shaving of the surgical site the night before an operation is associated with a significantly higher SSI risk in comparison to the use of depilatory agents or no hair removal. In addition, the earlier the preoperative hair removal, the higher the risk of SSIs

(3) Peculiarity of urological surgeries

The peculiarity of urological surgeries is that urine exposure in the surgical field is unavoidable. Therefore, preoperative UTI is a high risk factor. While preoperative UTIs are easily detectable using urine cultures, intraprostatic bacteria are not easily detected. Therefore, we should keep in mind that bacterial contamination is possible in surgical procedures of the prostate. Another peculiarity of urological surgeries is the indwelt catheter in the urinary tract. The indwelling time of the catheter after urological surgeries is longer than that after other types of surgery. In addition, an intracorporeal stent, a kind of foreign body, is sometimes indwelt. Therefore, the management of these catheters is an important issue. They should be placed aseptically. The indwelling time should be as short as possible and a closed drainage system should be used.

(4) Antimicrobial prophylaxis (AMP)

AMP for the prevention of perioperative infections is routinely performed, however AMP is empiric, as the evidences are limited concerning which antimicrobial agent should be administered, or for how long antimicrobial prophylaxis should be continued. The CDC recommends that AMP be initiated just before surgery and terminated as early as possible. The role of prophylactic antimicrobials is not to sterilize the surgical field, but to reduce the bacterial number so that it does not overwhelm the host's defenses. Therefore, we should not depend only on antimicrobials for the prevention of perioperative infections. The CDC emphasized the appropriate antimicrobial use as follows:

- Antimicrobials should be administered intravenously.
- AMP should be initiated 30 min before the beginning of the operation.
- First-generation cephems (CEPs) are recommended for clean or clean-contaminated operations.

Table 3 Antimicrobial prophylaxis in the perioperative period of open urological surgeries

Wound classification		Operation	Prophylactic antimicrobials	Duration (hours)
Class I	Clean	Operations in inguinal area Nephrectomy Retroperitoneal tumor resection, etc.	First-generation cephems Penicillins	Single-dose 24
Class II	Clean-contaminated	Nephroureterectomy Radical prostatectomy Cystectomy/ureterocutaneoustomy, etc.	First- or second-generation cephems Penicillins/BLI	48–72
Class III	Contaminated	Cystectomy/bowel-utilizing urinary diversion	Second-generation cephems Penicillins/BLI	72–96

BLI, beta-lactamase inhibitor.

- Second-generation CEPs or cephamycins are recommended for operations in the gastrointestinal tract.
- Additional dose should be administered every 2–3 h during surgery.
- Prophylactic antimicrobials are not appropriate treatment for dirty or infected operations.

I-III AMP in the urological field

(1) Open surgeries

AMP must be determined based on the expected contaminated bacteria and the distribution of pathogens in postoperative infections. In addition, it is necessary to choose antimicrobials not for prophylaxis, but for treatment against dirty or infected operations.

(2) Laparoscopic surgeries

Laparoscopic surgeries have been popular in the urological field, and the number of laparoscopic urological surgeries is increasing. In general, the incidence of postoperative infections after laparoscopic surgeries is lower than that after open surgeries, thus indicating that only shot-term prophylactic antimicrobial use is necessary for laparoscopic surgeries. However, their evidence is limited, and the prophylaxis is naturally empiric.

(3) Endoscopic surgeries

Transurethral surgeries, such as transurethral resection of the prostate (TUR-P) and transurethral resection of bladder tumor (TUR-Bt), are thought to be clean-contaminated operations, and it is important to clarify the presence or absence of preoperative bacteriuria. Patients with preoperative bacteriuria should be treated. Postoperative AMP after TUR-P should be longer depending on the individual, because of the possible presence of intraprostatic bacteria.

(4) Treatment of postoperative infections

Postoperative infections are caused by bacteria that are suspected to be resistant to prophylactic antimicrobials. Therefore, other antimicrobials with a different antibacterial spectrum in comparison to the initial prophylactic antimicrobials are naturally chosen. In addition, the antimicrobials chosen for treatment should also depend on the bacterial culture and drug-susceptibility tests. Every patient should be checked for postoperative infections on postoperative day (POD)-3.

I-IV Conclusions

Perioperative infections are prevented not only by AMP, but also by hand-hygiene, environmental care, glove use, and patient status.

This guideline was based on the ranking of scientific evidence of published reports: level A proven by at least one randomized comparative study or meta-analysis, level B proven by comparative study except randomized comparative study, or cohort study; and level C with retrospective study or opinions of specialists. The recommendation degrees of this guideline were determined according to the guidelines for the prevention of hospital infections (by the committee of the Japanese National Medical School affiliated hospitals);[2] rank A recommended strongly, rank B recommended generally, and rank C recommended optionally.

II. Detailed exposition

II-I. Open urological surgeries

(1) Peculiarities related to open urological surgery

In open urological surgery, the urinary tract is opened in many procedures, such as prostatectomy and cystectomy. Urine is exposed to the surgical field in urinary tract-opening surgery. Although the urinary tract is originally sterile, most patients receiving urological surgeries have a high risk of UTIs, because of the presence of underlying diseases of the urinary tract. In addition, the urinary catheter tends to be indwelt for a long time postoperatively in order to keep the surgical sites of the urinary tract at rest. Therefore, it is necessary to keep uropathogenic bacteria as the pathogens of postoperative infections in mind. Perioperative care of urinary diversion using the ileum or colon is similar to that of surgeries of the lower digestive tract.

(2) The guidelines of CDC and the European Association of Urology (EAU)

In the CDC guidelines,[1] the details of effective antimicrobial use for the prevention of SSIs after urinary tract opening surgery or bowel-utilizing operations, which are characteristic in the urological field, were not described. On the other hand, the EAU published a recommendation concerning the prevention of perioperative infections in a portion of the guidelines for genitourinary tract infections[3] (Table 3). Interestingly, they emphasized that antimicrobials shoulder a part of the prevention of perioperative infections, and surgical skills and

Table 4 Incidence of surgical site infections (SSIs) after urological surgeries and antimicrobial prophylaxis in Japan[4]

Institution (investigated period)	Operation	*n*	SSI	Prophylactic antimicrobial used	Duration (days)
Kyoto University (2001–2002)	Clean, small & endoscopic	224	4 (1.8%)	Penicillins first- or second-generation cephems	1
	Clean, large & clean-contaminated	105	8 (7.6%)	Penicillins first- or second-generation cephems	3
	Bowel-utilizing	10	3 (30.0%)	Second- or third-generation cephems	4
Okayama University (1998–2002)	Clean, small	41	0	Penicillins/BLI first-generation cephems	1.10 ± 0.26
	Clean, large	64	1 (1.6%)	Penicillins/BLI first- or second-generation cephems	2.77 ± 1.15
	Clean-contaminated (low grade)	16	0	Penicillins/BLI third-generation cephems	3.06 ± 0.25
	Clean-contaminated (high grade)	70	10 (14.3%)	Penicillins/BLI third-generation cephems	3.11 ± 0.47
	Bowel-utilizing	10	6 (60.0%)	Penicillins/BLI first- or second generation cephems	4.05 ± 1.18

BLI, beta-lactamase inhibitor; SSIs, surgical site infections.

perioperative care were important in the guidelines. AMP is not necessary for patients without risk factors after clean operations or urinary tract-opening operations, and they recommend AMP only for patients with risk factors such as diabetes or immunosuppressed status. The combination of prophylaxis, metronidazole with second-generation CEPs or penicillins (PCs)/beta-lactamase inhibitors (BLI), is recommended for the prevention of perioperative infections after all bowel-utilizing surgeries. Single-dose prophylactic antimicrobials just before surgery are enough; however, additional doses based on the pharmacokinetics of the antimicrobials are necessary when the operation lasts for more than 3 h.

(3) Incidences of perioperative infections in open urological surgeries

Reports concerning perioperative infections in the urological field are limited. Therefore, the data from two institutes involving these guidelines are shown here (Table 4).

The incidence of perioperative infections has been published by the Department of Urology, Kyoto University. They determined prophylactic plans according to the classification of urological surgeries depending on the grade of invasiveness and contamination:[4] 1-day administration of PCs, first- or second-generation CEPs for small clean operations such as intrascrotal operations and laparoscopic surgeries; 3-day administration of PCs, first- or second-generation CEPs for large clean operations or clean-contaminated operations such as nephrectomy and prostatectomy; and 4-day administration of second- or third-generation CEPs for bowel-utilizing operations. The incidences of perioperative infections were 1.8% in small clean operations or laparoscopic surgeries; 7.6% in large clean operations or clean-contaminated operations; and 30% in bowel-utilizing operations. On the other hand, the incidences of perioperative infections with the determination of AMP were also published by the Department of Urology, Okayama University).[5] They used PCs/BLI or first-generation CEPs for 1 or 2 days in clean operations (intrascrotal operation or nephrectomy); for 3 days in clean-contaminated operations (nephroureterectomy or prostatectomy); and for 4 days in contaminated operations (cystectomy with bowel-utilizing operations), driving perioperative care completely. The incidences of SSIs including low-grade infections such as superficial infections in clean operations, clean-contaminated operations and bowel-utilizing operations were less than 2%, around 10%, and around 60%, respectively.

In these studies, the incidences of SSIs did not increase in spite of the decreased consumptions of antimicrobials for prophylaxis, because of the complete perioperative care. These results indicate that the incidences of SSIs can be reasonably reduced by the administration of PCs, first- or second-generation CEPs for 1 or 2 days in clean operations and for 2 or 3 days in clean-contaminated operations. The incidence of SSIs in bowel-utilizing operations was still high, however, and drug-resistant bacteria, such as methicillin-resistant *Staphylococcus aureus* (MRSA), was frequently isolated. Therefore, how to prevent these SSIs in bowel-utilizing operations remains an issue. Matsukawa and coworkers[6] reported that the incidence of SSIs caused by MRSA was not reduced (93.3%) when they prohibited third-generation-CEPs and used only PCs, first- or second-generation CEPs. Yamamoto and coworkers[7] similarly reported that Gram positives were mostly isolated from SSIs, and 58.8% of them were MRSA. The high incidence of SSIs caused by MRSA which has already colonized in Japanese hospitals cannot be resolved by the restriction of prophylactic antimicrobial use, but by long-term continuous measures against hospital infections and perioperative infections.

Table 5 Perioperative care in urological surgeries

1. Preoperative care
   - Shorten preoperative hospital stay
     (Preoperative evaluations should be done before hospital stay as far as possible)
   - Urinalysis and urine culture
     For urinary tract-opening surgeries
     Antimicrobial chemotherapy is necessary when preoperative UTIs are present
   - For preoperative UTIs
     Antimicrobial chemotherapy should be tried for curable preoperative UTIs.
     Antimicrobial chemotherapy should be started a day before operation for incurable preoperative UTIs.
   - Hair removal should be avoided.
     Hair in the limited operating area should be removed immediately before operation with electric clipper, if necessary.
2. Intraoperative care
   - Perioperative administration of antimicrobials
     Initial administration should be done 30 min before the beginning of operation
     Additional administration should be done when the operation lasts for longer than 3 h.
   - Keep aseptic manner.
   - Procedures
     Effective hemostasis
     Irrigation of surgical field
     Eradication of dead space with subcutaneous sutures
3. Postoperative care
   - Wound should be covered with sterile dressing for 48–72 h when the wound is not infected.
   - Early removal of urethral catheter and drain
   - Dressing should be changed with aseptic procedures such as hand-hygiene, use of gloves and sterile materials.
   - The patients with infections caused by drug-resistant bacteria should be visited lastly on rounds.
     The cart for dressing change should not be brought to the bedsides of the patients.
     Minimum required materials should be brought to the bedsides of the patients.

(4) Perioperative care for open urological surgery (Table 5)

Perioperative care is more important than AMP for the prevention of perioperative infections. It is not possible to prevent perioperative infections without appropriate perioperative care, even if AMP is appropriate.

As preoperative care, the preoperative hospital stay should be shortened (BII), above all. For that purpose, a preoperative check-up should be performed before hospitalization, if possible. Urinalysis and urine culture in the preoperative check-up are essential in order to determine the presence of preoperative UTIs before the urinary tract-opening operation. Preoperative UITs should be treated and operations should be performed after the patients are cured from preoperative UTIs (BII). Patients with incurable UTIs, such as catheter-indwelling UTIs and infectious stones, should be treated with antimicrobials from 1 or 2 days before the operation. In principle, hair removal should be avoided (AII), and a minimum amount of hair removal should be done using electric clippers immediately before the operation, if necessary (AII).

As intraoperative care, AMP is initiated 30 min before the beginning of the operation (AI). Additional doses are required when the operation lasts for longer than 3 h. In addition, special attention should be paid to aseptic techniques, effective hemostasis, the irrigation of the surgical field and surgical wound, and the eradication of dead space. A closed drainage system should be used (BII).

As postoperative care, the surgical wound should be covered with a sterile dressing for 48–72 h when high contamination is not present in the wound (BII). The urethral catheter or drain should be removed as early as possible (BII). The dressing should be changed with aseptic procedures such as hand-hygiene or the use of sterile gloves and equipments (BII). Patients with infections caused by drug-resistant bacteria should be visited lastly on rounds in order to carefully prevent cross infection. To be precise, the cart for dressing changes should not be brought to the bedsides of patients. Only the minimum required materials should be used and all of the materials for the dressing change of one patient should be single-use.

(5) AMP for open urological surgery

AMP should be determined by the classification of surgical procedures according to whether or not the urinary tract will be open, and with or without bowel utilization (Table 3). In principle, PCs, first- or second-generation CEPs should be used, however, beta-lactamase producing bacteria infections after urinary tract opening operations and anaerobic bacteria infections after bowel-utilizing operations are considered. AMP should be performed within 3 days (72 h). Single-dose or one-day AMP is recommended for a clean operation; two or three-day AMP is recommended for clean-contaminated operations; however, 4-day AMP should be the maximum for bowel-utilizing operations.

II-II. Laparoscopic urological surgeries

(1) Peculiarities of laparoscopic urological surgery

Recently, laparoscopic surgery has become popular in the urological field as well as in general surgery. Their indications will likely be expanded in the future, because of their minimal invasiveness. In spite of their popularity, a consensus concerning AMP for laparoscopic surgery in the urological field has not yet been unified. The objective of this guideline is not only the prevention of SSIs, but also the prevention of UTIs after surgery treating the urinary tract.

(2) Perioperative care for laparoscopic urological surgeries

Perioperative care for laparoscopic surgeries is basically similar to that for open surgeries. It is also important to keep aseptic manners and wound irrigation. Bowel preparation is the most important care before laparoscopic surgeries. Laparoscopic surgeries with the transperitoneal approach need a wide working space to make them safe and sure after bowel preparation such as mechanical irrigation by Niflec and an indwelling gastric tube. Bowel preparation is also important to avoid bowel injuries by trocar or inappropriate punctures. Preoperative treatment is necessary for patients with preoperative curable UTIs.

(3) Incidence of perioperative infections in laparoscopic urological surgeries

The CDC guidelines,[1] which do not describe AMP for laparoscopic surgery, serve as the reference for these guidelines. Laparoscopic

Table 6 Antimicrobial prophylaxis in perioperative period of laparoscopic urological surgeries

Wound classification		Operation	Prophylactic antimicrobials	Duration (hours)
Class I	Clean	Nephrectomy Reduction of renal cyst Adrenalectomy Removal of intraperitoneal testis High ligation	First- or second-generation cephems	Single-dose (30 min preoperatively) Additional dose (every 3–4 h intraoperatively)
Class II	Clean-contaminated	Partial nephrectomy Pyeloplasty Nephroureterectomy	Second generation cephems Penicillins/BLI	Single-dose (30 min preoperatively) Additional dose (every 3–4 h intraoperatively) Within 72 h

BLI, beta-lactamase inhibitor.

surgery in the urological field can be divided into two groups according to the CDC guidelines; the former is clean operations without opening the urinary tract, and the latter is clean-contaminated operations involving opening the urinary tract. In the EAU guidelines,[3] AMP is not recommended, even if the urinary tract is opened intraoperatively.

In general, laparoscopic surgery is less invasive than open surgeries, however, studies on the invasiveness of laparoscopic surgery are limited. In retrospective studies, the incidences of SSIs in laparoscopic cholecystectomy,[8] laparoscopic appendectomy[9] and laparoscopic hysterectomy[10] were lower than those in open surgery. In addition, the distribution of the pathogens of SSIs in a laparoscopic cholecystectomy was similar to that in an open cholecystectomy; the number of Gram positives was equal to that of Gram negatives.[8]

Reports concerning AMP for laparoscopic surgery in the urological field are also limited. Yamamoto and coworkers[7] and Takeyama and coworkers[11] from Japan reported the SSIs in laparoscopic surgeries in the urological field. In the former report, the incidence of SSIs in laparoscopic surgeries was 1.4% after the one-day administration of first- or second-generation CEPs, or PCs/BLI for prophylaxis. In the latter report, the incidence of SSIs in laparoscopic surgery in the urological field was 2.9% after the one-day administration of CEPs or PCs. Fahlenkamp and coworkers[12] from Germany also reported that the incidence of SSIs in laparoscopic surgeries in the urological field was 0.8%.

From these reports, AMP may be useful in laparoscopic surgery as well as in open surgery. The prophylactic effects of first- or second generation CEPs, or PCs are expected. As for administration time and timing, a preoperative single-dose is recommended, because laparoscopic surgery is less invasive than open surgery, however, additional doses are necessary when the operation lasts for longer than 3 h, and AMP should be continued within 72 h postoperatively after urinary tract-opening surgery such as nephroureterectomy for pelvic tumor or ureter tumor, and pyeloplasty, depending on the individual case.

(4) Wound classification of laparoscopic urological surgery

In laparoscopic surgeries in the urological field, nephrectomy, the plication of renal cyst, adrenalectomy, orchiectomy for intraperitoneal testis, and high ligation of the testicular vein are classified as clean operations; Partial nephrectomy, pyeloplasty, and nephroureterectomy are classified as clean-contaminated operations.

(5) AMP for laparoscopic urological surgery (Table 6)

The recommended AMP is similar to that for open surgery. Namely, first- or second-generation CEPs for clean operations and PCs/BLI or second-generation CEPs for clean-contaminated operations are recommended. Drug concentration in the blood and tissue should be at the maximum when the surgical field is mostly contaminated; therefore prophylactic antimicrobials should be administered when trocar is inserted in a clean operation, and 30 min before the urinary tract is opened in clean-contaminated operations. Additional doses are necessary when the operation lasts for longer than 3 h. Among the clean-contaminated operations, the effectiveness of AMP after bowel-utilizing operations has not been ruled out. Therefore, AMP should be performed within 72 h postoperatively, and another antimicrobial as treatment should be started when the patient shows signs of infection.

II-III. Transurethral resection of bladder tumor (TUR-Bt)

(1) Peculiarities of TUR-Bt

In TUR-Bt, endoscopic manipulations and a postoperative indwelling catheter are essential. Therefore, AMP for the prevention of postoperative infections is necessary, because postoperative UTIs frequently occur, and some of them progress to febrile UTIs. Although past studies on the usefulness of AMP after TUR-P are numerous, those focusing on after TUR-Bt are limited. The operating time of TUR-Bt and the postoperative indwelling time of the urethral catheter after TUR-Bt is shorter than those in TUR-P; therefore, TUR-Bt is less invasive than TUR-P. From the view of these findings, AMP for TUR-Bt is determined to be less or shorter than that for TUR-P in these guidelines.

(2) Perioperative infections in TUR-Bt[13–20]

The incidences of postoperative UTIs in TUR-Bt are ranged from 10 to 40%.[21,22] In a report,[23] bacterial adhesion to the bladder tumor caused postoperative UTIs, even if the preoperative urine was sterile, and the incidence of UTIs after TUR-Bt was higher than that after TUR-P. Therefore, AMP is recommended to prevent UTIs after TUR-Bt.[19,20,24–28] Most strains isolated from UTIs after TUR-Bt were Gram negatives.[22,25,27] However, the distribution of streptococci from postoperative UTIs in female patients was reported to be high.[29] Prophylactic

antimicrobials should be chosen to target these bacteria. The recommended antimicrobials to prevent UTIs after TUR-Bt are injective CEPs and oral fluoroquinolones (FQLs).[16–20,22,28,30–35] Attention to fluoroquinolone-resistant *Escherichia coli* should be paid, however, because its prevalence has been reported.[36] In Western countries, the dosages of antimicrobials are higher than that in Japan. For example, 500 mg of levofloxacin (LVFX) is orally administered in Western countries.[22] Although these high dosages may be appropriate for AMP based on their pharmacokinetics, further studies will be needed to elucidate whether these high dosages are suitable for Japanese patients. In most studies[15,17–20,24–30,32] AMP was included as a single-dose 30 min to 2 h preoperatively, and 1-day perioperatively. On the other hand, 3-day AMP has been recommended in some studies.[16,26] No past studies on the comparison between 1-day and 3-day administration are available. Furthermore, the catheter-indwelling time was not unified in all of the past studies.

(3) Japanese circumstances of AMP for TUR-Bt

The following results were obtained from a questionnaire survey concerning the prevention of postoperative infection in TUR-Bt.

1 AMP was performed in all hospitals.
2 Injective antimicrobials were used in most hospitals. First- and second-generation CEPs occupied 2/3 of all prophylactic antimicrobials in all patients with or without complications.
3 AMP was initiated 30–60 min before the beginning of the operation in most hospitals.
4 AMP was continued for 1–3 days postoperatively in most hospitals. Injective antimicrobials were changed to oral antimicrobials in 37% of all hospitals when the patients had no complications, and 42% of all hospitals when the patients had any complications. The oral antimicrobials mostly used were FQLs for a week.
5 Urethral catheter was removed within 3 days postoperatively in most hospitals.

(4) Perioperative care in TUR-Bt

The objective of these guidelines is to prevent postoperative febrile genitourinary tract infections (acute pyelonephritis, acute epidydimitis, and acute prostatitis) and bacteremia; therefore, these guidelines do not indicate the patients with preoperative UTIs (AI). Antimicrobial chemotherapy is necessary to eradicate bacteria in the urinary tract when preoperative UTIs are present.

Pyuria and bacteriuria are not always parameters to diagnose UTIs just after manipulations of the urinary tract, or with an indwelt urethral catheter (AI). Urethral catheter indwelt should be removed as soon as possible in order to prevent UTIs (AII).

The following observations and tests should be done immediately, when febrile UTIs or bacteremia are suspected postoperatively (AII).

1 Vital signs: body temperature, blood pressure, and pulse rate
2 Physical findings: tenderness of costovertebral angle (CVA), scrotal swelling, scrotal pain, perineal pain or discomfort, manipulation of the intrascrotal organs, and digital rectal examination
3 Blood tests: peripheral leukocyte count, leukocyte segment, C-reactive protein (CRP) value, and confirmation of multiorgan failure and disseminated intravascular coagulation (DIC) in serious patients
4 The isolation and quantification of pathogens from the urine and its drug-sensitivity test: It takes several days to get results, so microscopic observation of the Gram-stained urine sediment is useful for the selection of antimicrobials. The quantification of serum endotoxin is recommended in severe patients, because endotoxin-removal therapy is sometimes necessary.
5 CT and Ultrasound are auxiliary for diagnosis. The information concerning the spread of inflammation is obtained from these findings.

In principle, antimicrobial chemotherapy against postoperative febrile UTIs is with injective antimicrobials. Empiric therapy is performed until the results of urine culture and its drug susceptibility are obtained. For the treatment of postoperative UTIs, other antimicrobials with higher antimicrobial activities than prophylactic antimicrobials or the other group of antimicrobials should be used. Carbapenems are one of the options, keeping in mind that UTIs can easily progress to urosepsis in patients with complications. Empiric antimicrobials should be changed when they are not effective according to the results of urine culture and drug susceptibility.

(5) AMP for TUR-Bt (Table 7)

PCs, first- or second-generation CEPs, or aminoglycosides (AGs) are recommended for AMP. AMP should be initiated 30 min before the beginning of the operation. AMP should be concluded within 72 h postoperatively. Single-dose or 1-day prophylaxis can be considered; however, longer-term prophylaxis within 72 h should be done for the patients with lower urinary obstruction, diabetes, immunocompromised status, or a residual tumor.

II-IV. Ureterorenoscope and transurethral lithotripsy (TUL)

(1) Peculiarities of ureterorenoscopic procedures

Most objective patients have obstruction in the upper urinary tract, such as a stone, tumor, or stricture in the ureter. Postoperative UTIs easily occur and sometimes develop into febrile UTIs, when these obstructions are present or the procedure is invasive. Therefore, AMP is necessary during these procedures. Ureterorenoscopic observation of the upper urinary tract sometimes takes a long time, resulting in invasiveness. The operation time and the operative invasiveness depend on the individual. Operative invasiveness also depends on the kind of ureterorenoscope (rigid or flexible, size, etc.). For these reasons, it is difficult to unify AMP. Therefore, routine AMP is recommended in these guidelines based on Japanese circumstances.

(2) Perioperative infections in ureterorenoscopic procedures

Studies on AMP for ureterorenoscope or TUL were also limited,[37] because operative invasiveness is different individually, as mentioned above.

The incidence of perioperative infections ranged from 3.9 to 10%,[38,39] depending on operative invasiveness, in other words, the difficulty of the procedure.[40] The benefit of AMP is not clear; no benefit,[13,21,41] benefit,[26,42] and benefit only for patients with risk[39,43] were reported. A study[44] on the usefulness of a single-dose (500 mg) of levofloxacin (LVFX) elucidated that the incidences of postoperative infections in the LVFX prophylaxis group and the no prophylaxis group were 1.8% and 12.5%, respectively, indicating a significant reduction of the incidence of postoperative infections with LVFX. The authors of this study also described that AMP was necessary because unexpected complications such as ureteral perforation by surgical manipulations sometimes happened. Another study[45] on the comparison of the

Table 7 Antimicrobial prophylaxis in perioperative period of endourological surgeries

Operation	Prophylactic antimicrobials	Duration (hours)	Risk factors
TUR-Bt	Penicillins	Single-dose	Lower urinary tract obstruction
	First- or second-generation cephems	24–72 h†	Diabetes
	Aminoglycosides		Immunocompromised status
			Residual tumor
Ureterorenoscope	Penicillins	Single-dose§	Lower urinary tract obstruction
TUL	First- or second-generation cephems	24–72 h†	Diabetes
	Fluoroquinolones‡		Immunocompromised status
			Residual stones or tumors
TUR-P	Penicillins	Within 72 h	
	First- or second-generation cephems		
	Aminoglycosides		

†Longer duration within 72 h of antimicrobial prophylaxis is recommended for the patients with risk factors. ‡High dose of fluoroquinolones is recommended as much as possible. §No prophylaxis can be possible for the patients without risk factor.
TUL, transurethral ureterolithotripsy; TUR-BT, transurethral resection of bladder tumor; TUR-P, transurethral resection of the prostate.

prophylactic effect between a single-dose (500 mg) of ciprofloxacin and a single-dose (1 g) of cefazolin (CEZ) elucidated that the incidence of postoperative infections in the CPFX and CEZ groups were 8.1% and 10.0%, respectively. On the other hand, the other study[18] on the comparison between a single-dose (400 mg) of lomefloxacin and a single-dose (1 g) of cefotaxime showed no postoperative infection in both groups.

In other guidelines, no prophylaxis[32] or prophylaxis only for the prevention of endocarditis[33] were recommended. The EAU guidelines[35] explained in detail that postoperative infections were frequently caused by *Enterobacteriae*, *Staphylococci* and *Enterococci*; therefore, AMP with FQLs, PCs/BLI, or second-generation CEPs as first line is recommended for high risk patients. Attention should be paid to quinolone-resistant *E. coli* when FQLs are selected.

(3) Japanese circumstances of AMP for ureterorenoscopic procedures

The following results were obtained from a questionnaire survey concerning AMP in ureterorenoscopic procedures.

1 AMP for ureterorenoscope and TUL was performed in 97.1% and 99.2% of all hospitals, respectively.

2 Injective antimicrobials for prophylaxis in ureterorenoscope and TUL were used in 93.4% and 98.4% of all hospitals, respectively. Among these injective antimicrobials, PCs, first- or second-generation CEPs were used in around 2/3 of all hospitals.

3 AMP was initiated 30–60 min before the beginning of these procedures in most hospitals. For ureterorenoscope, 1-day AMP was in 40.6% and 29.0% and 2- or 3-day AMP was in 58.7% and 64.5% in all hospitals for patients with and without complications, respectively. For TUL, 1-day AMP was in 23.4% and 19.8% and 2- or 3-day AMP was in 75.8% and 78.5% in all hospitals for patients with and without complications, respectively. Most AMPs were completed within 3 days.

(4) Perioperative care in ureterorenoscopic procedures

The recommendation for perioperative care in ureterorenoscope and TUL is the same as that in TUR-Bt (see II-II-4).

(5) AMP for ureterorenoscopic procedures (Table 7)

FQLs, PCs with or without BLI, first- or second-generation CEPs are recommended for AMP. The dosage of FQLs is recommended to be as high as possible, considering their characteristics. AMP should be initiated 30 min before the beginning of the operation. AMP should be concluded within 72 h postoperatively. Single-dose, 1-day AMP or no AMP can be considered; however, longer-term AMP within 72 h should be done for patients with a lower urinary obstruction, diabetes, immunocompromised status, or a residual stone or tumor.

II-V. Transurethral resection of prostate (TUR-P)

(1) Perioperative infections in TUR-P

Postoperative UTIs and bacteremia were the typical complications of TUR-P, so effective AMP is necessary. Many studies on the necessity of AMP for TUR-P have been reported.[3,13,14,46–89] Among them, many randomized comparative studies and meta-analysis[88,89] were included. The incidence of postoperative bacteriuria and bacteremia, which are more severe than UTIs, are approximately 26% and 4.4%, respectively. AMP is essential because it reduces these incidences. The problems are the antimicrobial chosen, and its administration time.

1 AMP is recommended for patients without preoperative bacteriuria (AI)

2 Urinary bacteria should be eradicated by the therapeutic antimicrobials which are expected to be effective against the pathogens, when patients have preoperative bacteriuria (AII).

Table 8 Antimicrobial prophylaxis for prostate needle biopsy

	Recommended prescription	Alternative prescription
Low risk group	High dose of oral fluoroquinolones Started just before biopsy for a day†	Cephems or penicillins/BLI intravenously started‡ Just before biopsy 3 times for a day
High risk group§	High dose of oral fluoroquinolones Started just before biopsy for a day plus Standard dose of oral fluoroquinolones for 2–4 days, thereafter	Cephems or penicillins/BLI intravenously started Just before biopsy 3 times for a day plus Standard dose of oral fluoroquinolones for 2–4 days, thereafter

†LVFX 200 mg orally, 3 times; 0.5–2 h before biopsy, 2 and 8 h after biopsy. ‡PIPC/TAZ 2.5 g intravenously, 3 times; 0.5 h before biopsy, 4 and 12 h after biopsy. However, maximum dose of TAZ/PIPC approved by Japanese government to date (2007) is twice daily. §High risk group; prostate volume ≥75 mL, diabetes, steroids administered, highly obstructed lower urinary tract (IPSS ≥20 pts, Qmax ≤12 mL/s, or residual urine ≥100 mL). BLI, beta-lactamase inhibitor; LVFX, levofloxacin; TAZ/PIPC, tazobactam/piperacillin.

(2) AMP for TUR-P (Table 7)

1 Broad-spectrum PCs, first- or second-generation CEPs are administered 30 min before the beginning of the operation. Single- or multiple-dose within 72 h is recommended (BIII). The prophylactic effect of multiple-dose of CEPs for 24–72 h is more effective than that of single-dose (BI).

2 AGs are alternatives for the patients with drug-allergy against beta-lactams (BIII).

(3) A remarks column

The strong effectiveness of FQLs and third-generation CEPs for prophylaxis against perioperative infections in TUR-P has been proven. However, these agents should not be the first choice in order to prevent the emergence of a FQL- or third-generation CEP-resistant strain, and should be considered to be used only for severe postoperative infections, such as bacteremia. This recommendation of AMP was consistent with a questionnaire survey in Japan concerning AMP for TUR-P, resulting in 89% of all prophylactic antimicrobials being PCs, first- or second-generation CEPs (BIII). AMP should be terminated within 72 h postoperatively, whether the urethral catheter is present or not (BI), because there was no significant difference in the prophylactic effectiveness between short-term AMP within 3 days and long-term AMP longer than 3 days from the results of the meta-analysis. However, AMP is necessary each time, only when the urethral catheter is irrigated, exchanged or removed because of clot obstruction (BIII).

II-VI. Needle biopsy of prostate

(1) Introduction

A needle biopsy of the prostate is essential in order to diagnose prostate cancer; therefore, this procedure is used worldwide. It is performed under transrectal ultrasound with a transrectal approach in 80% and a transperineal approach in 20% of patients. Among them, antimicrobial prophylaxis is essential for a needle biopsy of prostate with a transrectal approach, because infections frequently occur after it (AII).

(2) Transrectal approach

Preparation. The necessity of bowel preparation is controversial,[90] although it has been reported to be necessary in a past study.[91] In these guidelines, bowel preparation is not necessary, according to Japanese circumstance (CII). The rectum is disinfected with 10% povidone-iodine before the procedure (BIII). Thirty milliliters of mixed solution with 2% lidocaine-jelly and 10% povidone-iodine as a lubricant can be alternatively used, when the ultrasound probe is inserted into the rectum (BIII).

AMP (Table 8*).* Prophylactic antimicrobials should be administered before the procedure, according to many reports.[92,93] Among the antimicrobials, FQLs are reported to be effective.[92,94] The UTI cooperative study group compared the prophylactic effect to prevent infections after a needle biopsy of the prostate between 200 mg of LVFX three times a day and 100 mg of LVFX three times for three days. There was no significant difference in the infection rate between the two groups; there were two cases with febrile infection in each group.[95] These results indicate that high-dose short-term administration of FQLs is suitable for prophylaxis (AII).

Example of prescription. For low risk group:

1 Oral administration of 200 mg of LVFX three times; 0.5–2 h before biopsy, 2 and 8 h after biopsy (AII).
There are 3 reasons for this recommendation. The first reason is that the oral administration of 500 mg of LVFX 0.5–1 h before biopsy is recommended in the US guidelines from 2002. Secondly, the prospective study described above can support this recommendation. Finally, 200 mg of LVFX three times daily is the standard dosage in Japan.

2 Intravenous administration of 2.5 g of tazobactam (TAZ)/piperacillin (PIPC) for three times; 0.5 h before biopsy, 4 and 12 h after biopsy (BII).
PIPC has broad spectrum and stability against beta-lactamases, so PIPC alone can also be recommended for prophylaxis. However, penicillinase-highly producing strains or broad-spectrum beta-lactamase producing strains are increasing. In addition, a few cases with severe infections after PIPC prophylaxis were reported.[96] PIPC, which has been the standard agent for prophylaxis, has been changed to TAZ/PIPC in these guidelines.

For high risk group:[92]

The high risk group includes patients with a large prostate (≥75 mL), diabetes, systemic steroid use, high grade obstruction of the lower urinary tract (IPSS ≥20, Qmax ≤12 mL/s, or residual urine ≥100 mL), and immunocompromised status.

1 Oral administration of 200 mg of LVFX three times followed by oral administration of 100 mg of LVFX three times for 2–4 days;

Table 9 Antimicrobial prophylaxis for cystoscope

	Antimicrobials	Beginning of administration	Duration
Low risk group	Not essential	Prophylaxis should be started before cystoscope	Single-dose if necessary
High risk group	Fluoroquinolones Aminoglycosides Penicillins First-generation cephems		• Single-dose in principle • Within 72 h when long-term administration is necessary

0.5–2 h before biopsy, 2 and 8 h after biopsy on day-1, and three times daily for 2–4 days thereafter (AII).

2 The intravenous administration of 2.5 g of TAZ/PIPC three times; 0.5 h before biopsy, 4 and 12 h after biopsy on day-1, and standard dosage of FQL for 2–4 days thereafter (BII). However, the maximum dose of TAZ/PIPC approved by the Japanese government to date (2007) is twice daily.

(3) Transperineal approach

Bowel preparation. Bowel preparation is not necessary; however, disinfection of the perineum with povidone-iodine is necessary (AIII).

AMP. AMP for a needle biopsy with the transperineal approach is controversial; both beneficial[97,98] and non-beneficial[99] effects have been reported. To date, a single-high dose of FQLs is recommended (AIII).

(4) Follow-up after biopsy

Bacteremia and acute bacterial prostatitis, which are unavoidable, occur in 1–2% of cases after biopsy. Therefore, attention should be paid to these occurrences after biopsy. Informed consent concerning these complications is essential from the patients. Minute observation of body temperature and urination for the early detection of these infections is necessary in all patients (AIII).

(5) Treatment for infections after biopsy

The most noteworthy strain is FQL-resistant *Escherichia coli*. Second- or third-generation CEPs or carbapenems are effective to this strain.[100] Another important strain is multiresistant *Pseudomonas aeruginosa* (MDRP). Some cases with sepsis caused by anaerobes have also been reported. Antimicrobial chemotherapy and general care including anti-shock therapy and anti-DIC therapy should be immediately started for febrile patients, after performing bacterial culture tests for blood and urine samples (AIII).

II-VII. Cystourethroscopy

(1) Introduction

Cystourethroscopy, which is a typical instrumentation of the urinary tract, creates UTIs or bacteremia in 2–21%.[101–104] Among patients with bacteriuria before cystourethroscopy, bacteremia occurs at a high rate.[101,105] Considering the importance of bacteremia after cystourethroscopy, antimicrobial chemotherapy before cystourethroscopy to eradicate urinary bacteria in the patients with bacteriuria.[103,106,107] On the other hand, necessity of AMP is determined depending on the presence or absence of risk factor in each patient without suspecting UTIs before cystourethroscopy. AMP for cystourethroscopy is not recommended for low-risk patients in the advisory statement[108] or EAU guidelines.[3] The opposite opinion, however, in which AMP for cystourethroscopy is necessary is still present[109] to date; therefore, the usefulness of AMP for cystourethroscopy has not yet been completely ruled out. Under Japanese circumstances, AMP is performed in 75% of all hospitals, and oral antimicrobials are used after cystourethroscopy in 69% of all hospitals. Prophylactic antimicrobials should be administered before cystourethroscopy, in principle.

(2) Risk factors

Risk factors for infections after cystourethroscopy are the presence of a urethral catheter or ureteral stent, intermittent self catheterization, urinary retention, and recent history of UTIs. A risk factor which causes complications after bacteremia is the placement of an artificial joint within 2 years.

(3) AMP for cystourethroscopy (Table 9)

1 In the absence of findings of bacteriuria or UTIs before cystourethroscopy AMP is recommended for patients with risk factors (AI). AMP is not essential for patients without risk factors. However, the usefulness of antimicrobials is not denied (BI).
2 In the presence of findings of bacteriuria or UTIs before cystourethroscopy: eradication of urinary bacteria should be tried with antimicrobials that are expected to be effective (AIII). Antimicrobials should be continuously administered after cystourethroscopy, even when urinary bacteria are eradicated before cystourethroscopy, because recent UTIs are a risk factor (AII).
3 FQLs such as LVFX (BII) and NFLX (BII) should be administered orally 1 h before cystourethroscopy (BII).
4 Single-dose AGs, such as gentamicin (BI) and isepacin (BII), should be administered intramuscularly before cystourethroscopy.
5 PCs, first- or second-generation CEPs should be administered when FQLs or AGs cannot be administered.
6 Single-dose AMP is recommended for patients without risk factor, however, multiple-dose AMP within 72 h is considered for patients with risk factors (CIII).

II-VIII. Pediatric urological surgery

(1) Peculiarities of pediatric urological surgery

Many types of pediatric urological surgery require plastic techniques. In addition, various procedures are performed for each disorder. The stent used and the duration of the indwelling stent in urinary

tract-opening operations are different in each institute. From these reasons, it is difficult to standardize prophylactic antimicrobial use in pediatric urological surgery. Therefore, there are no guidelines from any society of pediatric urology, or pediatric surgery in Western countries. We tried to establish the guideline for pediatric urology according to the questionnaire survey from the executive members of the Japanese Society of Pediatric Urology. These guidelines are also based on those established for adults.[110,111]

(2) Japanese circumstances regarding the use of AMP in pediatric urological surgery

A questionnaire survey was performed to clarify the reality of antimicrobial use in pediatric urology. There are 25 participate objective institutes, including pediatric urology specialized hospitals and experienced university hospitals. Among them, 19 institutes answered. From these results, most pediatric urologists administered prophylactic antimicrobials empirically, because neither guideline, nor large scaled clinical studies were present. In addition, the selected procedures and types of catheter indwelt were different in each institute. Therefore, it was too difficult to determine the guidelines. Objective disorders and procedures, for which most pediatric urologists had consensus were optical urethrotomy for the posterior urethral valve, urethroplasty for hypospadias, circumcision or dorsal incision for phimosis, orchiopexy for undiscerning testis or torsion of the testis, hydrocelectomy, and high legation of the testicular vein. For these operations, AMP was determined according to that for adults. On the other hand, long-term AMP with low-dose oral CEP was performed during urinary catheter was indwelt after pyeloplasty, ureteroplasty for megaureter, and antireflux surgeries in half of the institutes, because these plastic surgeries failed, when SSI occurred. Therefore, further studies are necessary to clarify its indications.

(3) Matters that require attention in antimicrobial use for children or neonates

When beta-lactam is administered to neonates, the peak value is lower and the half-life is longer than those in adults, because of the low plasma protein concentration, the large amount of extracellular fluid, dysfunction of the liver enzymes, and insufficient renal function. The dosage of antimicrobials is determined by body weight for children; however, administration times should be reduced without changing the dosage for neonates (AI).[112–115] Safety is another important point for the choice of antimicrobials. FQLs are not the first choice because they sometimes cause joint disorders in children. Table 10 shows all antimicrobials and the optimal dosage and administration methods for children or neonates.[114–118]

(4) Perioperative care in pediatric urological surgeries

Pediatric patients should be checked to see if they have febrile infections before they stay in the hospital (AI). The operation should be delayed when the patient has a general infection, which will get worse postoperatively, because most operations are planed operations. Preoperative antimicrobials should be administered when the patient has a UTI and the procedure will be urinary tract-opening. The operation should be performed after the patient is cured from preoperative UTIs (BII). When the preoperative UTIs are not curable such as catheter-associated UTIs, antimicrobials should be administered from one to two days before operation.[119]

Although antimicrobial use during the operation is determined according to the criteria establish for adults (AI),[119,120] the timing should be somewhat delayed for neonates (AI).[112–114]

Regarding postoperative care, urethral catheters, cystostomies, ureteral catheters, or nephrostomies should be removed as early as possible (BII).[119] Long-term administration of antimicrobials for patients with long-term indwelling of catheters should be avoided (CIII).[121]

(5) AMP for pediatric urological surgeries (Table 11)

1 Operations without opening the urinary tract include orchiopexy for undescended testis and torsion of the testis, ligation of the testicular vein, hydrocelectomy, circumcision or dorsal incision for phimosis.[122,123] These operations are classified as clean operations (class I) according to the CDC guidelines from 1999.[1] First- or second-generation CEPs are administered twice for 1 day; 30 min before the operation and in the evening. Alternatively, oral CEPs can be administered for 5 days, perioperatively.[114,116]

2 Endosurgery such as a urethral incision for posterior urethral valve: urinary bacteria should be eradicated preoperatively when patients have preoperative UTIs. PCs, first- or second-generation CEPs are administered from 30 min before the operation, and every 12 h within 72 h postoperatively.

3 Cystourethroscopy is often performed for patients with anomalies of the genitourinary tract which are possible risk factors. Therefore, AMP is necessary (AI). Urinary bacteria before cystourethroscopy should be eradicated before cystourethroscopy. Single-dose of PCs, first- or second-generation CEPs are intravenously administered before performing cystourethroscopy. Alternatively, single-dose of AGs is intramuscularly administered.[124] FQLs are not recommended from the reasons described above.[114–117]

4 Operations for opening the urinary tract include urethroplasty for hypospadias, pyeloplasty, ureteroplasty for megaureter, and reimplantation of the ureters for vesico-ureteral reflux.[125,126] These operations are classified as clean-contaminated operations (class II) according to the CDC guidelines.[1] Urinary bacteria should be eradicated by antimicrobials, preoperatively. PCs, first- or second-generation CEPs are administered from 30 min before the operation, and every 12 h within 72 h postoperatively. For plastic surgery of the urinary tract, oral administration of CEPs is recommended for 7 days as an alternative option (CIII).

5 Laparoscopic surgery is indicated in a nephrectomy for atrophic kidney, pyeloplasty for ureteropelvic obstruction; however, it is rare in pediatric urologic surgery. The former is classified as a clean surgery and the later is a clean-contaminated operations (class II) according to the CDC guidelines. AMP is the same as 1 and 4.

II-IX. Extracorporeal shock wave lithotripsy (ESWL)

(1) Peculiarity of ESWL

ESWL is now a common procedure for upper urinary tract calculi, breaking the calculi without making a wound. However, the shock wave creates minor injuries in the urinary tract and sometimes causes urinary obstruction due to stone fragments. Ureteral stents are sometimes inserted before ESWL to prevent urinary obstruction. In addition to infectious stones, such as magnesium, ammonium phosphate and carbonate apatite are also risk factors for perioperative infections of ESWL. These environments thus create an immunocompromised status in the urinary tract.

Table 10 Optimal dosages of injective antimicrobials

Category	Antimicrobial	Symbol	Optimal dosage (mg/kg/day)	Times daily	Administration root		
					iM	iV	DiV
Penicillin	piperacillin	PIPC	50~125	2~4		○	○
	Aspoxicillin	ASPC	40~80	2~4		○	○
	Ampicillin/cloxacillin	ABPC/MPIPC	50~100	3~4	○		
Cephem	Cefazolin	CEZ	20~50	2~3	○	○	○
	Cefotiam	CTM	40~80	3~4		○	○
	Cefmetazole	CMZ	25~100	2~4		○	○
	Cefotetan	CTT	40~60	2~3		○	○
	Cefminox	CMNX	60~80	3~4		○	○
	Cefbuperazone	CBPZ	40~80	2~4		○	○
	Cefsulodin	CFS	60~100	3~4		○	○
	Cefotaxime	CTX	50~100	3~4		○	○
	Cefoperazone	CPZ	25~100	2~4		○	○
	Cefmenoxime	CMX	40~80	3~4		○	○
	Ceftriaxone	CTRX	20~60	2		○	○
	Ceftazidime	CAZ	40~100	2~4		○	○
	Cefodizime	CDZM	60~80	3~4		○	○
	Cefpirome	CPR	60~80	3~4		○	○
	Cefozopran	CZOP	40~80	3~4		○	○
Oxacephem	Latamoxef	LMOX	40~80	2~4		○	○
	Flomoxef	FMOX	60~80	2~4		○	○
Monobactam	Aztreonam	AZT	40~80	2~4		○	○
Carbapenem	Imipenem/cilastatin	IPM/CS	40~80	2~4		○	○
	Panipenem/betamipron	PAPM/BP	30~60	3		○	○
	Meropenem	MEPM	30~60	3		○	○
BLI compounded	Sulbactam/cefoperazone	SBT/CPZ	40~80	2~4		○	○
beta-lactam	Sulbactam/ampicillin	SBT/ABPC	60~150	3~4		○	○
	Tazobactam/piperacillin	TAZ/PIPC	60~150	3~4		○	○
Aminoglycoside	Kanamycin	KM	30~50	1~2	○		
	Gentamicin	GM	0.8~2.4	2~3	○		
	Tobramycin	TOB	3	2~3	○		○
	Dibekacin	DKB	1~2	1~2	○		
	Amikacin	AMK	4~8	1~2	○		○
	Bekanamycin	AKM	10~20	2	○		
	Ribostamycin	RSM	20~40	1~2	○		
	Arbekacin	ABK	4~6	2		○	
Lincomycin	Lincomycin	LCM	20~45	2~3	○		
	Clindamycin	CLDM	15~25	3~4			○
Others	Fosfomycin	FOM	100~200	2~4		○	○
	Vancomycin	VCM	40	2~4			○
	Teicoplanin	TEIC	6~10	2			○

DiV, for drip infusion; iM, intramuscularly; iV, intravenously.

(2) Incidence of perioperative infections in ESWL[127–139]

The incidences of asymptomatic bacteriuria and symptomatic UTIs after ESWL without preoperative bacteriuria were approximately 10% (ranging from 0 to 24%) and 3% (ranging from 0 to 10%), resp ectively. In addition, the incidence of bacteremia was 0–7.7%, most of which were suspected skin contamination. Based on such evidence, the possibility of clinically significant infections such as symptomatic UTIs or bacteremia is low without AMP.

On the other hand, bacteriuria, symptomatic UTIs and bacteremia occurred in 16–21%, 7.9 to 11%, and 0%, respectively, when preoperative bacteriuria was present. Therefore, the incidences of bacteriuria and symptomatic UTIs in the presence of preoperative bacteriuria were higher than those in the absence of bacteriuria; however, the incidence of bacteremia with or without preoperative bacteriuria was not substantially different.

Five placebo-controlled prospective randomized studies on AMP for ESWL were reported.[127–131] In each study, the antimicrobial used, dosage, duration of administration, and evaluation time were different; however, no antimicrobial reduced the incidence of postoperative infections in all studies. These results indicate that AMP is not necessary when preoperative bacteriuria is absent. A study on AMP for

Table 11 Antimicrobial prophylaxis in perioperative period of pediatric urological surgeries

Classification of operation	Operation	Antimicrobials
Operations without opening urinary tract	Orchiopexy for undescended testis	First- or second-generation cephems
	Orchiopexy for torsion	
	Ligation for varicocele	
	Hydrocelectomy	
	Circumcision or dorsal incision	Oral cephems
Endourological surgeries	Incision of posterior urethral valve	First- or second-generation cephems
		Penicillins
Endoscopic examination	Cystoscope	First- or second-generation cephems
		Penicillins
		Aminoglycosides
Operations with opening urinary tract	Pyeloplasty	First- or second-generation cephems
	Urethroplasty for hypospadias	Penicillins
	Operations for megaureter	
	Antireflux surgeries	
Laparoscopic surgeries	Nephrectomy	First- or second-generation cephems
	Pyeloplasty	First- or second-generation cephems
		Penicillins

Table 12 Antimicrobial prophylaxis for ESWL

1	In the absence of preoperative UTIs
	• Antimicrobial prophylaxis is not necessary. (AI)
2	In the presence of preoperative UTIs
	• Antimicrobial which has antimicrobial activity against isolated strains according to the susceptibility test is administered, preoperatively. (BIII)
3	For High risk group
	• Preoperative antimicrobial prophylaxis is recommended. (BIII)
	• High risk group includes the patients with known infection stones, such as magnesium ammonium and phosphate mixed with carbonate apatite, and the past history of symptomatic UTIs or bacteremia after ESWL.

ESWL, extracorporeal shock wave lithotripsy; UTIs, urinary tract infections.

postoperative bacteremia in ESWL showed drug-resistant strain caused bacteremia when antimicrobials were administered, thus indicating that antimicrobials do not prevent bacteremia.[140]

(3) AMP for ESWL (Table 12)

AMP is not necessary for patients without preoperative bacteriuria (AI), because of the low incidence of postoperative symptomatic UTIs or bacteremia. However, AMP should be necessary for patients with preoperative bacteriuria, known infectious stones, a past history of symptomatic UTIs or bacteremia after ESWL, and ureteral stent indwelt just before ESWL (BIII). The appropriate antimicrobial agent should be determined according to the preoperative urine culture.

(4) Diagnostic points of symptomatic UTIs and bacteremia after ESWL

When symptomatic UTIs and bacteremia are suspected, the patient should be evaluated. Diagnostic points are as follows.

1 Vital signs such as body temperature, blood pressure, and heart rate
2 Urine and blood cultures
3 Leukocyte count, CRP, and other biochemical factors to evaluate renal and liver functions
4 Kidneys, Ureter, Bladder (KUB) to evaluate the location and size of stone fragments, and ultrasound (US) to evaluate hydronephrosis

(5) Treatment for symptomatic UTIs and bacteremia after ESWL

Therapeutic antimicrobials should be administered intravenously. Empirically, second-generation CEPs or pazufloxacin (injective FQLs) are recommended as a first line treatment, and carbapenems should be a second line treatment. Antimicrobials should be changed to an appropriate one, when an empiric antimicrobial agent is inappropriate according to the culture results.

Urinary obstruction should be removed by either a nephrostomy or ureteral stent immediately when hydronephrosis is present and empiric antimicrobial therapy is not effective.

II-X. Febrile neutropenia in chemotherapy

(1) Background

Lethal infections can easily occur in patients with neutropenia in antitumor chemotherapy. In general, it is very difficult to detect the pathogen from patients with febrile neutropenia by various microbial cultures. The detection rate of pathogens is reported to be 5–40%.[141,142] Febrile neutropenia is suspected to be an infection because antibacterial or antifungal agents can resolve approximately 80% of fever of unknown origins.[142–145] In recent international trends, febrile neutropenia is thought to be an infection, and it should be immediately treated with empiric therapy. Bodey reported that the cure rates of 410 patients with pseudomonal infections were approximately 73%, 46%, and 20% when empiric therapy was started on the first day of fever, 1–2 days later, 3 days or later, respectively.[146]

Among the many guidelines established worldwide, the guidelines of Infectious Diseases Society of America (IDSA) have been famous

since they were first published in 1990.[147] It was revised in 1997[148] and 2002.[149] In the early IDSA guidelines, oral agents such as trimethoprim-sulfamethoxazole (ST) or FQLs are recommended for prophylaxis because these agents were reported to reduce the incidence of febrile neutropenia. Later, it was elucidated that FQLs and antifungal agents were not useful for prophylaxis, and these prophylactic antimicrobials were not strongly recommended from the view of appearance of drug-resistant strains in many prospective randomized studies.[150–152]

Further studies including cycling or rotation therapy for the appearance-reduction of drug-resistant strains are needed to conclude this issue of AMP in febrile neutropenia. Cycling therapy is defined as a therapy which regularly changes the first choice of antimicrobial in each unit of the hospital for patients with infections caused by unknown pathogen. Various cycling therapies have been reported with different cycling periods and different antimicrobials. In most of them, FQLs, AGs, carbapenems and CEPs were rotated every 3–6 months, resulting in the prevention of drug-resistant strains.[153] On the other hand, negative results of cycling therapy have also been reported,[154–157] and the cost-effectiveness of cycling therapy is another problem, because used broad-spectrum antimicrobials are expensive. Therefore, further studies are also needed to elucidate the true usefulness of cycling therapy.

In all guidelines for the prevention of infections, the importance of rapid detection of pathogen and immediate empiric therapy in febrile neutropenia is emphasized. In the last IDSA guidelines (2002), the oral administration of FQLs for the low-risk group and the intravenous administration of cefepime, ceftazidime, or carbapenems with or without AGs or vancomycin for the high-risk group were recommended.[149]

In Japan, 'The recommendations concerning antimicrobial use for the patients with febrile neutropenia based on evidence'[142] is present.

(2) Guidelines of antimicrobial use for febrile neutropenia

Definition of febrile neutropenia. Febrile neutropenia is defined as when the neutrophil count is less than 100/μl and the axillary temperature is higher than 38.0°C.

Evaluation of risk based on the presence of complications. According to the IDSA guidelines (2002),[149] the high risk group is defined as when the neutrophil count is less than 100/μl, the maximum axillary temperature is above 39.0°C, the duration of neutropenia is longer than 7 days, abnormal findings in the chest X-ray, liver or renal dysfunction, intravenous catheter related infections, illness with symptoms, disorientation, abdominal pain, dehydration, hypotension, chronic obstructive pulmonary diseases, diabetes, history of fungal infections, and age older than 60 years.

(3) Evaluation of febrile neutropenia

When the patient is diagnosed with febrile neutropenia, careful history taking and physical examination to find the infection site, and various microbial cultures to detect the pathogen are necessary.

1 Physical examination to find the infection site includes the oral cavity, eyes, ears, nose, pharynx, skin, perineum, anus, chest, abdomen, insertion site of intravenous catheter, presence or absence of diarrhea.
2 Monitoring by blood and biochemical tests includes complete blood count (CBC) with leukocyte segments, CRP, liver and renal function.
3 Imaging diagnosis includes chest and abdominal X-ray or computed tomography (CT), and abdominal US.
4 Detection of pathogen and drug-susceptibility test: Blood culture should be performed more than twice, from more than two different sites. Multiple cultures increase the possibility of detection of the pathogen, and make it easier to exclude contamination. Cultivations of urine, nasal swab, sputum, stool, when abdominal symptoms are present, are necessary.
5 Cerebrospinal fluid (CSF) test for meningitis and skin biopsy for skin infections caused by staphylococci and fungi are considered.

(4) Initial antimicrobial chemotherapy

Oral FQLs are mainly administered for febrile neutropenia in low risk group (BII; Fig. 1).

Monotherapy or combination therapy of antimicrobials which are intravenously administered are recommended for the high risk group. (AI) Drug selection should be based on the antibiogram against isolates in each hospital. The standard choice of antimicrobials for the high risk group is as follows.

1 Monotherapy: fourth-generation CEPs such as cefepime or carbapenems are the first choice. (AI) The other fourth-generation CEPs, ceftazidime and PIPC/TAZ can be used, when they have good antibiogram against the isolates from the hospital.[150] (BII)
2 Combination therapy with AGs: AGs are added to the antimicrobial, which is mentioned in 'monotherapy', intramuscularly once a day. Although AGs do not have any antimicrobial activity against a part of Gram positives, the incidence of superinfection is reduced by combination therapy. (BII) Attention should be paid to nephrotoxicity of AGs.
3 Combination therapy with anti-MRSA agent: Vancomycin or teicoplanin is considered to be added to the antimicrobial, which is mentioned in 'monotherapy', for severe infections with body temperature above 40°C, carriers with multidrug-resistant strains, and patients with Gram positives isolated from the blood. (BII) This combination should be started immediately without waiting for the results of the bacterial culture. However, the administration of vancomycin or teicoplanin should be immediately stopped when Gram negatives are isolated.
4 The effectiveness of immunoglobulin agents for febrile neutropenia is unclear. Therefore, it should be used within the permission level of the Japanese health insurance system. (CIII)

(5) Evaluation of empiric therapy

Clinical efficacy is evaluated 3–5 days after the beginning of empiric therapy. Antimicrobial is changed to a more appropriate agent, if necessary, according to the results of the drug susceptibility test of the isolated strain. (AI)

1 When empiric therapy is successful with an improvement of the general condition, blood tests including leukocyte count and CRP value, the empiric therapy should be continued for around a week. When the neutrophil count is still less than 1000/μl at the time of improvement of the general condition, antimicrobial therapy should be continued for several days until the general condition is improved. (BII)
2 When the patient is still febrile 3–5 days after the beginning of empiric therapy, the next therapy should be chosen from the

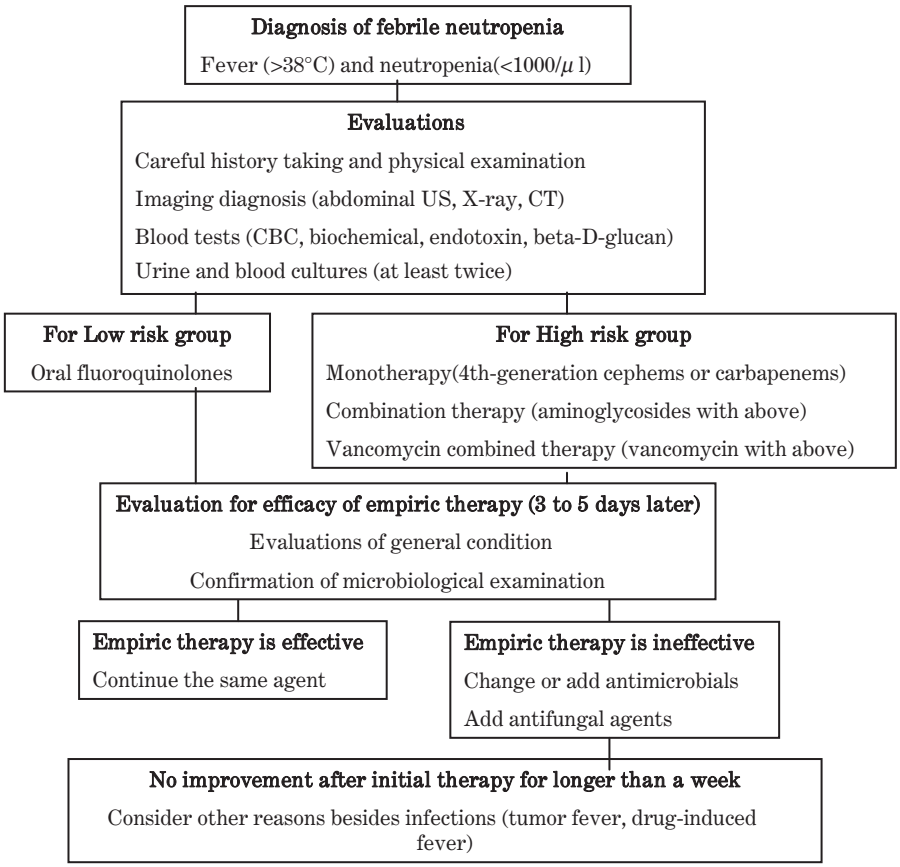

Fig. 1 Flow chart for febrile neutropenia.

following three options. In addition, careful history taking and physical examination are necessary, again (see 2–3).

i The empiric antimicrobial, which is known to be effective to the pathogen isolated, is continued, when the general condition of the patient is well-balanced. (AI)

ii Antimicrobial empirically used is changed to another categorized antimicrobial (from fourth-generation-CEPs to carbapenems, for example), or another antimicrobial is added (for example, vancomycin). (BII)

iii The addition of antifungal agents, such as amphotericin B is considered with or without the change of empiric antimicrobials, especially when the neutrophil count is less than 500/μ for longer than five days. (BII)

3 No improvement in the febrile condition in spite of the continuation of empiric therapy for longer than seven days without detecting the pathogen or infection focus by repeated tests, the possibility of non-infectious diseases, such as tumor fever and drug-induced fever, is considered. In this situation, the discontinuation of antimicrobial therapy is one of the options. (BII)

(6) The use of granulocyte-colony stimulating factor (G-CSF) in febrile neutropenia

The routine use of G-CSF is not recommended in the 2002 Guidelines for the Use of Antimicrobial Agents in Neutropenic Patients with Cancer and The Guideline for the Appropriate Use of G-CSF by the Committee of Clinical Studies of the Japanese Society of Cancer Therapy. G-CSF shortens the period of neutropenia; however, whether or not G-CSF does reduce the mortality of infections, antimicrobial consumption, and the cost of medical care has not yet been elucidated. The indications of G-CSF as well as antimicrobials are pneumonia, hypotension, severe phlegmone or sinusitis, systemic fungal infection, and multiple organ failure.[149,158,159] Therefore, it should be used within the permission level of the Japanese health insurance system. (BII)

(7) Febrile neutropenia in the urological field

In the urological field, reports concerning febrile neutropenia in chemotherapy are limited. Yamazaki and coworkers[160] reported in 1989 that neutropenia with less than 500/μ occurred 62.6% in 110 courses of Cisplatin, Vinblastine, Bleomycin (PVB) therapy for testicular cancer and 45.5% in 13 courses of Methotrexate, Vinblastine, Adriamycin, Cisplatin (M-VAC) therapy for bladder cancer. Among them, febrile neutropenia occurred in 15.4% in each group, and the positive rate of blood culture was 9.1%. Matsumoto and coworkers[161] reported recently that fever above 38°C happened in 12%, and the risk factors were urinary diversion, hydronephrosis and the duration of neutropenia with 500/μ. Kotake and coworkers[162] reported that G-CSF reduced the incidence of infections in chemotherapy and febrile neutropenia from 23.5% to 14.1%, and from 14.1% to 1.0%, respectively. In reports from abroad, Counsell and coworkers[163] reported that FQLs reduced the incidence of febrile neutropenia in chemotherapy for testicular cancer from 15% to 5%. This report was in the era when AMP was affirmed before the IDSA guidelines of 2002. Nowadays, it is not positively recommended from the view of reduction of infections caused by multidrug-resistant strains. (BII)

(8) Catheter-associated blood stream infections

Catheter-associated blood stream infection is defined as bacteremia or fungemia in patients with an intravenous catheter indwelt. It is diagnosed when the bacterial culture from the peripheral blood is positive and there is obvious infection, except the intravenous catheter is absent.[2]

Central venous catheter. The central venous catheter is frequently inserted in chemotherapy for high-dose of antitumor agents and a large amount of hydration. It should be inserted under high barrier precautions using sterile gloves, a gown with long sleeves, mask, cap, and large covering sheet. (AI) It is not necessary to change the central venous catheter regularly for the prevention of infection. Sterile gauze dressing or film typed dressing is used and exchanged once or twice a week. The junction of the catheter and the infusion line is carefully disinfected with ethanol solution. A unified type of infusion line should be used, and lateral lines or a 3-sided plug should not be used except in the operation room or intensive care unit. (BII) Bacterial contamination can easily occur in the 3-sided plug; therefore, careful disinfection of this site is necessary when the infusion line is connected to the 3-sided plug. The infusion system is exchanged twice a week; however, it should be exchanged within 24 h when fatty milk liquids, which stimulate bacterial growth, are administered. (BII) A mixture of medicines should be performed in pharmacy under sterile conditions, as much as possible. However, it should be done in a place without crossing any dirty areas, if it has to be done in a ward.

Peripheral venous catheter. A peripheral venous catheter should be inserted in the upper limbs rather than in the lower limbs. The catheter is generally exchanged every 72–96 h. It should be removed immediately when patients have the symptom of phlebitis. (BII)

Peripheral arterial catheter. The blood pressure monitoring system should be disposable. The incidence of infections from peripheral arterial catheter is similar to that from a central venous catheter; therefore, it should be exchanged every 96 h. However, it is not necessary to exchange it within 4 days in order to prevent infections. (BII)

III. Future aspects

The evidence concerning perioperative infections in the urological field are limited. Further studies for additional evidence are necessary in order to make these guidelines more appropriate. First, prospective clinical studies on AMP according to these guidelines should be carried out to clarify the usefulness and validity of these guidelines. In addition, short-term AMP should also be studied. On the other hand, alternative precautions for high risk patients such as aged patients and diabetic patients, and high risk operations such as cystectomy with (bowel-utilizing) neobladder are required. To date, we have no evidence to reduce the incidence of perioperative infections by the choice of broad-spectrum antimicrobials or longer-administration time of antimicrobials for high risk patients or high risk operations. In principle, careful attention should be paid to the early diagnosis and treatment of perioperative infections in high risk patients or high risk operations without changing the antimicrobials or the administration time.

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