

ANTIBIOTIC RESISTANCE IN URINARY TRACT INFECTIONS: CURRENT PROBLEMS, ANTIMICROBIAL THERAPY STRATEGIES AND PREVENTION PROSPECTS

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Abstract

Urinary tract infections (UTIs) are among the most common bacterial infections in humans and represent a significant source of medical care. Modern urology faces a fundamentally new challenge: the rapid spread of antibiotic-resistant uropathogens, primarily members of the Enterobacterales family, including strains producing extended-spectrum β -lactamases and carbapenemases. Complicated UTIs, urinary catheter-associated infections, recurrent infections, and infections in patients with urologic obstruction, stones, neurogenic bladder, and post-instrumentation procedures pose particular clinical challenges.

The purpose of this review is to systematize current understanding of the causes of increasing antibiotic resistance in UTIs, analyze current principles of diagnosis and antibacterial therapy, and assess promising areas for prevention and reduction of antibiotic burden. Particular attention is paid to the principles of antimicrobial stewardship, personalized empirical therapy based on risk factors for resistant pathogens, the use of local antibiograms, early de-escalation of treatment, shortening the duration of antibiotic therapy, switching from intravenous to oral administration, and the development of non-antibiotic methods for relapse prevention.

The scientific novelty of this review lies in the systematization of modern approaches to the problem of antibiotic resistance in urology as a unified clinical and organizational system that combines early diagnosis, risk stratification, personalized empirical therapy, microbiologically based de-escalation, control of the source of infection and antibiotic-sparing prophylaxis.

A systemic approach to managing antibiotic resistance in urinary tract infections is proposed, combining stratification of individual risk of resistant uropathogens, local epidemiological information, early microbiological verification, targeted de-escalation of antibacterial therapy, control of the urological source of infection, and antibiotic-sparing prevention of relapse.

Keywords: Urology, urinary tract infections, antibiotic resistance, complicated urinary tract infection, uropathogens, ESBL, carbapenemases, antibiotic therapy, antimicrobial stewardship, recurrent UTI, catheter-associated infection, prevention.

Introduction

Urinary tract infections are one of the most common groups of infectious diseases and are of particular importance to urology practice. They occur in patients of all ages, but the risk of developing the disease increases significantly in the presence of factors specific to urology patients: urinary obstruction, urolithiasis, benign prostatic hyperplasia, neurogenic bladder dysfunction, indwelling or intermittent catheters, urological surgeries, and instrumental interventions.

Traditionally, most bacterial UTIs responded well to standard antibiotic therapy. However, in recent decades, the situation has changed significantly due to the spread of antibiotic resistance. This problem is global in scope and is considered by the World Health Organization as one of the key threats to modern medicine. According to the WHO, antibiotic resistance is already associated with millions of deaths annually, and research priorities should focus on resistant bacterial and fungal pathogens.

A distinctive feature of UTIs is that the primary pathogen pool is represented by gram-negative microorganisms, among which *Escherichia coli* plays a leading role. Furthermore, gram-negative bacteria demonstrate a significant potential for developing multidrug resistance. Analysis of the global burden of antibiotic resistance in UTIs shows that antibiotic use contributes to the selection of resistant uropathogenic strains, and the high prevalence of UTIs creates conditions for the constant selection of resistant microflora [5].

The current problem isn't just that some antibiotics are becoming ineffective. The treatment model itself is changing. Physicians must simultaneously address several challenges: ensuring rapid initiation of effective therapy, preventing the progression of infection and sepsis, and avoiding the use of an unnecessarily broad spectrum of antibiotics or creating additional selection pressure.

The emergence of a new concept of complicated urinary tract infection is particularly significant. In 2025, the IDSA published the first specialized guideline for the diagnosis and treatment of complicated UTIs. It proposes a practical model for selecting empirical therapy based on the severity of the disease, individual risk factors for resistant microorganisms, individual patient characteristics, and, in sepsis, local antibiogram data.

The 2026 EAU guidelines also continue to develop a personalized approach. They updated recommendations for the diagnosis and treatment of cystitis, antibiotic prophylaxis during prostate biopsy, and, for the first time, a separate section on fungal urinary tract infections.

Thus, the problem of antibiotic resistance today is not just a narrow infectious problem, but one of the central issues of modern urology, as it affects diagnostics, surgical treatment, prevention of complications, the organization of inpatient care, and long-term treatment outcomes.

Antibiotic resistance as a new clinical reality in urology. The spread of antibiotic resistance is driven by several interrelated factors. The primary one remains the excessive and irrational use of antibacterial drugs. In urology, antibiotics are prescribed not only to treat confirmed

infections but also prophylactically—before surgeries, endoscopic procedures, and prostate biopsies. The widespread use of antibiotics in outpatient practice is also significant.

The use of antibiotics in asymptomatic bacteriuria presents a particular challenge. Bacteria can be detected in urine without clinical manifestations of infection, especially in elderly patients, those with catheters, neurogenic bladder dysfunction, and certain urological diseases. International guidelines emphasize that asymptomatic bacteriuria does not require antibacterial treatment in most situations. Exceptions include pregnancy and certain urological procedures, which pose a risk of mucosal damage and bacterial entry into the bloodstream [4].

Thus, one of the approaches to combating antibiotic resistance lies not in finding a new antibiotic for every infection, but in preventing unnecessary use of existing drugs. It is crucial for urologists to distinguish between:

- asymptomatic bacteriuria;
- localized lower urinary tract infection;
- systemic urinary tract infection;
- complicated UTI;
- catheter-associated UTI;
- infections with bacteremia;
- infections in patients with urinary tract obstruction.

This classification has direct implications for treatment selection. Modern classification increasingly focuses not only on the anatomical location of infection but also on the presence of systemic manifestations, risk factors, and the likelihood of resistant pathogens. This reflects the shift from formal diagnosis to clinical risk stratification.

The main mechanisms of resistance development in uropathogens. The most significant mechanisms of resistance in Gram-negative bacteria are the production of extended-spectrum β -lactamases (ESBLs), AmpC β -lactamases, carbapenemases, altered cell wall permeability, modification of antibiotic targets, and activation of efflux pumps.

The practical significance of ESBL lies in the fact that bacteria are becoming resistant to a large number of widely used β -lactam antibiotics. Carbapenemase-producing strains pose an even more complex situation, as carbapenems have long been considered one of the main groups of drugs of choice for severe infections. This creates a paradoxical situation. The more frequently broad-spectrum antibiotics are used, the greater the likelihood of selecting for microorganisms against which these same drugs become ineffective. Urological patients are particularly vulnerable to this process. Multiple hospitalizations, surgical interventions, the presence of catheters, and previous courses of antibiotics create conditions for colonization by resistant microorganisms.

A global analysis of the problem shows that antibiotic resistance in UTIs should be considered as an interaction of three factors: microorganism characteristics, patient characteristics, and the conditions of care [5]. Therefore, modern antibiotic selection should be based not only on the typical spectrum of pathogens but also on the individual risk of resistance.

Complicated urinary tract infections: a changing concept. Complicated UTIs are one of the most challenging categories for modern urology. It is in this group that problems of antibiotic resistance, recurrence, and the need for hospitalization are most pronounced. In 2025, the IDSA first released a separate guideline on complicated UTIs. The authors note that current levels of resistance in urinary pathogens make many traditional empirical treatment regimens unreliable. Therefore, drug selection should be performed stepwise. The proposed approach includes four sequential stages:

1. assessment of disease severity;
2. assessment of individual risk of resistant pathogens;
3. taking into account contraindications and individual characteristics of the patient;
4. use of local antibiogram in severe infection and sepsis.

A history of previous urine cultures is particularly important. If a patient has recently isolated a resistant microorganism, the likelihood of recurrence of the same pathogen significantly influences the choice of initial therapy. Equally important is previous antibiotic treatment. For example, the IDSA recommends considering fluoroquinolone use within the previous 12 months as a factor increasing the likelihood of resistance to this class of drugs. Thus, the concept of "empirical therapy" in modern urology is gradually changing. It is no longer the same for all patients with the same diagnosis.

Local antibiogram and personalized empirical therapy. One of the most practical tools for combating antibiotic resistance is a local antibiogram. An antibiogram reflects the susceptibility patterns of microorganisms isolated in a specific medical facility or region. Its advantage is that national or international data may not reflect the local situation. Antibiograms are especially important in severe systemic infections and sepsis. In such situations, delaying effective therapy can have serious consequences.

At the same time, the widespread use of antibiotics "just in case" also poses a risk. Therefore, the optimal model is a combination of two principles: **early provision of adequate empirical therapy → earliest possible identification of the pathogen → de-escalation**. This sequence is one of the central principles of modern antimicrobial stewardship. In cases of confirmed infection, IDSA recommends switching from empirical therapy to a drug with a narrower spectrum, consistent with the results of culture and antibiogram, rather than continuing unnecessarily broad therapy.

De-escalation of antibacterial therapy. De-escalation means changing the initial empirical regimen after obtaining microbiological data. For example, if a patient with a severe UTI was initially prescribed a broad-spectrum antibiotic and culture revealed a microorganism sensitive to a more narrow-spectrum drug, it would be appropriate to switch to a more targeted therapy. This has several advantages:

- reduces the antibiotic load;
- reduces the selection of resistant microorganisms;
- reduces the likelihood of drug complications;

- reduces the cost of treatment;
- promotes the preservation of reserve antibiotics.

The modern strategy therefore focuses not on maximizing the drug's spectrum of activity, but **on maximizing the likelihood of clinical efficacy with the minimum necessary spectrum**. This principle is particularly important when treating patients with ESBL-producing bacteria and other MDR pathogens.

Reducing the duration of antibiotic therapy. Another key trend in modern urology is reducing the duration of treatment. Traditionally, many UTIs were treated for 10–14 days or more. However, accumulated research shows that in some clinical situations, shorter courses provide comparable clinical effects with a lower antibiotic burden.

IDSA 2025 recommends shorter courses for patients with complicated UTIs who demonstrate clinical improvement with effective therapy: typically 5–7 days for fluoroquinolones or approximately 7 days for non-fluoroquinolone agents, instead of the traditional 10–14 days. However, there are exceptions, such as severe immunodeficiency, abscesses, persistent obstruction, some cases of bacterial prostatitis, and other complicating conditions. The principle itself is particularly important: **treatment duration should be determined by clinical need, not historical practice**. Each additional day of unnecessary antibiotic therapy increases the drug burden and potential selection pressure.

Transition from intravenous to oral therapy. The development of effective oral medications allows for a reconsideration of the traditional practice of long-term intravenous treatment. When clinical improvement occurs, the patient is stable, oral medication can be administered, and an effective oral antibiotic is available, continued intravenous therapy is often not advantageous. Early transition to oral therapy can:

- reduce the length of hospital stay;
- reduce the risk of intravenous complications;
- reduce the cost of treatment;
- improve patient comfort;
- to promote more rational use of hospital resources.

However, the transition should be based on the drug's pharmacokinetics, the pathogen's susceptibility, the location of the infection, and the patient's clinical condition. The problem is particularly challenging for infections caused by MDR microorganisms, as the number of reliable oral options is limited. Therefore, the development of new oral drugs is considered a priority area of modern antibacterial therapy [9].

New antibacterial drugs: potential and limitations. Recent years have seen the emergence of new antibiotics and combinations of β -lactams and β -lactamase inhibitors. Modern drugs and combinations used for infections caused by drug-resistant gram-negative bacteria include ceftazidime/avibactam, meropenem/vaborbactam, imipenem/relebactam and other modern drugs.

A systematic review and meta-analysis of randomized trials of new β -lactams for complicated UTIs, including 10 studies and 5925 patients, found no significant deterioration in clinical outcomes compared with traditional antibacterial regimens [9]. However, the emergence of new antibiotics alone does not solve the problem of resistance. On the contrary, their inappropriate or excessive use can accelerate the emergence of resistance to reserve drugs. Therefore, new antibiotics should be considered as part of a comprehensive strategy, not as a replacement for rational diagnosis and prevention.

Recurrent urinary tract infections and antibiotic-sparing prophylaxis. Recurrent UTIs present a particular challenge, as patients may receive multiple courses of antibiotics over several years. The traditional method of prevention is long-term use of low-dose antibiotics. However, this strategy creates the conditions for the development of resistance. In this regard, non-antibiotic methods of prevention are becoming increasingly important.

One of the most well-known studies was the ALTAR randomized trial, which compared methenamine hippurate with daily antibiotic prophylaxis in women with recurrent UTIs. It was shown that methenamine did not exceed the pre-established clinical failure threshold compared with antibiotic prophylaxis, and antibiotic use was associated with more pronounced *E. coli* resistance in several assays [6]. This study is of fundamental importance: relapse prevention can be viewed not only as a matter of suppressing bacteria with antibiotics but also as a matter of reducing the antibiotic burden.

Another promising area is bacterial vaccines and immunomodulatory therapies. A 2024 systematic review and meta-analysis demonstrated the potential of bacterial vaccines for the prevention of recurrent UTIs, although the authors note the need for further high-quality research and standardization of drugs [10].

Catheter-associated infections. Infections associated with the use of urinary catheters occupy a special place in the structure of urological infections. A catheter disrupts the urinary tract's natural defense mechanisms and creates a surface for biofilm formation. Bacteria within the biofilm can be significantly more resistant to antibiotics and the body's immune mechanisms. Therefore, not only the choice of antibiotic is of fundamental importance, but also the prevention of unnecessary catheterization.

The updated position of the International Society for Infectious Diseases emphasizes the importance of limiting indications for catheterization, proper insertion technique, catheter care, and timely removal of the device [7]. This is especially important in hospitals, where catheterization may last longer than necessary. Prevention of catheter-associated infection should be considered as part of antibiotic stewardship: every prevented episode of infection means a prevented course of antibiotics.

Infectious complications during prostate biopsy. The problem of antibiotic resistance is directly related to prostate cancer diagnosis. Transrectal prostate biopsy carries a risk of transferring intestinal flora into the urinary tract and bloodstream, which can lead to infectious complications. With the spread of fluoroquinolone-resistant bacteria, traditional antibiotic prophylaxis is becoming increasingly unreliable.

One of the most important areas of practice change has been transperineal biopsy. The PREVENT study demonstrated that the transperineal approach significantly reduces the risk of infection and potentially reduces the need for antibiotic prophylaxis compared with the transrectal approach [8]. This trend is reflected in the 2026 EAU guidelines, which updated the provisions on antibiotic prophylaxis for prostate biopsy.

Thus, preventing antibiotic resistance can be achieved not only by changing the drug but also **by changing the surgical technique itself**. This represents an important conceptual shift in modern urology.

Rapid microbiological diagnostics is a promising approach. One of the key unresolved issues is that traditional urine culture takes time, whereas in severe infections, decisions about antibiotic therapy must be made immediately. In the future, molecular methods will play a significant role, allowing for faster identification of the pathogen and key resistance mechanisms. Potential benefits of rapid diagnosis:

- reducing the time to effective therapy;
- reducing the duration of unjustifiably broad treatment;
- earlier de-escalation;
- reducing the risk of septic complications;
- reducing the length of hospital stay.

However, the implementation of molecular methods requires addressing a number of challenges: cost, standardization, interpretation of results, and correlating the detection of resistance genes with the actual susceptibility phenotype. In the long term, the integration of clinical risk stratification, local antibiograms, standard culture, and rapid molecular technologies may prove most effective.

The Role of Infection Source Control

One of the fundamental characteristics of urologic infections is the possibility of an anatomical source of infection. These include:

- urinary tract obstruction;
- infected stones;
- abscess;
- foreign body;
- long-term catheter;
- residual urine;
- ureteral or urethral stricture;
- infected prostate tissue.

In such situations, an antibiotic may temporarily suppress the bacterial infection but not eliminate its cause. Therefore, if the expected clinical response is not achieved, it is necessary to search for the remaining source of infection.

Infected obstruction of the upper urinary tract is particularly dangerous. In this situation, decompression of the urinary system may be more important for the outcome than expanding the antibiotic regimen. Therefore, a modern approach to UTIs should integrate infectious therapy and urological surgery.

Antimicrobial stewardship as a new model of urological practice

Antimicrobial stewardship can be defined as a system of measures aimed at ensuring the correct choice of antibiotic, dose, route of administration, and duration of therapy while simultaneously reducing unnecessary use of antibacterial drugs. For urology, this means several principles: **an antibiotic should be prescribed when there is a clinical indication; The empirical drug should be appropriate for the severity of the disease and the risk of resistance; culture results should be used to adjust treatment; the antibiotic should be discontinued or replaced if the initial diagnosis of infection is not confirmed; the duration of treatment should be minimal but sufficient; infection prophylaxis should use non-antibiotic methods as much as possible.**

This approach is especially important for urologists, since a significant portion of the antibiotic burden is associated not only with treatment, but also with the prevention of infectious complications after procedures.



Figure 1. Modern conceptual model of antibiotic resistance management.

Note: Analysis of current guidelines and research allows us to conceptualize the management of antibiotic resistance in UTIs as a sequence of interrelated steps. This algorithm allows us to view antibiotic resistance not as an isolated microbiological problem, but as a manageable clinical process.

Table 1. Modern directions for reducing antibiotic resistance in urinary tract infections.

Direction	Modern approach	Expected effect
Diagnostics	Distinction between asymptomatic bacteriuria, localized and systemic UTI	Reducing unnecessary antibiotic prescribing
Risk stratification	Consideration of infection severity, sepsis, and MDR risk factors	Increasing the likelihood of adequate initial therapy
Antibiogram	Using local sensitivity data	More precise choice of empirical drug
Microbiology	Urine culture and susceptibility testing	The possibility of targeted therapy
De-escalation	Switching from a broad spectrum to a narrow one after receiving results	Reducing the antibiotic burden
Duration of therapy	Using the minimum effective rate	Reducing selection pressure
Route of administration	Early transition from intravenous to oral therapy	Reduction of hospitalization and complications
Recurrent UTIs	Non-antibiotic prophylaxis, including methenamine and immunoprophylactic approaches	Reducing antibiotic consumption
Catheters	Limitation of indications and early removal	Prevention of catheter-associated UTIs
Prostate biopsy	Transition to transperineal access	Reduction of infectious complications and antibiotic burden
Resistant pathogens	Modern β -lactams/ β -lactamase inhibitors and other new drugs	Expanding treatment options for MDR infections
Source control	Elimination of obstruction, stones, abscesses and other causes of persistent infection	Increasing the effectiveness of therapy and reducing relapses

Conclusion

Antibiotic resistance has become one of the most significant problems in modern urology. Its importance is determined not only by the increasing number of resistant uropathogens but also by changes in the clinical model for treating urinary tract infections.

Current data demonstrate the need to shift from universal antibacterial treatment regimens to individualized strategies. Antibiotic selection should take into account the severity of the infection, the presence of sepsis, previous culture results, prior antibiotic therapy, local resistance patterns, and the patient's individual risk factors. This approach is enshrined in the new IDSA guidelines for complicated UTIs and updated EAU guidelines.

Antimicrobial stewardship is a key component of the modern strategy. Its key elements include preventing unnecessary antibiotic therapy, early microbiological diagnosis, de-escalation,

shortening treatment duration, and switching from intravenous to oral therapy when clinically feasible.

Equally important is eliminating the source of infection. In cases of obstruction, infected stones, abscesses, catheters, or other anatomical factors, antibacterial therapy alone is not always capable of ensuring a lasting recovery.

Non-antibiotic methods for preventing recurrent UTIs hold great promise. Results from the ALTAR study indicate that methenamine may be considered as an antibiotic-sparing alternative to long-term antibiotic prophylaxis in some women with recurrent UTIs [6]. Bacterial vaccines and immunoprophylactic approaches also hold promise [10].

An important area of change in urological practice is reducing infectious complications through improvements in the procedures themselves. The transition to transperineal prostate biopsy demonstrates that preventing antibiotic resistance can be achieved not only by changing drug regimens but also by modifying surgical techniques [8].

Thus, **the scientifically and clinically sound strategy for the future lies not in the constant expansion of the antibiotic arsenal, but in the development of a comprehensive infection management system** that includes prevention, early diagnosis, individual risk assessment, rational empirical therapy, microbiological verification, de-escalation, the minimum sufficient duration of treatment, and control of the source of infection.

References

1. European Association of Urology. EAU Guidelines on Urological Infections 2026. Arnhem: EAU Guidelines Office; 2026. <https://d56bochluxqnz.cloudfront.net/documents/full-guideline/EAU-Guidelines-on-Urological-Infections-2026.pdf>
2. Trautner BW, Cortes-Penfield NW, Gupta K., et al. IDSA 2025 Guideline Update on Complicated Urinary Tract Infections. Infectious Diseases Society of America; 2025. <https://www.idsociety.org/practice-guideline/complicated-urinary-tract-infections/>
3. World Health Organization. Global research agenda for antimicrobial resistance in human health. Geneva: WHO; 2024. <https://www.who.int/publications/i/item/9789240102309>
4. Nicolle LE, Gupta K, Bradley SF, et al. Clinical Practice Guideline for the Management of Asymptomatic Bacteriuria: 2019 Update by the Infectious Diseases Society of America. Clinical Infectious Diseases. 2019;68(10):e83-e110. doi:10.1093/cid/ciy1121. <https://academic.oup.com/cid/article/68/10/e83/5407612>
5. Von Vietinghoff S., Shevchuk O., Dobrindt U., et al. The global burden of antimicrobial resistance - urinary tract infections. Nephrology Dialysis Transplantation. 2024;39(4):581-588. doi:10.1093/ndt/gfad233. <https://pubmed.ncbi.nlm.nih.gov/37891013/>
6. Harding C., Chadwick T., Homer T., et al. Methenamine hippurate compared with antibiotic prophylaxis to prevent recurrent urinary tract infections in women: the ALTAR non-inferiority RCT. Health Technology Assessment. 2022;26(23):1-172. doi:10.3310/QOIZ6538. <https://pubmed.ncbi.nlm.nih.gov/35535708/>
7. Rosenthal VD, Memish ZA, Nicastrì E., et al. Preventing catheter-associated urinary tract infections: a position paper of the International Society for Infectious Diseases, 2024 update.

International Journal of Infectious Diseases . 2025;151:107304.
doi:10.1016/j.ijid.2024.107304. <https://pubmed.ncbi.nlm.nih.gov/39551089/>

8. Hu JC, Assel M, Allaf ME, et al. Transperineal Versus Transrectal Magnetic Resonance Imaging-targeted and Systematic Prostate Biopsy to Prevent Infectious Complications: The PREVENT Randomized Trial. European Urology . 2024;86(1):61-68.
doi:10.1016/j.eururo.2023.12.015. <https://pubmed.ncbi.nlm.nih.gov/38212178/>

9. Xiang Hua Quan , Xin Yi Wang , Chun Hua Han . Novel β -lactam antibiotics versus other antibiotics for treatment of complicated urinary tract infections: a systematic review and meta-analysis. 2024. <https://pubmed.ncbi.nlm.nih.gov/39449969/>

10. Mak Q., Greig J., Dasgupta P., Malde S., Raison N. Bacterial Vaccines for the Management of Recurrent Urinary Tract Infections: A Systematic Review and Meta-analysis. European Urology Focus. 2024;10(5):761-769. doi:10.1016/j.euf.2024.04.002.
<https://pubmed.ncbi.nlm.nih.gov/38644097/>.