

PROTOCOL OF TREATMENT OF URINARY TRACT INFECTIONS (UTI)

SUA recommendations

TRANSLATION



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PROTOCOL OF TREATMENT OF URINARY TRACT INFECTIONS (UTI)

CONCEPT AND CLASSIFICATION OF UTIs

UTIs are one of the most frequent problems seen in adults by Primary Care Physicians. If we consider that approximately 30% of the visits in Primary Care (PC) are infectious processes, of which around 10% are UTIs, we are getting a glimpse of the magnitude of the problem. In terms of the number of UTIs, the number of cases and the in terms of number of cases, antibiotic consumption, sick leave, etc. And the problem becomes magnitude if we consider the not inconsiderable number of episodes of self-treatment or non-treatment, treatment in the emergency room, etc.

Fortunately, most UTIs tend to be uncomplicated, mainly affecting women without urinary tract anomalies, and are usually satisfactorily controlled by both the urologist and, especially, the PC physician with a short treatment. Although in volume they represent an important number of patients, from the health point of view they do not represent a serious health problem, as the UTIs that we call complicated. The latter are a serious problem in terms of their control, the indiscriminate use of antibiotics, the consumption of resources and the number of visits they generate both in PC and in hospital care, as well as the loss of quality of life they entail for the patients affected by them.

Following the definition and outline of the EAU guidelines on urinary tract infections, published in 2021, we can generally classify urinary tract infections (UTIs) as follows 2021, we can broadly classify urinary tract infections (UTIs) as follows: Urinary tract infection (UTI) as follows:

CLASSIFICATION OF URINARY TRACT INFECTIONS (ITUS)	
Uncomplicated urinary infections	Acute, sporadic or recurrent urinary infection of the lower tract (uncomplicated cystitis) and/or upper tract (uncomplicated pyelonephritis) urinary tract infection, limited to non-pregnant women without known relevant anatomical and functional abnormalities within the urinary tract or comorbidities.
Complicated urinary infections	All UTIs that are not defined as uncomplicated: <ul style="list-style-type: none">• Males.• Pregnant women.• Patients with anatomical or functional abnormalities of the urinary tract.• Urinary catheter wearers.• Renal and/or other concomitant diseases, e.g. diabetes.
Recurrent urinary tract infections (RUTI)	Recurrences of uncomplicated and/or complicated urinary tract infections, with a frequency of at least three UTIs/year or two UTIs in the last six months.
Catheter-associated urinary tract infections	Urinary tract infections occurring in patients with catheters in at least the last 48 hours.

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Following this classification, and completing it, we will basically deal with complicated UTIs, as it does not seem that the treatment of uncomplicated UTIs in women requires special management. We will follow the following outline:

- 1- Patients with permanent catheterisation.
- 2- Recurrent UTI.
- 3- Antibiotic resistance and multi-resistance.
- 4- UTI in men: management of prostatitis.
- 5- Asymptomatic bacteriuria in special situations.

TREATMENT GUIDELINES IN UNCOMPLICATED ITU

Suggested regimens for antimicrobial therapy in uncomplicated cystitis:

Antimicrobial	Daily dose	Duration of therapy	Comments
FIRST-LINE TREATMENT FOR WOMEN			
Fosfomycin trometamol	3 g	1 day	Recommended only in women with cystitis, including each episode of reinfection, without complications.
Nitrofurantoin	50-100 mg four times per day	5 days	
Nitrofurantoin prolonged-release	100 mg twice per day	5 days	
ALTERNATIVES			
Cefadroxil	500 mg/12 h	3 days	
IF LOCAL RESISTANCE PATTERN FOR E.COLI IS <20%.			
Trimethoprim-sulfamethoxazole	160/800 mg twice per day	3 days	Not in the last trimester of pregnancy.
TRAITEMENT CHEZ LES HOMMES			
Triméthoprime-sulfaméthoxazole	160/800 mg twice per day	7 days	Betalactams or fluoroquinolones may also be prescribed according to local susceptibility testing.



1. PATIENTS WITH PERMANENT CATHETERISATION

The percentage of the population with indwelling catheters in the community is around 0.02-0.07%, with up to 20% in patients admitted to nursing homes. Another group of patients who may also have an indwelling urinary catheter are patients with spinal cord injury, of whom approximately 15% will have a urinary catheter 5 years after the accident.

The importance of this group of patients is that after a catheter insertion time of more than one month, practically 100% of the patients are colonised by germs potentially triggering symptomatic UTI. Fortunately, most patients have asymptomatic bacteraemia, with symptomatic infection rates ranging from 10 to 40% of the series, being symptomatic bacteraemia rare. Thus, 2 to 11 episodes of febrile symptomatic UTI are described for every 1000 days that the patient has an indwelling bladder catheter.

1.1. Infection prevention in catheter wearers

A number of considerations should be taken into account with regard to prevention:

- 1.1.1. Assess the strict need to use or not to use a urinary catheter: try to use it only in case of real need, keep it as short as possible, try to use intermittent self-catheterisation.**
- 1.1.2. In cases where removal is not possible and periodic and definitive replacement is necessary, a number of precautions should be taken:**
 - 1.1.2.1. Use of sterile equipment and aseptic technique.
 - 1.1.2.2. Use of silicone catheters, which make bacterial adhesion difficult, and timely replacement.
 - 1.1.2.3. Use of closed drainage systems, avoiding ectasia that causes the catheter clogging.
 - 1.1.2.4. To prevent catheter-associated UTIs, do not use antibiotic prophylaxis. In these cases, the use of prolonged-release (24 h) D-Mannose is recommended.
 - 1.1.2.5. Do not routinely use antibiotic prophylaxis to prevent UTIs after urethral catheter removal or in patients performing intermittent self-catheterisation, to avoid bacterial resistance. Restrict prophylactic use of antibiotics only to patients at high risk or with a history of symptomatic UTI and/or urosepsis or traumatic replacement with hematuria, after catheter replacement.

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- 1.1.2.6. If antibiotics are used to prevent UTI, the preferential use of urinary elimination antibiotics (Fosfomycin trometamol, cefixime) is recommended, avoiding those that cause alteration of the intestinal flora such as quinolones, co-trimoxazole and nitrofurantoin.
- 1.1.2.7. Occasionally, when the patient does not tolerate the catheter and the UTIs are very frequent and symptomatic, it may be considered to replace the urethral catheter with a suprapubic catheter, which reduces the rate of infections and improves patient tolerance.

1.2. Treatment of patients with catheters

There is a range of treatment options depending on the severity of the condition, from asymptomatic bacteriuria. In general, patients with asymptomatic bacteriuria should not receive antibiotic treatment, except in those cases where the number of symptomatic infections is high, associated with catheter replacement, in which case the prophylactic use of antibiotherapy before and after the replacement would be recommended, always trying to use a sensitive antibiotic seen in previous cultures, with preferential elimination via urine, orally and for a limited time, for example, the day before the replacement and the two days after. Prolonged -release (24 h) D-Mannose would be recommended during these changes.

Patients with symptomatic febrile UTIs and very pyuric urine should be treated, trying to use antibiotics with proven sensitivity in previous cultures, as they are usually multi-resistant and BLEE-producing germs, and other aggressive and unusual germs such as Pseudomonas and Enterococcus.

1.3. Role of the family doctor in primary care and referral criteria

Most bladder catheterised patients can probably be managed on an outpatient basis and by the family doctor. Sometimes the participation of the urologist is necessary, so the criteria for referral of these patients are as follows:

- 1.3.1. Frequent symptomatic UTIs requiring intensive treatment and repeated use of subsequent antibiotic prophylaxis.
- 1.3.2. Intolerance to bladder catheterisation, in order to assess alternatives to catheterisation, such as surgery or replacement of the urethral catheter by a suprapubic cystostomy or learning to self-catheterise.
- 1.3.3. In both cases, once the condition has been resolved, the patient will undergo annual check-ups by the urologist if there are no incidents, and quarterly and then six-monthly check-ups by the family doctor in Primary Care, with periodic urine cultures for microbiological confirmation in case treatment would be necessary at any time.



2. RECURRENT ITU (ITUR)

A recurrent UTI is defined as the presence of at least 3 episodes of UTI per year or 2 in the last 6 months. Recurrences may be caused by reinfection or relapse-recurrence. For clinical management it is considered appropriate to differentiate between them:

- a) **Relapse-recurrence:** UTI caused by the same germ as the initial infection and with recurrence of bacteriuria within 2 weeks after completion of treatment or which may persist during treatment over time (persistent UTI).
- b) **Reinfection:** a new-onset infection following complete clinical resolution of the previous infection that occurs at least 15 days after the end of treatment, usually several weeks or months later, and is caused by a different germ (or strain) than the previous episode.

Most episodes of UTI (0-90%) are reinfections. It is a common condition in sexually active women, in menopausal women and when there are urological conditioning. The presence of uropathogenic germs in the vaginal and periurethral area in women is a real reservoir that perpetuates these UTIs. They represent a major public health problem, not only because of the loss of quality of life they entail and the frequent use of antimicrobials and other drugs, but also because of the significant health care costs related to treatment, complementary tests and visits to the doctor. Women are the most frequent sufferers of recurrent UTIs, and the causes vary according to their age and habits, as reflected in this table from the European Guidelines:

YOUNG AND PRE-MENOPAUSAL WOMEN	POSTMENOPAUSAL AND OLDER WOMEN
<ul style="list-style-type: none">• Sexual intercourse.• Spermicide use.• New sexual partner.• Mother with a history of UTI.• History of UTI during childhood.	<ul style="list-style-type: none">• History of UTI before menopause.• Urinary incontinence• Atrophic vaginitis due to oestrogen deficiency.• Cystocele• Post-void urine volume increase.• Urinary catheterisation and deterioration of functional status in elderly institutionalised women.

With regard to the evaluation of these patients, complementary tests such as ultrasound, cystoscopy, and simple or contrast radiological studies have proven to be of little use. In general, if there is no clinical suspicion of complicated UTI, no specific complementary tests are required, only a urine culture to confirm the UTI. Therefore, in the treatment and prevention of these infections, in addition to pharmacological treatment, we must intervene on all the factors that trigger and perpetuate them. The European Association of Urology in its latest guidelines on urological infections (2021) establishes that the management and follow-up of UTIs should include hygienic-dietary measures, non-antimicrobial measures and antimicrobial prophylaxis, in this order of application.

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2.1. Changes in lifestyle habits

General behavioural measures for those affected include: drinking more fluids than usual, urinating after intercourse, scheduled urination, avoiding long hours without emptying the bladder, avoiding constipation, avoiding tight clothing, cleaning the genital area from the urethra to the rectum, avoiding the use of spermicidal creams and diaphragms.

2.2. Non-pharmacological treatments

- 2.2.1. Use of prolonged-release D-Mannose for 24 hours.** D-Mannose is a monosaccharide that is not metabolised and is excreted in the urine 3-4 hours after ingestion. It acts by blocking the fimbriae of uropathogens, preventing their adhesion to the bladder wall. The use of 24-hour prolonged-release D-Mannose is recommended to ensure the presence of this compound in urine and thus significantly reduce the amount of bacteriuria and the number of active episodes of UTI. D-Mannose prolonged-release 24 h is useful in patients who link episodes of UTI after sexual intercourse. In addition, in pregnant patients with a history of recurrent UTIs, 24-hour extended-release D-Mannose is recommended for use during the gestational period. It is a safe, effective and contraindication-free alternative that avoids the use of antibiotics in many patients.
- 2.2.2. Use of probiotics:** Lactobacillus spp, not orally but topically, where they would play a competitive inhibitory role with vaginal uropathogens. Vaginal administration of food preparations containing these Lactobacillus has long been popular. At present, no convincing benefit of Lactobacillus products in the prophylaxis of UTIs has been shown. Further studies are needed to assess the effectiveness among the available preparations before a definitive recommendation for or against their use can be made.
- 2.2.3. Cranberry extract prophylaxis.** The most important mechanism, produced by its proanthocyanidin content, is the inhibition of the adhesiveness of a type of bacterial fimbriae to the bladder wall. There are conflicting results on the efficacy of cranberry juice/extract in reducing the occurrence of new episodes of symptomatic UTI in women with UTI. Although its actual usefulness is unclear, it is one more element contributing to patient improvement, provided it is used for a prolonged period of time and in conjunction with other alternatives such as prolonged-release (24 h) D-mannose.
- 2.2.4. Topical vaginal oestrogen administration in menopausal women,** in where vaginal dryness and postmenopausal changes are a clear cause of recurrent UTI.
- 2.2.5. Endovesical instillations with Glycosaminoglycans (GAGs) or Hyaluronic Acid,** or combination of both to replenish the bladder wall lining. The rationale is that there is a genetic condition related to the absence of secretion by the urothelial cells in some women of the ABO group, which increases the adhesiveness to the bladder wall of bacteria and makes it more difficult to eradicate the bacteria. This would explain the familial predisposition for this type of UTI. Large-scale trials are currently pending to assess the benefit of this type of therapy.



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2.2.6. Use of autovaccines: although they can be effective, their effect is usually transient and short-lived. These vaccines, which are administered orally or intranasally, are obtained from inactivated uropathogenic bacterial strains, but with potential antigenic capacity, stimulating the host immune reaction, activating macrophages and the production of cytokines, such as interleukin and interferon, leading to an increased inflammatory response.

If the above measures have been applied and do not work, antimicrobial treatments should be prescribed.

2.3. Pharmacological treatments

2.3.1. Continuous antibiotic prophylaxis: sometimes, despite all the measures mentioned in previous points, the number of UTIs is unbearable, causing a significant loss of quality of life, and some of them may even lead to more serious conditions such as acute pyelonephritis. In these circumstances, continuous low-dose prophylaxis over long periods of time is necessary. This prophylaxis must fulfil several conditions:

- 2.3.1.1. That when it is started there is no active infection by any germ, so that it would be ideal to have a negative culture at the start of it.
- 2.3.1.2. The dose of the drug must be minimal to be effective and to minimise side effects.
- 2.3.1.3. Preferably drugs with priority elimination in the urine should be used to avoid selection of strains from the digestive tract.
- 2.3.1.4. The rationale is, although it is not possible to eradicate the germs from their reservoirs, to try to keep the number of bacterial colonies as low as possible to prevent active infection even if colonisation occurs.
- 2.3.1.5. Prophylaxis is often random and depends on the doctor's experience: it may be daily or weekly nightly depending on the type of antibiotic, it may be one week per month, or every other week, etc. All this leads to a decrease in the number of germs that can cause an active infection. The duration is also variable, depending on the severity and intensity of the symptoms, number of episodes, etc., and can last 1 month, 3, 6, 12 or even permanently with interruptions.

2.3.2. Postcoital prophylaxis: This is mainly used in sexually active women who have a clear relationship with the number of episodes after intercourse. Women who are very sexually active tend to benefit more from continuous weekly prophylaxis.

2.3.3. Self-treatment of cystitis: is a very good option for women who recognise their episodes of cystitis and when they start with symptoms begin self-treatment with drugs such as Nitrofurantoin or similar for periods of 2-3 days. They must be motivated, sensitive and aware of their problem and have a good intellectual level.

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The following table details the most commonly used antibiotics and their dosage:

ANTIBIOTIC	CONTINUOUS PROPHYLAXIS	POSTCOITAL PROPHYLAXIS
Cotrimoxazole	4/200 mg/day	40/200 mg/day 80/400 mg/day
Fosfomicin Trometamol	3g every 7-10 days	3 g every 7-10 days
Cephalexin	125-250 mg/days	125-250 mg/day
Norfloxacin ^a	200 mg/day	200-400 mg/day

(a) avoid the use of quinolones as far as possible to avoid increasing the risk of resistance and altering the gut microbiota.

2.4. Referral criteria and role of the primary care physician

In general, if there is no clinical suspicion of complicated UTI, specific complementary tests are not required. Only a urine culture to confirm UTI is required.

The clinical management of most patients with UTI can be adequately performed by general practitioners in the primary care setting, without the need for additional diagnostic studies. In some circumstances requiring further evaluation, specific therapeutic management will be undertaken. After the initial assessment of the patient with UTI by the family doctor, 3 intervention options will be established.

CLINICAL SITUATION	RECOMMENDED APPROACH IN FAMILY MEDICINE
ITUR without risk factors for complicated infection or other clinical situations warranting further evaluation in the urology clinic (tables 2 and 3).	<ul style="list-style-type: none"> It is not necessary to perform additional studies, including urine cultures. Perform therapeutic management of episodes of UTI and preventive management from PC.
ITUR due to relapse, persistent or presence of risk factors for complicated infection, with no other clinical situations warranting urological assessment.	<ul style="list-style-type: none"> Perform additional studies in PC (ultrasound, renal function tests, urine culture). Refer to urology if urogynecological abnormalities susceptible to correction are detected or if there is a need for further functional studies.
Selected clinical factors warranting further evaluation by the urology specialist.	<ul style="list-style-type: none"> Refer to the urology specialist ^(a). Collaboration in the follow-up of the pathologies detected.

(a) In these situations, collaboration between the family doctor and the urology department to assess the options for referral can be carried out by means of a telematic inter-consultation (e-consultation).



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There are no specific guidelines or indications for imaging studies in women with ITUR, in whom there are not known underlying structural, functional or anatomical abnormalities.

These abnormalities are rare <10-15% of UTI cases. Several studies have shown a low yield from routine performance imaging studies for the detection of non-incidental findings in UTI. Ultrasonography is the first-line diagnostic test.

The indications for the use of ultrasound in cases of ITUR are:

- Infections not related to sexual activity.
- Suspected urinary obstruction or renal lithiasis (sometimes an abdominal X-ray is required).
- Alterations in renal function tests.
- Persistent microhaematuria associated with urinary tract infections.
- Acute pyelonephritis.
- Pregnant women.

The request and/or performance and interpretation of ultrasound can/should be performed in PC.

The following are indications for referral to a urology specialist for urological evaluation:

- ITUR in patients with high clinical suspicion of severe lower urinary tract anomalies or dysfunction to establish a diagnosis of certainty and rule out urinary tract dysfunction (table 3).
- Presence of a known surgically correctable structural or anatomical urogynaecological abnormality (urinary incontinence, cystocele, vesicoureteral reflux, bladder outlet obstruction).
- Uncertain diagnosis of UTI as a cause of recurrent lower urinary tract symptoms.
- Lack of response to preventive treatment with antibiotic therapy.

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TABLE 2. HOST FACTORS THAT CLASSIFY A URINARY TRACT INFECTION AS COMPLICATED THAT WARRANT FURTHER EVALUATION IN PATIENTS WITH ITUR

Structural, functional abnormalities of the urinary tract:

- Structural or anatomical abnormality of the genitourinary tract: renal or bladder stones, polycystic kidney disease, cystocele, diverticulum, fistula.
- Voiding dysfunction: vesicoureteral reflux, neurological disease, neurogenic bladder, pelvic floor dysfunction, high postvoid residual (>150 cc), urinary incontinence.
- Urinary tract obstruction: bladder outlet obstruction, ureteral stricture, ureteropelvic junction obstruction.
- Previous urinary tract surgery.
- Carriers of an indwelling urinary catheter or intermittent catheterisation.
- Pregnancy.

Other risk factors, in patients with a normal tract:

- Diabetes, immunosuppression.
- Postoperative infection or after urological manipulation.
- Chronic renal insufficiency.
- Nosocomial infection.
- History of infection by multi-resistant germs.
- Prolonged infection or relapse.

TABLE 3. SELECTED CLINICAL FACTORS WARRANTING FURTHER EVALUATION BY THE UROLOGICAL SPECIALIST IN PATIENTS WITH ITUR ("RED FLAGS")

- Haematuria (gross or microscopic) persisting after clearance of infection.
- History of abdominopelvic or urinary tract malignancy.
- History of urinary tract surgery or trauma, or diverticular disease.
- Obstructive symptoms (straining, weak flow, intermittency, hesitancy).
- Renal or bladder stones proven by imaging or if high suspicion ^(a).
- Symptoms of a fistula such as pneumaturia, faecaluria, urine culture with anaerobic bacteria or history of diverticulitis.
- Severe immunosuppression.
- Repeated episodes of pyelonephritis.

(a) Consider further investigations if urine culture shows the presence of pathogenic urease-positive (urea cleavage) organisms, including: *Proteus*, *Klebsiella*, *Morganella*, *Pseudomonas*.



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2.5. Criteria for return to primary care

Once the patient with UTI referred from primary care has been evaluated in the urology department, The patient will be referred to the family doctor, specifying the follow-up needs if necessary.

TABLE 4. CRITERIA FOR INTER-LEVEL REFERRAL OF THE PATIENT WITH ITUR		
Reason for referral from PC to specialised urological care.	Criteria for return to primary care.	Need for follow-up.
ITUR in patients with high clinical suspicion of serious anomalies or dysfunctions of the lower urinary tract to establish a diagnosis of certainty.	Absence of structural or functional abnormalities.	Yes, from PC for episodes of RUTI.
	Abnormalities corrected	NO
Presence of a known structural or anatomical urogynaecological abnormality that can be surgically corrected (urinary incontinence, pelvic organ prolapse, etc.).	Abnormalities corrected	NO
	Uncorrected abnormalities.	Yes, coordinated follow-up between PC and urology.
Uncertain diagnosis of RUTI as a cause of recurrent lower urinary tract symptoms.	Diagnosis of uncomplicated RUTI.	Yes, follow-up by PC.
	Diagnosis of other clinical entities responsible for urinary tract symptoms	Depending on the entity diagnosed.
Absence of response to preventive treatment with antibiotherapy.	Absence of structural or functional abnormalities.	Yes, from PC for episodes of RUTI.
	Abnormalities corrected	NO

3. ITUR MONITORING

3.1. Follow-up from PC

It is not easy to establish a specific follow-up plan for patients with UTI due to the variability of clinical situations and patient profiles. Most of the follow-up activities can be performed through non presential consultation.

3.1.1. Indications

ITUR cases that can be followed up in PC are:

- 3.1.1.1. ITUR in preventive treatment with antibiotherapy and topical vaginal oestrogens.
- 3.1.1.2. Patients with RUTI and structural, anatomical or functional alterations that cannot be corrected. If there is a risk of renal damage, preventive treatment with antibiotics will be considered and management will be similar to the rest of RUTI.

3.1.2. Content

Follow-up should include clinical monitoring and, if necessary, bacteriological monitoring by urine culture. The effectiveness of preventive treatment should be assessed by anamnesis and, if necessary, by microbiological tests (urine culture). The most important indicators for evaluation are:

- Number of episodes of infections (continuous antibiotic prophylaxis or topical vaginal oestrogen).
- Number of repeat prescriptions (post-coital antibiotic prophylaxis or self-treatment after self-diagnosis).
- Bacteriological monitoring (episodes of infection during continuous or post-coital antibiotic prophylaxis or symptomatic symptoms 48 hours after self-treatment).

3.1.3. Periodicity

The periodicity and duration of follow-up will depend on the preventive treatment used:

3.1.3.1. Preventive treatment with antibiotic therapy and self-treatment

- First month after starting treatment: check tolerance and adverse effects.
- Sixth month: check efficacy and assess completion of continuous antibiotic prophylaxis if there is a good response.



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- First year: check efficacy of postcoital antibiotic prophylaxis or self-treatment and continuous antibiotic prophylaxis if continued for up to 12 months.
 - If treatment is maintained for longer, clinical follow-up should be performed every 6 months.
- 3.1.3.2.** Preventive treatment with antibiotic therapy and topical vaginal oestrogens: check effectiveness 6 and 12 months after initiation of treatment and annually thereafter.
- 3.1.3.3.** ITUR with structural or functional abnormalities not amenable to restorative treatment. If antibiotic prophylaxis is used due to risk of renal function impairment, follow-up will be similar to other patients with uncomplicated UTI. In this case, renal function should be monitored by annual renal function tests (creatinine or estimated glomerular filtration rate).

3.1.4. Management of urinary tract infections in patients receiving antibiotic prophylaxis

Urine culture shall be performed in all cases. When breakthrough infection is diagnosed, it should be treated according to the results of the antibiogram and the original prophylaxis should be restarted after resolution of the infection if the culture confirms that it is still sensitive to the prophylactic agent.

If urine cultures show uropathogens resistant to the antibiotic used in prevention, or frequent urinary tract infections occur (≥ 2 UTIs in 6 months), prophylaxis is considered ineffective and will be discontinued. Referral to urology is then considered.

3.1.5. Recurrence of UTI after discontinuation of antibiotic prophylaxis

If the patient has no any anomaly and there are no other warning symptoms (table 3), continuation of prophylaxis for a longer time ($>$ one year) may be considered. In this case the follow-up is similar to the first course of preventive antibiotherapy.

The management algorithm for women with symptoms of urinary tract infection (**Figure 1**) and recurrent urinary tract infections (**Figure 2**) is shown in Figures 1 and 2, which are attached.

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FIGURE 1. ASSESSMENT OF WOMEN WITH UTI SYMPTOMS

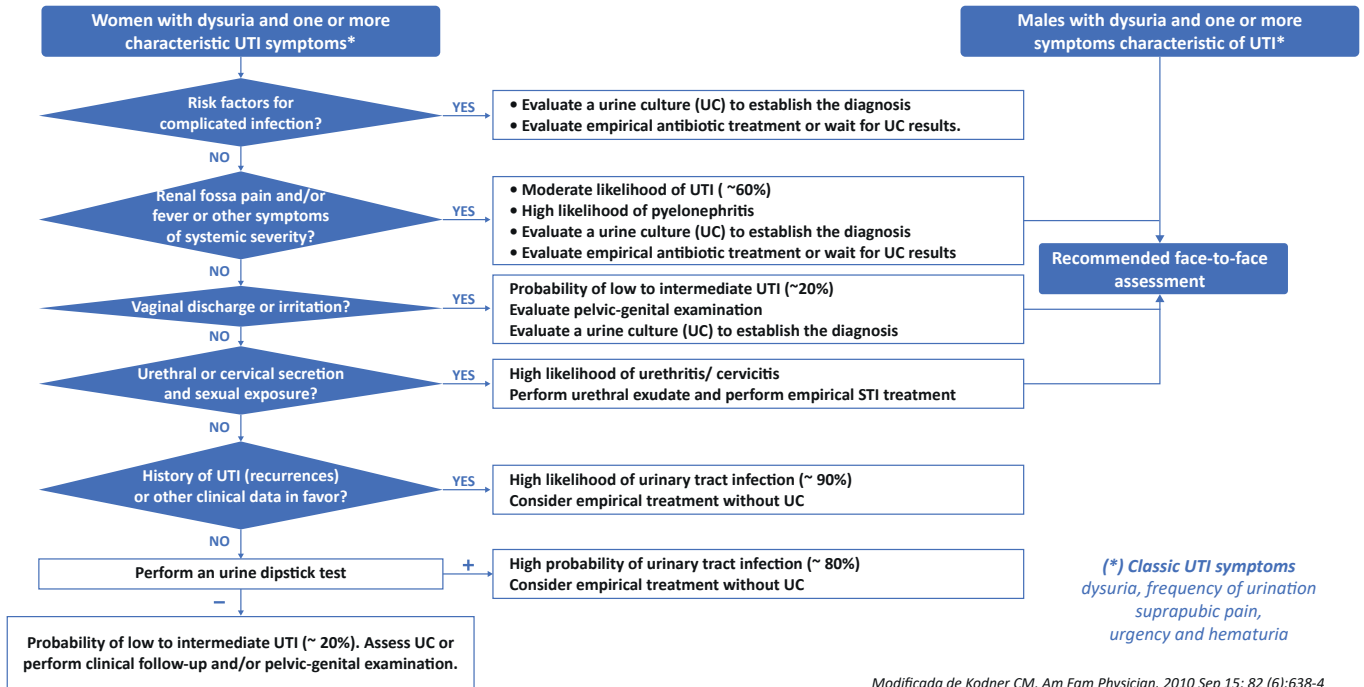
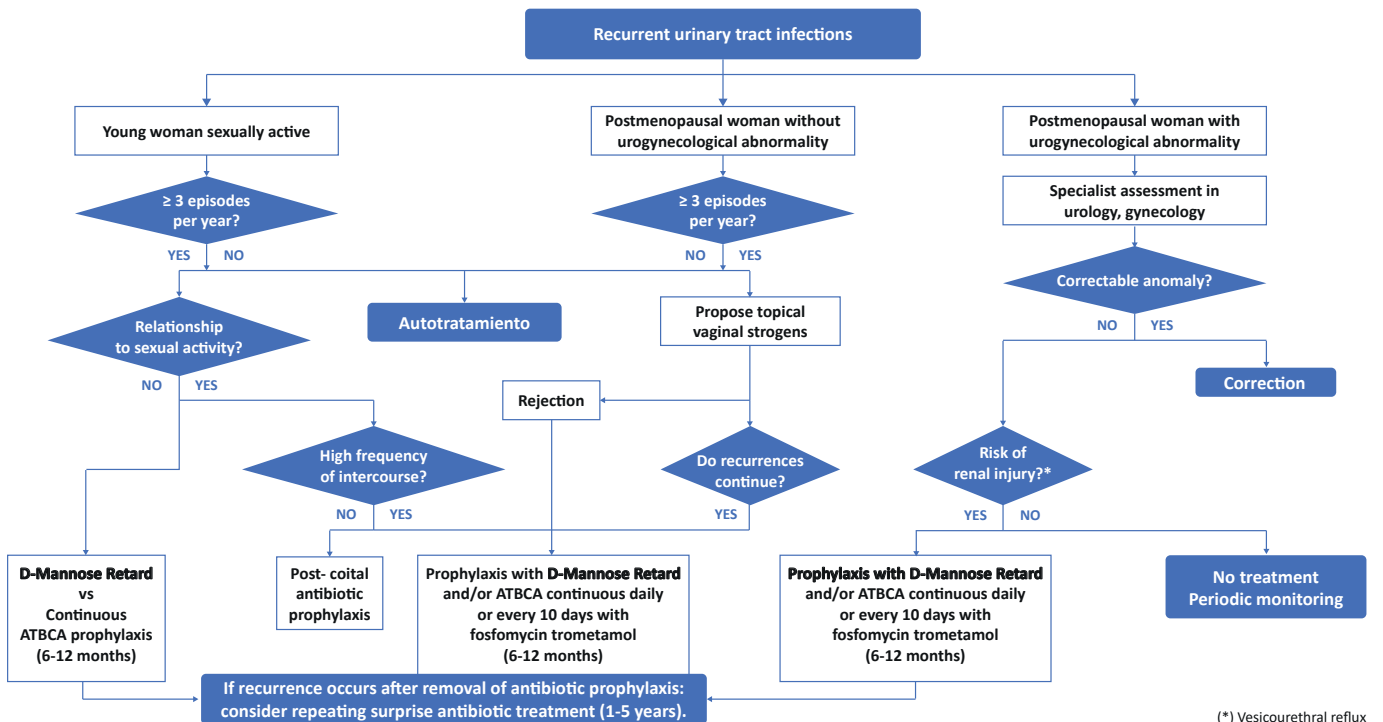


FIGURE 2. RECURRENT URINARY TRACT INFECTIONS



(*) Vesicourethral reflux



4. ANTIBIOTIC RESISTANCE AND MULTI-RESISTANCE

Antibiotic resistance is increasing daily, not only to beta-lactams, but also to quinolones, cephalosporins and aminoglycosides, with the added public health problem that this entails.

The so-called extended-spectrum beta-lactamases (ESBLs), found mainly in enterobacteria, cause resistance to penicillins and cephalosporins (including 3rd and 4th generation), but can also be resistant to other antibiotics, such as aminoglycosides and quinolones, becoming in these cases multi-resistant bacteria.

These types of UTIs are beyond the scope of this chapter, as their treatment is complex and requires parenteral drugs and hospitalisation for varying lengths of time; but we can take action to prevent their appearance by considering the factors that increase their risk and acting on them: elderly patients, diabetics with poor control, repeated UTIs, urinary catheter carriers, use of broad-spectrum antibiotics (cephalosporins and quinolones).

Hygienic-dietary measures and non-pharmacological alternatives such as prolonged-release (24 h) D-mannose help to reduce antibiotic use and therefore reduce morbidity, mortality, length of hospitalisation and healthcare costs associated with antibiotic resistance.



5. ITU IN MEN. MANAGEMENT OF PROSTATITIS

This is a UTI in the male that affects the prostatic parenchyma. Traditionally, when there is symptomatic colonisation of the lower urinary tract in the male usually results in the majority of cases of parenchymal involvement through the prostatic ducts leading to the urethra. We will only consider bacterial prostatitis, which can be acute and chronic. So only acute prostatitis is a problem that can be treated in conjunction with primary care.

The summary of the evidence in the European guidelines is as follows:

RECOMMENDATIONS	DEGREE OF STRENGTH
Do not perform prostate massage in acute bacterial prostatitis.	Strong
Medium-flow urine dipstick to check nitrites and leukocytes in patients with clinical suspicion.	Weak
Perform urine culture in patients with symptoms to guide diagnosis and tailor antibiotic treatment.	Weak
Perform blood culture and blood count in patients with symptoms.	Weak
Perform accurate microbiological evaluation for atypical pathogens such as <i>Chlamydia trachomatis</i> or <i>Mycoplasma</i> in patients with chronic bacterial prostatitis.	Weak
Perform Stamey test in patients with chronic bacterial prostatitis.	Strong
Perform transrectal ultrasound in selected cases to rule out prostatic abscess.	Weak
Do not routinely perform microbiological analysis of ejaculate alone to diagnose chronic prostatitis.	Weak

With regard to therapeutic recommendations, it should be noted that when we are faced with a male patient with UTI symptoms, we should always think that it is prostatitis and treat at a sufficient dose and for a minimum of one month on average, although there are exceptions.

The treatment recommendations are given in the following table:

ANTIMICROBIAL	DAILY DOSE	DURATION OF THERAPY	COMMENTS
Fluoroquinolone	Optimal oral daily dose.	4-6 weeks	
Doxycycline	100 mg twice daily.	10 days	Only for <i>C. trachomatis</i> or <i>mycoplasma</i> infections.
Azithromycin	500 mg once a day	3 weeks	For <i>C. trachomatis</i> infections only.
Metronidazole	500 mg three times per day	14 days	For <i>T. vaginalis</i> infections only.



6. ASYMPTOMATIC BACTERIURIA IN SPECIAL SITUATIONS

It is the growth of bacteria in significant quantity without the patient presenting symptoms of UTI. Diagnosis in a healthy person assumes the presence of more than 10⁵ CFU/ml of a single uropathogen in two consecutive urine samples, with only one sample being necessary in the case of the male. In the case of patients with catheters, asymptomatic bacteriuria (AB) is considered when there are more than 10² CFU/ml.

In general, the germs responsible for AB are the same as those responsible for symptomatic UTIs, generally enterobacteria and especially *E. coli*. It is said that the non-appearance of symptoms could be related to less virulent germs with less adhesive capacity to the bladder wall. In general, treatment of AB would be indicated because of the likelihood of developing symptomatic or potentially severe UTIs but, on the other hand, continuous treatment of UTIs may lead to adverse treatment may cause adverse effects such as the development of bacterial resistance, irrespective of the adverse effects of the drugs used and the economic cost. For all these reasons, it is necessary to define the management of AB in special situations.

6.1. AB in healthy women with recurrent UTIs

It has been shown that treatment of women with BA without risk factors and with previous recurrent UTIs increases the risk of symptomatic UTIs has been found to increase the risk of developing symptomatic UTIs, so treatment is not recommended.

6.2. BA in pregnant women

In this group of patients, the treatment of AB significantly reduces the number of symptomatic episodes, as well as being associated with a decrease in the number of premature deliveries and the number of low birth weight neonates.

The treatment options would be:

- Single- dose.
- Short treatment (2-7 days).
- Long treatment (8-14 days).
- Treatment up to delivery.

The EUA guidelines recommend short courses of treatment (2-7 days) versus single doses, even though the latter minimize adverse effects, they increase the rate of low birth weight neonates.

SUA recommendations

The following table shows the treatment regimens:

ANTIBIOTIC	DOSAGE	DURATION
Fosfomycin trometamol	3 g/day	1 day
Nitrofurantoin	100 mg/12h	5 days
Amoxicillin	250 mg/8 h	5 days
Amoxicillin-clavulanic acid	250 mg/8 h	5 days
Cefuroxime	250 mg/12 h	5 days
Fluoroquinolones	Contraindicated	3 days
Sulfonamides	Avoid 1 and 3 trimester	NO

An alternative that we believe to be useful and effective is prolonged-release D-Mannose 24 h during the period of gestation until delivery.

6.3. Diabetic patients

In general, screening and treatment of AB is not recommended in these patients. Good control of their diabetes is recommended to avoid symptomatic UTIs and septic complications.

An alternative that we believe to be useful and effective is 24-hour prolonged-release D-Mannose.

6.4. Postmenopausal women:

Do not require treatment and for practical purposes should be considered as non-menopausal women.

6.5. Patients with urinary tract diseases

Prostatism, neurogenic bladder, neobladder with self-catheterisation, spinal cord injury: no treatment of BA is indicated.

6.6. Patients with urinary catheters

Already discussed in previous sections.



PROTOCOL OF TREATMENT OF URINARY TRACT INFECTIONS (UTI)

By way of summary, and following the recommendations of the European clinical guidelines:

RECOMMENDATIONS	CLASSIFICATION STRENGTH
<p>Do not assess or treat asymptomatic bacteriuria in the following conditions:</p> <ul style="list-style-type: none">• women without risk factors;• patients with well-regulated diabetes mellitus;• postmenopausal women;• elderly institutionalised patients;• patients with dysfunctional and/or reconstructed lower urinary tracts;• patients with renal transplants;• patients before arthroplasty surgeries;• patients with recurrent urinary tract infections.	Strong
<p>Detect and treat asymptomatic bacteriuria before mucosal disruptive procedures.</p>	Strong
<p>Detect and treat asymptomatic bacteriuria in pregnant women with standard short-course treatment.</p>	Weak



7. APPROACH BY THE FAMILY DOCTOR IN PRIMARY CARE IN NON-FACE-TO-FACE CONSULTATIONS

The clinical management of UTIs by means of a telephone consultation has been successfully evaluated in different studies and the results are comparable with the usual telephone consultation.

This approach has proven to be feasible in terms of patient satisfaction and cure rates.

On certain other occasions, a face-to-face clinical evaluation is required, usually to assess general condition or to complete the physical examination to establish the clinical diagnosis:

CRITERIA FOR FACE-TO-FACE MANAGEMENT OF ITU BY THE FAMILY PHYSICIAN IN PC

- Symptoms of alarming or serious systemic involvement (suspected sepsis, complicated pyelonephritis) or recent alteration of cognitive and/or functional status.
- Suspicion of other acute infection conditions different from cystitis:
 - Pyelonephritis
 - Prostatitis
 - Orchiepididymitis
 - Urethritis/cervicitis
- Suspicion of UTI in a patient with an indwelling urinary catheter.
- Poor tolerance of oral medication.

The diagnosis of UTI is essentially clinical. Complementary tests can help to confirm the diagnosis in cases where it cannot be established by clinical findings. In relation to clinical findings, a diagnosis of UTI is unlikely without the presence of the symptom dysuria, as most patients with UTI present with dysuria. However, dysuria as an isolated symptom does not establish a diagnosis of UTI.

In addition to dysuria, other classic symptoms of acute cystitis are increased frequency of urination (pollakiuria), suprapubic pain, urgency, haematuria and nocturia. The combination of two or more of these symptoms, especially if dysuria is present, increases the likelihood of UTI. In recurrences in young women, self-diagnosis of UTI from the symptoms of urinary tract infection themselves has good accuracy.

A diagnosis of cystitis (classical symptoms) or pyelonephritis (fever with/without chills, pain in the costovertebral angle and/or flank, which may be accompanied by nausea and/ or vomiting and usually with voiding symptoms) can be established by means of an appropriate anamnesis. It is also possible to establish the diagnosis of UTI, detect the presence of risk factors for complicated UTI or the alarm criteria or severity of UTI and to obtain data that help to make the differential diagnosis of UTI, as opposed to differential diagnosis of UTI, compared to other prevalent conditions such as vulvovaginitis (women), urethritis and prostatitis (men).



PROTOCOL OF TREATMENT OF URINARY TRACT INFECTIONS (UTI)

The presence of vaginal discharge or irritation substantially reduces the likelihood of urinary tract infection, by about 20%. Therefore, in women without risk factors for complications, the presence of dysuria and one or more typical UTI symptoms, in the absence of vaginal symptoms (irritation, vaginal discharge) and pyelonephritis, can be considered as the presence of uncomplicated acute cystitis with high probability. Currently the Acute Cystitis Symptom Score Questionnaire [ACSS] which is being validated in different languages (www.acss.world) is a good tool for the diagnosis of uncomplicated cystitis (94.75% sensitivity, 82.4% specificity). This questionnaire also assesses the severity of symptoms and the course of the disease.

Cystitis in men presents a similar clinical picture to that in women, but symptoms have a lower positive predictive value. The risk of tissue invasion (prostatitis in the young and adult male, or occult pyelonephritis in the prostatic patient with obstruction) should always be considered. Therefore a differential diagnosis with other pathologies such as prostatitis or urethritis must be made and requires a face-to-face evaluation.

In uncomplicated UTI in women, empirical treatment can usually be performed without further diagnostic tests. However, in the presence of inconclusive clinical findings, complementary tests such as the dipstick, urine sediment and urine culture (UC) should be used to make a presumptive diagnosis and to confirm or rule out the diagnosis of UTI:

- 1-** The dipstick indirectly measures pyuria (detection of leukocyte esterase) and bacteriuria (detection of nitrites in urine). It has a low sensitivity. However, a negative result of the two tests improves the negative predictive value and rules out the diagnosis of UTI in the presence of inconclusive clinical findings. If one or more symptoms of UTI are present, any positive dipstick result (nitrite or leukocyte esterase alone or in combination), further increases the likelihood of a UTI.
- 2-** The urine sediment is more valid and reliable than the dipstick. The presence of pyuria (>10 leukocytes/mm³) confirms the diagnosis of UTI in adults, provided that there are accompanying symptoms.
- 3-** UC is the reference technique for the diagnosis of UTI. It is indicated in probable or confirmed cases of UTI, in which the identification of the uropathogen and analysis of sensitivity to antibiotics is important in order to select the most appropriate antibiotherapy regimen:

INDICATIONS FOR PRE-TREATMENT URINE CULTURE IN UTIS

- Uncomplicated UTI that does not respond to treatment.
- Complicated UTI in the absence of pyelonephritis.
- Pyelonephritis.
- UTI during pregnancy.
- Relapse/recurrence of UTI or persistent UTI.
- UTI in the patient with permanent catheterisation (perform catheter replacement previously).
- Acute prostatitis.
- Orchiepididymitis.
- Urethral syndrome (together with urethral exudate).

8. ORGANISATION AND METHODOLOGY

This approach has consisted of a review of the literature and also based on our own experience, considering the different situations that are considered in patients with UTI, establishing forms of joint management of the pathology that can be most beneficial for patients and can be managed in the most appropriate setting, either in Primary Care or in the Hospital.

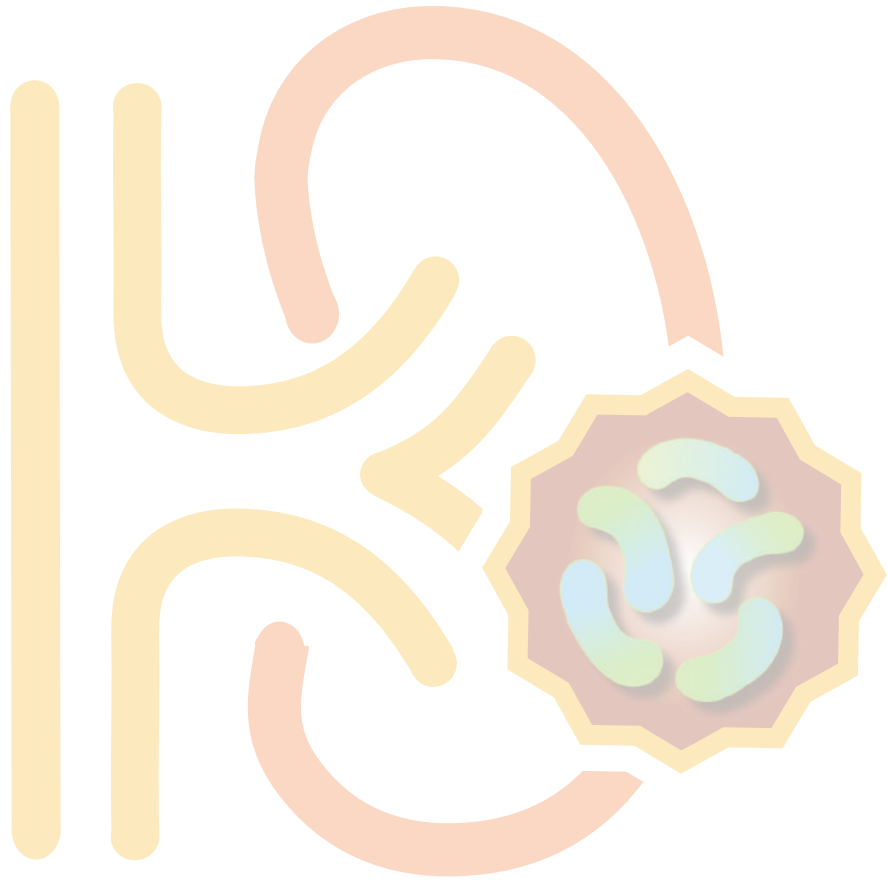
But logically, it is necessary to establish a common infrastructure and strategy for both levels of care. In this way, several actors are needed:

- 1-** The Primary Care Family Doctor who is the point of reference for urological pathologies in each health centre. Who is able to convey the common actions with the urologist and communicate to the rest of his colleagues any cross-cutting joint management protocol.
- 2-** Primary care urologist in each health area, who meets periodically with the Primary Care with the referring Primary Care Doctor but also with the rest of the Doctors in the Health Centres.
- 3-** Development of preferential communication circuits in special situations to coordinate specific actions: use of e-mail, telephone, fax, email, etc. This would be used to consult in exceptional circumstances that are not protocolised or agreed or that go beyond the established protocols, so it will always be something exceptional. It would be for cases of preferential management and/or referral.
- 4-** Development of regular communication circuits: with an established frequency, meetings to discuss the evolution of each of the agreed programmes, between the consultant urologist and the urological pathology referrals. We have the tool, which teleconferencing, and the frequency must be agreed.



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SUA recommendations

