STICHTING WERKGROEP ANTIBIOTICABELEID

# Optimalization of the antibiotic policy in the Netherlands X: SWAB guidelines for antimicrobial therapy of complicated urinary tract infections

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**ABSTRACT**

- The "SWAB" (Dutch Study Group for Antibiotic Policy) develops evidence-based guidelines for the administration of antibiotics to hospitalized adults.
- This guideline "Antimicrobial treatment of complicated urinary tract infections (UTIs)" focuses on the empirical antibiotic treatment of the hospitalized adult with a complicated UTI.
- The choice of treatment is based on recently published percentages of resistance for uropathogens in the Netherlands.
- First choice for empirical antibiotic treatment of a patient with a complicated UTI is a 2nd or 3rd generation cephalosporin or the combination of amoxicillin + gentamicin. Amoxicillin/clavulanic acid administered intravenously is the second empirical choice. Treatment duration must be at least 10 days.
- Treatment has to be adjusted on the basis of the definitive culture results and tailored, when possible. Oral treatment can be given when feasible, depending on the clinical condition of the patient.
- The treatment of UTIs in the following patient categories will be discussed separately: men, pregnant women, patients with a urinary catheter, patients with urine retention, patients with diabetes mellitus and patients with renal disease, congenital polycystic kidney disease and pyocystis.

SWAB (The Dutch Study Group for Antibiotic Policy) develops guidelines for the administration of antibiotics to adults in hospitals. The aims and the method of development of these guidelines were recently described in this journal.[1] In this guideline we, the members of the Study Group who drew up this guideline, will discuss antimicrobial therapy for complicated urinary tract infections (UTIs).
The complete text of the guideline is available at www.swab.nl.

## DEFINITIONS

The differentiation between uncomplicated and complicated UTIs has implications for the therapy, because the risks of complications or treatment failure are increased for patients with a complicated UTI. We have used the following definitions: an uncomplicated UTI is cystitis in a woman who is not pregnant, is not immunocompromised, has no anatomical and functional abnormalities of the urogenital tract and does not exhibit signs of tissue invasion and systemic infection. All UTIs which are not uncomplicated are considered to be complicated UTIs.

As a result a pyelonephritis is also considered to be a complicated UTI.[2]

Empirical therapies is the initial therapy chosen before the culture results are known.

## POSITIONING AND STRUCTURE OF THE GUIDELINE

The guideline described here is meant for empirical antimicrobial therapy (and not diagnostics) for adult patients (for this guideline ≥ 12 years) with a complicated UTI admitted to a hospital. Uncomplicated UTIs will be treated predominantly by the general practitioner. For the relevant guidelines, see the recently published Standard for Urinary Tract Infections of the Dutch Society of General Practitioners (NHG)[3]. We have tried to adhere to this standard insofar as possible. In addition to the general section on antimicrobial therapy for a UTI with systemic symptoms, we have chosen to describe complicated UTIs for certain groups of patients separately. The Study Group prefers to discuss a UTI with systemic symptoms because it is not always possible at first presentation of a patient to differentiate between a pyelonephritis and a urosepsis. In addition this differentiation has no consequences for the choice of empirical antimicrobial therapy.

## CAUSATIVE FACTORS AND RESISTANCE

Although there is a greater diversity in causative micro-organisms of complicated UTIs than uncomplicated UTIs, *Escherichia coli* remains in most cases of complicated UTIs the causative organism. The most useful resistance data on the above-mentioned micro-organisms was provided by the report “Nethmap”

2005.[4,5] In this report information has been collected on the prevalence of resistance against antibiotics in the Netherlands in the period 1998-2004 (see Table 1). Recent data on co-trimoxazole resistance in the Netherlands is not available, but previous investigations have shown that it is comparable to the resistance percentage for trimethoprim.[6]

## EMPIRICAL THERAPY

### General

Upon suspicion of a complicated UTI, urine must be collected for culturing, preferably before the start of therapy; whenever it appears to be a UTI with systemic symptoms (for example, the patient has fever) blood cultures must be performed.

Choice of drug.

For treatment of a complicated UTI, the antimicrobial drug must occur in high concentrations in urine, kidney tissue and prostate. Nitrofurantoine and fosfomycin are not registered for the treatment of a complicated UTI. On the basis of resistance data, it appears that a 2nd or 3rd generation cephalosporin or the combination of amoxicillin + gentamicin is suitable for empirical antimicrobial therapy for a complicated UTI (see Table 3). At present, good comparative studies are not available to determine a preference for a 2nd or 3rd generation cephalosporin, the combination amoxicillin + gentamicin or amoxicillin-clavulanic acid as empirical antimicrobial therapy. In view of the high percentage of intermediate sensitivity for amoxicillin-clavulanic acid, the Study Group is of the opinion that this drug is not the first but a second choice. In addition this drug must for this reason be administered intravenously.

Because there is only a small chance that cross-hypersensitivity exists, the Study Group means that in the event of hypersensitivity for penicillin derivatives (rash but not a systemic anaphylactic reaction), a 2nd or 3rd generation cephalosporin can still be prescribed.[7] If β-lactam antibiotics cause anaphylaxis, a fluoroquinolone is recommended. Results of Dutch studies demonstrated a correlation between the increase in the percentage resistance for fluoroquinolones

and use of these drugs.[8] This explains why, except in the above-mentioned cases, they should only be prescribed in the event of an indication, thus after the resistance pattern of the causative micro-organism is known or when the entire treatment is to be administered orally. In view of the high degree of resistance among patients admitted to the Department of Urology, fluoroquinolones are not automatically suitable as empirical antimicrobial therapy.

Duration of therapy.

A retrospective study of the duration of treatment of pyelonephritis showed that, independent of the drug administered, there is a strong chance of treatment failure whenever the treatment lasts less than 10 days.[9] According to the guidelines of the Infectious Diseases Society of America (IDSA) a total duration of treatment for an acute pyelonephritis of 10-14 days should be adequate. For women with this disease even 7-14 days should be sufficient.[10] When ciprofloxacin is prescribed, a course of 7 days for women with pyelonephritis is sufficient, [11] but when β-lactam antibiotics are prescribed treatment for 7 days would be too short.[10] In view of these data, the Study Group recommends that the duration of treatment must be at least 10 days.

Once the results of the urine culture are known, therapy must be adjusted and if possible narrowed down. Long-term treatment with gentamicin is not recommended. If the condition of the patient allows it and if the patient does not vomit, then oral therapy can be prescribed.[10] If the patient no longer has symptoms, then there is no indication for follow-up cultures.

**Men**

As a rule a UTI in a man is considered to be a complicated UTI because there is often a urological abnormality.[12] As far as the urine culture is concerned, it is recommended on the basis of one study to use $10^3$ colony-forming units (CFU) /ml instead of $10^5$ CFU/ml as the cut-off point for a positive urine culture.[13]

Choice of drug and duration of therapy

In general, treatment with nitrofurantoine is not recommended, because this drug does not penetrate into tissue sufficiently.[12] The fluoroquinolones and to a lesser degree trimethoprim have certain characteristics (soluble in fat, low protein

binding) which result in high penetration into the prostate.[14] During an acute inflammation however better penetration of the prostate can also be achieved with other antibiotics and therefore an acute bacterial prostatitis can be treated empirically with β-lactam antibiotics, if necessary in combination with gentamicin.[14, 15]

The Study Group reached the conclusion that men with a UTI can be separated into three groups. Therapy is different for each group.

1. Young men with a UTI without systemic symptoms (fever, feeling ill), where the patient's medical history and physical examination do not suggest a causative factor. The UTIs in this group can be considered uncomplicated UTI and can therefore be treated with nitrofurantoine for 7 days (in accordance with the NHG standard[3]). Since this SWAB guideline is written for patients who are seen in the hospital, the Study Group believes that this rare group of patients need not be discussed further here.
2. Men with a UTI and systemic symptoms or with a medical history and physical examination that suggest a causative factor. These UTIs must be considered complicated UTIs. The systemic symptoms indicate invasion of the tissue in the prostate (acute bacterial prostatitis) or the kidney (pyelonephritis). The empirical therapy is then the same as that described in the General section of this guideline.
3. Men with complaints which fit a chronic bacterial prostatitis. It would seem best to wait for the results of the culture. For men with a chronic bacterial prostatitis a fluoroquinolone is recommended as first choice because these drugs are supposed to be more effective than co-trimoxazole.[14] In an open randomized trial treatment with norfloxacin was more effective than co-trimoxazole therapy. [16] In general, for the treatment of a chronic bacterial prostatitis duration of at least 4 weeks is recommended. Since it is not an acute illness, the results of the culture (urine, if necessary after massage of the prostate, semen) can be awaited before therapy is initiated.

**Pregnancy**

During pregnancy there is an elevated risk of a more severe course of an UTI with consequences for mother and child.[17] The conclusions of a Cochrane review of

asymptomatic bacteriuria (ABS) during pregnancy made it clear that antibiotics are effective again ABS during pregnancy and lower the incidence of pyelonephritis as well as prematurity and dysmaturity.[18]

Choice of drug

In view of the lack of the teratogenic effects described and the previously mentioned resistance percentages, the β-lactam antibiotics are a good choice for the treatment of a UTI during pregnancy. Amoxicillin-clavulanic acid or nitrofurantoine are first-choice drugs for the treatment of cystitis during pregnancy (nitrofurantoine must not however be used just before delivery).[19,20]
The recommendation in the guideline of the Dutch Society for Obstetrics and Gynaecology (NVOG) [21] is to treat a cystitis for 7 days with amoxicillin, amoxicillin-clavulanic acid, or nitrofurantoine (not around the time of the delivery) (www.nvog.nl) . In view of the high resistance percentage of the uropathogens for amoxicillin, we believe that this drug is not suitable for empirical treatment.
A 2nd or 3rd generation cephalosporin is the drug of first choice and amoxicillin-clavulanic acid is second choice for treatment of a pyelonephritis during pregnancy.
Whenever a group B streptococcus (GBS) is found in the urine culture, this is a sign of maternal colonization with GBS. Intravenous antibiotic treatment of the mother during delivery reduces the number of neonatal infections with GBS.[22]
As far as GBS is concerned, in the NVOG guideline Prevention of Perinatal Group B Streptococcus Disease published in 1998, screening is not recommended, but in the event of severe maternal GBS colonization (and therefore GBS in the urine) consultation with the gynaecologist is advised and in all cases administration of antibiotic prophylaxis during delivery is necessary.

Duration of therapy

On the basis of the literature it is recommended that pregnant and non-pregnant women with cystitis should be treated for 3-7 days and for at least 5 days if β-lactam antibiotics are administered.[17]
We agree with the recommendation of the NVOG guideline to hospitalize a pregnant woman with a pyelonephritis and to administer antibiotics intravenously.

After a fever-free period of 24-48 hours, oral antibiotics can be given; the total duration of therapy must be at least 10 days.
After completion of the treatment of a (high and low) UTI, urine must be checked since approximately 1/3 of the women with a cured UTI develop a bacteriuria later during their pregnancy.[12, 23] That's why there are good reasons to perform urinalysis at every check-up for pregnant women who have been treated for UTI.

**Catheter**

Every patient with an indwelling catheter develops bacteriuria. In general it is not a question of an infection but colonization. In that case the patients will not have the complaints of a UTI. Patients (male and female) with an indwelling catheter can best be separated into three groups:

1. catheter in place for ≤ 10 days
2. cather in place for longer period (years)
3. over prolonged period intermittent catheterization

*Prophylaxis*

According to the literature on this subject, it can be concluded that antibiotic prophylaxis decreases the chance of bacteriuria for patients with a short-term indwelling catheter or those who catheterize themselves intermittently over prolonged periods.[24, 25] Furthermore antibiotic prophylaxis decreases the chance of a symptomatic UTI for patients with either a short-term or long-term indwelling catheter.[24] What the effect will be of antibiotic prophylaxis is not known on the development of resistance. The differences in the incidence of symptomatic UTIs between groups of patients who did and did not receive antibiotic prophylaxis were very small. Therefore we do not recommend antibiotic prophylaxis and as a result there is no need to screen for bacteriuria.[26]
It is not known whether it is worthwhile to treat an eventual existing bacteriuria after removal of the indwelling catheter. We recommend that a patient with bacteriuria should not receive antibiotic treatment at the time of removal of the indwelling catheter, because studies on the clearance of bacteriuria and the incidence of symptomatic low UTI, yield contradictory results.[27, 28]

*Therapy*

Patients with a long-term indwelling catheter may carry in addition to Enterobacteriaceae, such as *Serratia, Providencia* and *Acinetobacter,* also enterococci, yeasts and staphylococci.

If the indwelling catheter is changed at the time of treatment of a symptomatic UTI, a higher percentage of patients will exhibit disappearance of the bacteriuria and a more rapid recovery from the symptoms.[29]

Choice of antibiotic

When the patient with a catheter has only local symptoms and exhibits no signs of a systemic infection, it is recommended to wait for the results of the cultures.

If there is a systemic infection, the patient should be treated as described under the General section for patients with UTI and systemic symptoms, with the restriction that the patient who has had an indwelling catheter for a prolonged period or was catheterized intermittently can better be treated empirically with a fluoroquinolone or an aminoglycoside and not with a β-lactam antibiotic due to the insensitivity for β-lactam antibiotics of the most commonly cultured micro-organisms.[12]

Duration of therapy

In the diverse (not systematic) reviews and guidelines, different recommendations for the duration of therapy are given, ranging from 3-21 days.[12, 30] In view of the results of a trial,[27] in which no difference in efficacy was found after removal of the catheter for symptomatic patients with a low UTI after treatment with one dose or 10 days of co-trimoxazole, we mean that prolonged treatment of a symptomatic low UTI is not worthwhile. On the other hand if it is a complicated UTI and the patient only has local symptoms and no signs of systemic infection, we recommend treatment for 5 days, for systemic phenomena at least 10 days.

**Patients with retention abnormalities as a result of neurological or obstructing problems**

The general recommendation is to remove the obstruction; therefore the guideline is for patients for whom this is not (yet) possible. Experts believe that

prophylaxis is not indicated, with the exception of patients with urethral reflux and/or recurrent UTIs[31] or in the event of stones.[12]

*Therapy*

Choice of drug: In the case of UTI in a patient with a spinal cord lesion, the most common causative agents cultured are Gram-negative bacteria and enterococci. In the event of kidney stones, *Proteus, Pseudomonas* and other urease-producing bacteria are more common.[12]

Duration of therapy:
In the only prospective randomized trial of patients with a low UTI (51 men and 9 women) with a spinal cord lesion and without a long-term indwelling catheter (83% intermittent catheterization), the effects of ciprofloxacine for 3 and 14 days were compared. The general clinical recovery at the end of therapy and after 6 weeks were equal for the two groups, but the percentage clinical and microbiological relapses after six weeks was significantly higher for the 3-day group.[32]
See also for this group the section Catheter.

**Diabetes mellitus**

Patients with diabetes mellitus (DM) have a higher prevalence of UTIs than patients without DM.[33] In addition complications of the UTI develop more often in this group of patients.[34] For this reason a cystitis in a patient with DM is considered a complicated UTI.

*Therapy*

Choice of drug:
Because the resistance percentages for *E. coli* from the urine of patients with and without DM are comparable,[35] the previously mentioned arguments (see General) for the choice of therapy for this group of patients can also be used. For women

with DM and only cystitis, nitrofurantoine or amoxicillin-clavulanic acid seem to be a good choice.

Duration of therapy:

It is not clear whether the chance of therapeutic failure is increased after treatment of UTI among women with DM compared to women without DM. The results of the various studies of treatment failure are contradictory.[9, 36, 37] Since we mean that a cystitis in a woman with DM should be considered a complicated UTI, we have decided to recommend, in accordance with the NHG standard, a longer duration of therapy, namely 7 days, than for a woman without DM. For the treatment of a pyelonephritis in a woman with DM, see the above General section.

**Kidney disease, congenital cystic kidneys and pyocystis**

UTIs in dialysis patients are by definition complicated UTIs because the immunity of patients with uraemia is decreased.[38] Asymptomatic bacteriuria and UTIs occur frequently in patients with renal insufficiency and congenital cystic kidneys and often lead to complications.

*Therapy*

During the treatment of UTIs in patients with terminal renal insufficiency, the pharmacokinetics of various antibiotics are influenced by changes in protein binding and/or renal elimination.[12] For adaptation of the dosages, see the SWAB National Book of Antibiotics (www.swab.nl).

**Patients with congenital cystic kidneys**

Patients with congenital cystic kidneys often have high and low UTIs.[39] This is not always clear at presentation so that the clinician must always be alert for a cystic infection.

*Therapy*

The efficacy of an antibiotic in the event of a cystic infection is dependent upon adequate activity of the antibiotic in the cyst. Options are an aminoglycoside combined with a continuous infusion of β-lactam antibiotics, fluoroquinolones or eventually co-trimoxazole.
When a patient with congenital cystic kidneys develops a UTI, there need not always be a cystic infection. It is however not clear after a literature study whether a patient with congenital cystic kidneys and a UTI should be handled primarily as a complicated UTI or that each patient with congenital cystic kidneys who develops a UTI has an infected cyst and thus that the duration of treatment must be prolonged to 4-6 weeks. Because the Study Group could not reach consensus no recommendations are given.

**Patients with a pyocystis**

A pyocystis is a vesicular empyema which can occur in the "low flow state" of the bladder of a patient who has undergone urinal deviation or patients with oligo-anuria due to terminal renal insufficiency.[40] Clinically this condition often presents as atypical with fever, swollen and/or painful abdomen, especially suprapubic pain. For therapy see the complete guideline (www.swab.nl).

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Table 1

| ***Escherichia coli***<br><br>Antibiotic | **Resistance percentages 1998** | **Resistance percentages 2004** |
|---|---|---|
| Amoxicillin (Clamoxyl) | 29% | 37% |
| Trimethoprim (Monotrim) | 18% | 25% |
| Ciprofloxacin (Ciproxin) | 0% | 5% |
| Ciprofloxacin[1] (Ciproxin) | 7% (year 2000) | 11% |
| Amoxicillin-clavulanic acid (Augmentin) | 4% | 4% |
| Amoxicillin-clavulanic acid (Augmentin): intermediate sensitivity | | 9% |
| Nitrofurantoine (Furabid, Furadantine) | 4% | 2% |
| Gentamicin | 4% | 4% |
| Cefuroxime (Zinacef, Cefofix) | | 3%(n=500)[1], 5%(n=128)[2] |
| Ceftazidime (Fortum) | | 1%(n=500)[1], 0%(n=128)[2] |
| ***Klebsiella pneumoniae***<br><br>Antibiotic | **Resistance percentages 1998** | **Resistance percentages 2004** |
| Trimethoprim (Monotrim) | 11% | 16% |
| Ciprofloxacin (Ciproxin) | 0% | <3% |
| Amoxicillin-clavulanic acid (Augmentin) | 5% | 4% |
| Gentamicin | | <3% |
| Ceftazidime (Fortum) | | <3% |
| ***Proteus mirabilis***<br>Antibiotic | **Resistance percentages 1998** | **Resistance percentages 2004** |
| Amoxicillin (Clamoxyl) | 14% | 24% |
| Trimethoprim (Monotrim) | 24% | >50% |
| Ciprofloxacin (Ciproxin) | | <3% |
| Amoxicillin-clavulanic acid (Augmentin) | | 5% |
| Gentamicin | | <3% |
| Ceftazidime (Fortum) | | 0% |

Table 2

| | |
|---|---|
| * | The resistance percentages of the different uropathogens for amoxicillin and trimethoprim are high (37% and 25%, respectively).<br>*[4] |
| * | The resistance percentages of the different uropathogens for amoxicillin-clavulanic acid, a 2nd or 3rd generation cephalosporin, gentamicin, nitrofurantoine and the fluoroquinolones are low (all <5%). The percentage for intermediate sensitivity amoxicillin-clavulanic acid is relatively high, namely 9%.<br>*[4],B[5] |
| * | The resistance percentage for fluoroquinolones of *E. coli* isolated from patients admitted to the Department of Urology is high (11%)<br>*[4] |
| Level 3 | If therapy for pyelonephritis lasts less than 10 days, the chance of treatment failure is increased.<br>B[9] |
| Level 3 | When β-lactam antibiotics are prescribed for pyelonephritis, then 7 days of therapy is too short.<br>B[41] |
| Level 3 | A urine culture with at least $10^3$ CFU/ml must be considered positive for men.<br>B[13] |
| Level 3 | A UTI in a male is usually accompanied by prostatitis.<br>B[42],C[43, 44] |
| Level 4 | It is better not to treat acute prostatitis empirically with nitrofurantoine, although it is possible to prescribe fluoroquinolones or β-lactam antibiotics with or without gentamicin.<br>D[14, 15] |
| Level 4 | The duration of therapy for an acute prostatitis must lie between 7 and 28 days.<br>D[45, 15, 14] |
| Level 3 | For men with a chronic bacterial prostatitis the choice of drug is dependent on the results of the culture, whereby fluoroquinolone is recommended as the drug of first choice and co-trimoxazole as the second.<br>B[16],C[14, 15] |
| Level 4 | The duration of therapy for a chronic prostatitis must be at least 28 days.<br>D[14, 15] |
| Level 1 | Treatment of ABS during pregnancy decreases the incidence of pyelonephritis and prematurity and dysmaturity, but the optimal duration of treatment is not clear.<br>A1[18, 46] |
| Level 3 | The β-lactam antibiotics and nitrofurantoine (not close to the time of delivery) are suitable drugs for treatment of cystitis during pregnancy.<br>The β-lactam antibiotics are suitable drugs for the treatment of pyelonephritis during pregnancy.<br>B[19], C[20], D[47] |
| Level 1 | The optimal duration of therapy for cystitis during pregnancy is not known, but a period of at least 5 days is sufficient. |

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| | A1[17], B[48] |
| Level 2 | In general it is recommended that a pregnant woman with pyelonephritis should be admitted to the hospital for at least 24 hours, intravenous antibiotics are prescribed and that treatment lasts for a minimum of 10 days.<br>A2[9], B[49, 50] |
| * | Approximately 1/3 of the women treated for UTI develop bacteriuria again later in their pregnancy.<br>D[23, 12] |
| Level 1 | The presence of Group B streptococci (GBS) in the urine is a sign of maternal colonization with this micro-organism. Intravenous antibiotic treatment during the delivery reduces the number of neonatal infections with GBS.<br>A1[51], A2[22] |
| Level 2 | For patients with a short-term transurethral indwelling catheter, *E. coli* are usually found in the culture; in the case of a short-term suprapubic catheter the culture usually yields *E. coli,* enterococci and/or Staphylococcus epidermidis.<br>A2[52], B[53] |
| Level 4 | For patients with a longtem indwelling catheter, not only Gram negative bacteria such as *Serratia, Providencia,* and *Acinetobacter* but also enterococci, yeasts and staphylococci are found in the culture.<br>D[12, 54] |
| Level 1 | Antibiotic prophylaxis decreases the chance of bacteriuria for patients who have a short-term (≤10 days) indwelling catheter.<br>A1[24] |
| Level 1 | Antibiotic prophylaxis decreases the chance of bacteriuria for patients who perform catheterization themselves over the long-term.<br>A1[25] |
| Level 1 | Antibiotic prophylaxis decreases the chance of a symptomatic UTI among patients with a short-term indwelling catheter (≤10 days).<br>A1[24] |
| Level 3 | Antibiotic prophylaxis decreases the chance of a symptomatic UTI among patients who have a long-term indwelling catheter (>10 days).<br>B[55] |
| Level 2 | Reports on the results of the administration of antibiotics after removal of a (short-term) indwelling catheter show a faster clearance of bacteriuria and lower symptomatic UTI values.<br>B[27, 56, 28] |
| Level 3 | When the catheter has been removed, there is no difference in clearance of the bacteriuria after a single dose or after 10 days of antibiotics.<br>B[27] |
| Level 3 | When the indwelling catheter is removed during treatment of a symptomatic UTI, the percentage patients who exhibit elimination of the bacteriuria is higher and recovery from symptoms is faster.<br>B[29] |
| Level 3 | For the treatment of a low UTI in male patients with a spinal cord lesion, treatment for 3 days is presumably too short – but the optimal duration of treatment is unknown.<br>A2[32] |

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| Level 2 | Patients with DM suffer more often from UTIs and complications of UTIs than patients without DM.<br>B[58.34.59.33] |
| Level 3 | It is not clear whether the chance of treatment failure after treatment of a UTI is greater for women with DM compared to those without DM.<br>B[36, 37, 9] |
| * | ASB and UTIs are common in patients with renal insufficiency as well as congenital cystic kidneys and often lead to complications.<br>B[60]. C[61] |
| * | The microbial spectrum of UTI for patients with terminal renal insufficiency, congenital cystic kidneys or a pyocystis is comparable to that for the general population of patients with a complicated UTI, whereby *E. coli*, enterococci, Proteus, Klebsiella amd Pseudomonas species are prevalent.<br>B[60], C[61] |
| Level 4 | The treatment of UTIs in terminal renal insufficiency is in general the same as treatment of patients with a normal renal function with the exception that the pharmacokinetics of various antibiotics are influenced by changes in protein binding and/or renal elimination.<br>D[12] |
| Level 4 | The treatment of a patient with a UTI and congenital cystic kidneys with a marked suspicion of a cystic infection must be carried out with antibiotics which are highly active against Gram-negative micro-organisms and exhibit sufficient activity in the cyst. Options are a continuous infusion with β-lactam antibiotics combined with an aminoglycoside, the fluoroquinolones or eventually co-trimoxazole.<br>D[39] |
| Level 4 | The treatment of a pyocystis differs markedly from the treatment of a UTI for patients with normal urine output and consists of repeated catheterization or use of an indwelling catheter for bladder instillation of antibiotics, or physiological saline, with systemic antibiotics as support.<br>D[40] |

Table 3

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| General | Amoxicillin + gentamicin iv, 2nd or 3rd generation cephalosporin iv. Second choice: amoxicillin-clavulanic acid iv<br><br>Duration: at least 10 days. | In case of hypersensitivity for penicillin derivatives with only rash: 2nd or 3rd generation cephalosporin iv. Prolonged treatment with gentamicin is not recommended. Fluoroquinolones only if β-lactam antibiotics cause anaphylaxis or the entire course of treatment is oral. |
| Men with UTI | Amoxicillin + gentamicin iv, 2nd or 3rd generation cephalosporin iv. Second choice: amoxicillin-clavulanic acid iv<br><br>Duration: at least 10 days | In case of hypersensitivity for penicillin derivatives with only rash: 2nd or 3rd generation cephalosporin iv. Prolonged treatment with gentamicin is not recommended. Fluoroquinolones only if β-lactam antibiotics cause anaphylaxis or entire course of treatment is oral. |
| Chronic bacterial prostatitis | Choice of treatment determined by results of culture. A floroquinolone is first choice and co-trimoxazole is second choice.<br><br>Duration: at least 28 days | |
| Pregnant women with cystitis | Amoxicillin-clavulanic acid or nitrofurantoin (not close to delivery)<br><br>Duration: at least 5 days. | Culture of group B streptococcus is indication for antibiotic prophylaxis at the time of delivery, then consultation with gynaecologist is indicated. After completion of therapy, repeat urinalysis. |
| Pregnant women with pyelonephritis | A 2nd or 3rd generation cephalosporin iv. Second choice: amoxicillin-clavulanic acid iv<br><br>Duration: at least 10 days. | At the start of therapy, hospitalize patient. Culture of group B streptococcus is indication for antibiotic prophylaxis at the time of delivery, then consultation with gynaecologist is indicated. After completion of therapy, repeat urinalysis. |
| UTI without systemic symptoms in case of catheter ≤10 days. | Choose drug on basis of results of culture. Oral therapy is also possible.<br><br>Duration: 5 days | In case of hypersensitivity for penicillin derivatives with only a rash: 2nd or 3rd generation cephalosporin iv. Prolonged treatment with gentamicin is not recommended. Fluoroquinolones are only indicated if β-lactam antibiotics cause anaphylaxis or when the entire course is given orally. As part of treatment, change the catheter. |

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| UTI with systemic symptoms in case of catheter ≤10 days | Amoxicillin + gentamicin iv; 2nd or 3rd generation cephalosporin iv. Second choice: amoxicillin-clavulanic acid iv.<br><br>Duration: 10 days | In case of hypersensitivity for penicillin derivatives with only rash: 2nd or 3rd generation cephalosporin iv. Prolonged treatment with gentamicin is not recommended. Fluoroquinolones are only indicated if β-lactam antibiotics cause anaphylaxis or the entire course is oral. As part of treatment, change the catheter. |
| UTI without systemic symptoms in case of (intermittent) catheter >10 days | Choose drug on the basis of culture results. Empirical therapy: a fluoroquinolone or gentamicin iv.<br><br>Duration: 5 days. | As part of treatment, change the catheter. |
| UTI with systemic symptoms in case of (intermittent) catheter >10 days | Empirical treatment: fluoroquinolone or gentamicin iv.<br><br>Duration: at least 10 days. | As part of treatment, change the catheter. |
| Female with DM and cystitis | Amoxicillin-clavulanic acid or nitrofurantoin.<br><br>Duration: 7 days | |
| Female with DM and pyelonephritis | Amoxicillin + gentamicin iv, 2nd or 3rd generation cephalosporin ic. Second choice: amoxicillin-clavulanic-acid.<br><br>Duration: at least 10 days. | In case of hypersensitivity for penicillin derivatives with only rash: 2nd or 3rd generation cephalosporin iv. Prolonged treatment with gentamicin is not recommended. Fluoroquinolone only if β-lactam antibiotics cause anaphylaxis or the entire course is oral. |
| UTI in patients with congenital cystic kidneys with an infected cyst. | A fluoroquinolone or a β-lactam antibiotic with aminoglycoside. Second choice: co-trimoxazole.<br><br>Duration 4-6 weeks. | A continuous infusion of a β-lactam antibiotic can be considered. |
| Patients with pyocystis | Systemic antibiotics on the basis of the results of the culture.<br><br>Duration: at least 10 days. | In addition repeated catherization or indwelling catheter for instillation into the bladder of antibiotic, physiological saline. |

## Legends

Table 1

Resistance percentages of Escherichia *coli, Klebsiella pneumoniae* and *Proteus mirabilis* from patients admitted to a non-selected department (not Urology, not Intensive Care).[4, 5] In addition data from Ellen Stobberingh, medical microbiologist (personal communication). Eventual brand name in parentheses behind generic names. For further explanation, see text.

1. Isolates from the Department of Urology in 2003
2. Isolates from Intensive Care in 2002

Table 2

**Conclusions from the literature**

For the classification of the literature according to the degree of value as evidence, which applies for literature for diagnostics and intervention, and the search strategy, see the CBO classification. The study group means that this system is not applicable to some rare diseases, such as pyocystis, and some literature (such as "Nethmap" by SWAB). Despite the lack of a level the report "Nethmap" must be awarded a certain weight because the results cover 30% of the Dutch population. There where the level of the literature cannot be applied, we have placed an asterisk (*).

Table 3

Summary of the recommended guidelines for the various groups of patients. Empirical therapy is the therapy chosen before the results of cultures are known. After the results are known the therapy must be adjusted and if possible the spectrum must be narrowed down. Intravenous is abbreviated as iv.

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