Urinary tract infections in adult general practice patients

Eva Hummers-Pradier and Michael M Kochen

SUMMARY
Urinary tract infections (UTIs) are symptomatic infections of the urinary tract, mainly caused by the bacterium Escherichia coli. One in two women suffers from a UTI at least once in her life. The young and sexually active are particularly affected, but it is also seen in elderly, postmenopausal women. The likelihood of recurrence is high. Diagnosis is made with regard to typical complaints and the presence of leucocytes and nitrites in the urine. A culture is unnecessary in most cases. Uncomplicated UTI should be distinguished from complicated UTI, which has a risk of severe illness. The treatment of choice — short-term therapy with trimethoprim or nitrofurantoin — is successful in over 80% of the cases. Co-trimoxazole, fluoroquinolones or cephalosporins are not considered first-choice drugs. There are indications that general practitioners’ (GPs’) management of UTI is not always optimal, specifically concerning diagnostic tests, the application of second-choice antibiotics, and the length of prescribed treatment courses. Many points relevant to GPs require further research, such as epidemiology and resistance of urinary pathogens in the community and natural history of UTI, as well as optimal management in elderly or complicated patients and men.

Keywords: urinary tract infection; antibiotics; bacterial resistance; optimal treatment.

Introduction
INCREASING concern about the use — or misuse — of antibiotics, resulting in increasing resistance, has highlighted the need for rational pharmacotherapy of common infections in general practice. Relatively little is known about how general practitioners (GPs) actually manage urinary tract infection (UTI). A prospective study in Dutch general practices,1 three vignette-based studies from the United States2 and several European countries3,4 as well as prescribing surveys from the United States5 and The Netherlands, Norway and Sweden6 and prescription statistics6 indicate that management (of uncomplicated cases) could be improved: Diagnostic tests are not always employed appropriately; for example, more urine cultures than necessary are being performed. Second choice antibiotics (e.g. fluoroquinolones, co-trimoxazol) are frequently used in some countries5,7 and longer treatment courses than recommended are often prescribed.8,9 In some countries, use of irrational medication, such as antispasmodics or plant extracts, is high.6

Method
Literature was researched in MedLine, using the American National Library of Medicine internet page (PubMed) (1966–2002). Relevant articles were identified using the following keywords: ‘urinary tract infection’, ‘cystitis’, ‘pyelonephritis’, ‘dysuria’, ‘urethral syndrome’, ‘irritable bladder’, ‘bacteriuria’, ‘urethritis’, and ‘urinary symptoms’, as well as drug names (international non-proprietary names). A similar search was performed in EMBASE and the Cochrane Register of Randomised Controlled Trials. Articles with relevance for general practice were identified manually, and searched using the keywords ‘family practice’, ‘general practice’, and ‘primary care’. However, the search was not limited to articles with these keywords. The Cochrane Library was searched for relevant reviews. Non-indexed journals were scrutinised manually. Additionally, a manual literature search was performed using the reference lists of recent reviews and guidelines.10 Studies clearly not relevant to general practice (such as, for example, those referring to hospitalised patients) were eliminated and the remaining articles were read and assessed for their validity. Both authors searched and identified relevant articles and cross-checked their results. Oxman’s criteria11 were used to assess the quality of articles. While all articles were read, assessed, and summarised by the leading author (EH-P), this was done in close cooperation with MMK, who also evaluated literature on key or critical points. Grades of recommendation (US Agency for Health Care Policy and Research, 1992) are given for therapeutic proposals: grade A indicates the presence of at least one randomised controlled trial (RCT) as
Urinary tract infection mainly affects women. One out of two suffers from UTI at least once in her life — 12% of women with an initial infection and 48% who already had recurrent UTI will have a further episode within one year. Risk factors in young women are previous UTIs, sexual intercourse, the use of diaphragms and spermicides, young age at first UTI (below 15 years), and maternal history of UTI. Genetic factors also influence susceptibility to UTI. In the elderly, particularly if they live in senior citizen’s or nursing homes, asymptomatic bacteriuria (which does not require treatment), is common. However, symptomatic UTI also occurs frequently.

Urinary tract infection is one of the most frequent reasons for consulting a GP. It is the ninth most frequent reason (equivalent to 1.6%) of all outpatient consultations in Sweden. In Dutch general practices, the frequency of UTI within one year was 23.3 per 1000 patients. In German primary care practices the figure was 37.4 per 1000 patients in 1995 (IMS, Frankfurt, unpublished data). Typical symptoms of UTI are frequent, urgent and/or painful micturition and pain in the lower abdomen. Usually, these symptoms occur suddenly in an otherwise healthy person.

A general practice-based Scandinavian study showed that Escherichia coli was the causative agent in 80% of UTI cases acquired outside hospitals or nursing homes (13% were caused by Staphylococcus saprophyticus, and less frequently by other enterobacteria).

Complicated UTI, i.e. all UTIs in patients with particular risk factors or concomitant diseases, have to be regarded separately (Box 1). In some healthcare settings; for example, in Germany, up to 40% of GP patients with symptoms evoking UTI present with complicating factors. Experts claim that these patients are at a higher risk of developing complications; (evidence grade C); in particular, in the event of an obstruction of the urinary tract (e.g. urolithiasis or pregnancy), uresepsis may occur. In geriatric patients, oligosymptomatic pyelonephritis can be confused with uncomplicated UTI; these patients are considered susceptible to septic disease. As patients with chronic conditions or complicating factors are usually excluded from RCTs on treatment of UTI, little is known about optimal management.

Uncomplicated or complicated UTI has to be distinguished from pyelonephritis. In the latter, fever, kidney pain (on palpation/percussion) and a general feeling of illness are present, sometimes in addition to the symptoms of UTI. Oligo- or asymptomatic pyelonephritis can occur in infants or geriatric patients.

**Results**

Literature on urinary tract infection is extensive: a MedLine search on ‘urinary tract infection’ without time limits retrieves over 29 000 articles; additional papers were found using the other keywords, other databases or through manual search.

**Epidemiological overview**

Urinary tract infection mainly affects women. One out of two suffers from UTI at least once in her life — 12% of women with an initial infection and 48% who already had recurrent UTI will have a further episode within one year. Risk factors in young women are previous UTIs, sexual intercourse, the use of diaphragms and spermicides, young age at first UTI (below 15 years), and maternal history of UTI. Genetic factors also influence susceptibility to UTI. In the elderly, particularly if they live in senior citizen’s or nursing homes, asymptomatic bacteriuria (which does not require treatment), is common. However, symptomatic UTI also occurs frequently.

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**Prognosis**

Experts agree that the prognosis of uncomplicated UTI in adult women is good. In the absence of predisposing factors (anatomical or functional abnormalities are rare in adult women), there are no grounds for fear of renal damage and failure. A questionnaire-based study of patients in one British general practice showed that many women try to treat an episode of dysuria with home remedies. If they consult their doctor at all, they often wait several days before seeing their GP; apparently without suffering damage (evidence grade B). This may imply that the treatment of uncomplicated UTI serves above all to control symptoms rather than to prevent complications. Nevertheless, studies on a wait-and-see approach or the natural history of untreated UTI could not be located.

In complicated UTI, the prognosis depends on the underlying condition. No literature on the prognosis of general practice patients with underlying ‘complicating conditions’, such as diabetes or urolithiasis, could be identified.

**Diagnosis**

The patient’s history and description of symptoms serve to determine the diagnosis and to exclude complicated UTI. Enquiries should be made about predisposing factors, such as previous UTI, concurrence of UTI and sexual intercourse, and the use of diaphragms or spermicides.

Differential diagnoses of uncomplicated UTI include urethritis (caused by chlamydia, gonococci or herpes simplex viruses), and colpitis. In most cases the history and the detailed description of complaints will already lead to the
correct diagnosis. In some women presenting with symptoms evoking UTI, standard urine culture fails to identify a causative organism (17% to 53%, depending on inclusion criteria and diagnostic techniques). This condition is often labelled as ‘urethral syndrome’, ‘interstitial cystitis’ or ‘irritable bladder’ (a term mainly promoted by the pharmaceutical industry) and has not been well explained. A multitude of possible explanations has been postulated and (controversially) discussed, including bacteria that are present in low concentrations or

Table 1. Recommendations and their evidence.

<table>
<thead>
<tr>
<th>Statement/recommendation</th>
<th>Reason</th>
<th>Grade of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diagnostic strategies</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Identify complicated patients</td>
<td>Higher risk of developing complications</td>
<td>C</td>
</tr>
<tr>
<td>Good prognosis for women with uncomplicated UTI</td>
<td>No grounds for fearing renal damage and failure</td>
<td>A</td>
</tr>
<tr>
<td>No harm in delayed or no consultation</td>
<td></td>
<td>B — observational study from a single practice</td>
</tr>
<tr>
<td>Physical examination unnecessary in patients with uncomplicated UTI, who communicate well</td>
<td>Telephone management feasible and safe</td>
<td>B</td>
</tr>
<tr>
<td>Urine examination instead of empirical treatment</td>
<td>Limits use/misuse of antibiotics: possibly identifies patients who may benefit from exploration</td>
<td>?</td>
</tr>
<tr>
<td>10^2 CFU/ml sufficient for the diagnosis of UTI</td>
<td></td>
<td>B</td>
</tr>
<tr>
<td>Urine culture not necessary for uncomplicated UTI</td>
<td></td>
<td>B</td>
</tr>
<tr>
<td>No midstream or clean-voided specimen necessary</td>
<td></td>
<td>B</td>
</tr>
<tr>
<td>No sediment</td>
<td>No improved diagnostic certainty compared with dipsticks</td>
<td>A</td>
</tr>
<tr>
<td>Use dipsticks</td>
<td>In general practice conditions, a positive nitrite test has high positive predictive value (90–100%), but low sensitivity (46%). The leukocyte esterase test is very sensitive (83%). If both tests are negative, probability of UTI is low.</td>
<td>A</td>
</tr>
<tr>
<td><strong>Culture in all complicated patients</strong></td>
<td></td>
<td>? — no evaluated management strategy</td>
</tr>
<tr>
<td>Examine pregnant women after treatment</td>
<td>Treatment of asymptomatic bacteriuria is indicated in this patient group only</td>
<td>A</td>
</tr>
<tr>
<td>Re-examination after treatment</td>
<td>Asymptomatic bacteriuria not linked to morbidity or mortality</td>
<td>A</td>
</tr>
<tr>
<td>No additional diagnostic tests in premenopausal women with recurrent uncomplicated UTI</td>
<td>Anatomical or functional abnormalities very rare</td>
<td>A — small prospective trial</td>
</tr>
<tr>
<td>Gynaecological assessment in postmenopausal women with recurrent UTI</td>
<td>Descensus uteri/prolapse of the uterus with cystocele and residual urine promotes UTI</td>
<td>C</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trimethoprim or nitrofurantoin are first choice drugs</td>
<td></td>
<td>A</td>
</tr>
<tr>
<td>Studies on long-term prophylaxis with nitrofurantoin are favourable</td>
<td></td>
<td>B — retrospective cohort</td>
</tr>
<tr>
<td>Nitrofurantoin equivalent to trimethoprim, co-trimoxazole, and ciprofloxacin</td>
<td>In terms of both efficacy and tolerability</td>
<td>B</td>
</tr>
<tr>
<td>Fluoroquinolones offer no advantage over first-choice drugs</td>
<td></td>
<td>A</td>
</tr>
<tr>
<td>Patients prone to recurrent UTI should avoid getting cold</td>
<td></td>
<td>B — one small trial experimental</td>
</tr>
<tr>
<td>Avoid exaggerated genital ‘hygiene’ (deodorant sprays, vaginal lotions or douching, etc) and contraception by spermicides or diaphragms</td>
<td>Damage to the physiological vaginal flora facilitates UTI</td>
<td>A</td>
</tr>
<tr>
<td>Treat for three days in women aged under 65 years</td>
<td>As effective as a longer course, fewer adverse effects</td>
<td>A</td>
</tr>
<tr>
<td>Treat UTI recurring shortly after index episode with first-choice drug for 10 days</td>
<td></td>
<td>C</td>
</tr>
<tr>
<td>Treat recurrent UTI with first-choice drug for three days</td>
<td>Treat as if it was a first infection</td>
<td>B — no studies on reinfection, cited studies on self-treatment use fluoroquinolones</td>
</tr>
<tr>
<td>Use of second-choice drugs is usually not necessary</td>
<td></td>
<td>?</td>
</tr>
<tr>
<td>Concurrency with sexual intercourse: 100 mg trimethoprim after intercourse</td>
<td>Effective and well tolerated</td>
<td>A</td>
</tr>
<tr>
<td>Recurrence prophylaxis with with 50 mg trimethoprin daily or 50 mg nitrofurantoin daily for six months</td>
<td></td>
<td>A</td>
</tr>
<tr>
<td>Local oestrogen in post-menopausal women</td>
<td>Reduces the frequency of UTI</td>
<td>A</td>
</tr>
<tr>
<td>No treatment of asymptomatic bacteriuria except in pregnancy</td>
<td>No reduction in mortality or the rate of symptomatic UTI, instead it promotes colonisation with resistant bacteria or fungi</td>
<td>A</td>
</tr>
</tbody>
</table>
are difficult to culture, unspecific inflammation, psychological origin or muscular dysfunction.\textsuperscript{46-51}

There is no evidence for benefits of physical examination in patients with a good ability to communicate. In some countries (e.g. The Netherlands) patients with uncomplicated UTI are primarily managed by practice nurses or practice assistants,\textsuperscript{52,53} an approach also shown to be safe and effective in a small RCT\textsuperscript{54} (evidence grade B).

An American, as well as a British, study claim that treating all symptomatic women with antibiotics without any further diagnostic procedures is the most cost-effective procedure, even when possible adverse outcomes are taken into account.\textsuperscript{55,56} However, most authors agree that an examination of urine should be performed to ascertain the diagnosis of UTI, to limit unnecessary use of antibiotics, and to identify patients that may benefit from further exploration.\textsuperscript{38,52,56-58}

Several techniques are available; urine cultures are frequently used as the gold standard when evaluating different methods. If bacteriuria is assessed quantitatively, 10\textsuperscript{2} colony-forming units (CFU) per ml are sufficient for the diagnosis of UTI\textsuperscript{59-60} (grade B evidence). However, in most general practice cases, urine culture is not necessary for uncomplicated UTI\textsuperscript{61} (grade of evidence B), and has been shown to have little impact on management.\textsuperscript{62} Controversially, Ross, commenting on Fenwick’s paper about cost-effectiveness of UTI treatment,\textsuperscript{56} and Davey\textsuperscript{63} questioned whether GPs should be encouraged to use both near-patient testing (dipsticks or microscopy) and bacterial culture, to target antibiotic prescriptions more effectively,\textsuperscript{64} an approach not yet evaluated for feasibility, efficiency, and benefit. Different management strategies have not been studied in patients with complicating factors.

Dipsticks testing for leucocytes and nitrite, or microscopy of either native urine or sediment, can be used for a fast assessment of fresh urine of ‘uncomplicated’ symptomatic patients: Only freshly voided urine should be tested (nitrite produced by contaminating bacteria can induce false-positive results in older specimens). The recommendation to use a midstream or clean-voided specimen is not evidence-based\textsuperscript{56-68} (evidence grade B).

In symptomatic female general practice patients, the sensitivity of a positive dipstick test for nitrite has been reported to be 62%, with a specificity of 89% if performed under laboratory conditions.\textsuperscript{55} The test seems to be less reliable when performed in general practice: a sensitivity of 53% to 66% and a specificity of 75% to 95% have been reported.\textsuperscript{1,69} A dipstick positive for leucocytes has a higher sensitivity (88% to 96%), but a very low specificity (16% to 37%)\textsuperscript{1,70} when performed in general practice. Compared with the dipstick method, the examination of the urinary sediment is laborious and often incorrectly performed (owing to, for example, examination of insufficiently spun urine, using fewer than five fields or using fields chosen for cell content rather than chosen randomly) and does not improve diagnostic certainty\textsuperscript{68} (evidence grade A). As neither method exhibits superior performance, the time-saving dipstick test can be recommended for general practice (Table 2).

If nitrite (with or without leucocytes) is positive, the patient is very likely to have a UTI (according to culture as a gold standard) and antibiotic treatment is justified. If both nitrite and leucocytes are negative, four out of five patients will not have UTI and antibiotics should not be given. A culture (or gynaecological assessment) may be indicated in patients with severe or persistent symptoms. A dipstick result positive for leucocytes by itself is not helpful: half of these patients will have UTI and half will not, so no information is added to the 58% baseline probability of UTI. In this case, a culture should be performed (this applied to almost half of the study sample), and antibiotic treatment delayed until results are known, to avoid overtreatment. The utility of sediment microscopy as a second test for these cases of doubt has not been studied. Searching for leucocytes and bacteria in uncentrifuged urine using a counting chamber is valid under laboratory conditions\textsuperscript{71,72} (evidence grade B) but has not been evaluated under general practice conditions. The method is also quite time consuming. Sexually transmitted diseases or renal tuberculosis should be considered in patients presenting with urinary symptoms if no other diagnosis can be established, though we could not find data on the prevalence of these conditions in symptomatic general practice patients.

After clinically successful therapy of an uncomplicated UTI, an examination of the urine for bacteria is only required in pregnant women; treatment of asymptomatic bacteriuria is indicated in this patient group only (recommendation grade A), as there is a risk of pyelonephritis and preterm delivery, while asymptomatic bacteriuria is not linked to morbidity or mortality in other patients.\textsuperscript{12,20} Additional diagnostic tests should not be performed routinely in premenopausal women with recurrent uncomplicated UTI, as anatomical or functional abnormalities of the urinary tract are very rare in general practice patients\textsuperscript{59,73} (recommendation grade A). Postmenopausal women may benefit from a gynaecological assessment as descensus uteri/prolapse of the uterus with cystocele and residual urine promotes UTI\textsuperscript{67} (evidence grade C).

**Counselling and treatment**

A woman suffering from uncomplicated UTI should be informed about the harmlessness of her condition, but also about possible recurrences and — in this case — about the relationship between UTI and sexual intercourse. Asking a patient about her own conception of the illness may (as in many general practice consultations) improve mutual understanding.\textsuperscript{43} Non-pharmaceutical measures for the actual episode or recurrence prophylaxis (see below) can be recommended, though not all current concepts are based on
evidence. Generally, drug treatment is thought to be necessary to ensure quick symptom control.

**First-choice drugs**

Drugs of choice for UTI should be effective, safe, and suitable for short-term therapy. Both trimethoprim and nitrofurantoin fulfill these requirements for general practice patients (recommendation grade A, see later). They are well tolerated, and the patient’s physiological intestinal flora is hardly affected. Nevertheless, the local epidemiology and resistance patterns must be taken into account when prescribing an empirical treatment. Clinical outcomes do not always correlate with the level of sensitivity indicated in an antibiogram.63,74 Several studies (albeit with low patient numbers and various antibiotics) indicate that more than half the patients treated with a drug tested as resistant will be clinically and microbiologically cured;75,76 the implications of these findings have not been studied further. Hospital or laboratory-based surveys or studies of selected patients have to be considered carefully with respect to their validity for general practice.77 Further research is necessary. Few recent general practice-based systematic surveys on antibiotic resistance of urinary pathogens have been conducted in Europe; nevertheless, these studies indicate that resistance to trimethoprim or co-trimoxazole may be rising to levels compromising its use as a first-choice drug — 18% in Dutch practices78 and 14% in a Belgian practice.79 A cross-sectional survey in American patients in health maintenance organizations (HMOs)80 also indicates increasing resistance, though this study may be of limited relevance to general practice. Since recent antibiotic therapy has been shown to increase the likelihood of resistance, further studies evaluating risk factors for resistance and the impact on clinical failure could be helpful.81 Use of nitrofurantoin has been discussed somewhat controversially in Europe. Potentially dangerous side effects (polyneuropathy, interstitial pneumonia, hepatitis) have been discussed internationally82 and were put forth as arguments against its use in Germany,83 whereas it is considered a first-choice drug in many other European countries (e.g. The Netherlands, Norway, Sweden). Nevertheless, most adverse effects are mild and self-limiting and serious toxicity is extremely rare (similar to trimethoprim), tending to appear after prolonged exposure.84,85 Resistance to nitrofurantoin remains low at between 3% and 11%.78,80 An observational study on long-term prophylaxis with nitrofurantoin was favourable with regard to efficacy and safety86 (recommendation grade B). Concerning the treatment of acute UTI, only a few trials were identified: nitrofurantoin proved equivalent to trimethoprim, co-trimoxazole and ciprofloxacin, in terms of both efficacy and tolerability87,88 (recommendation grade B). Recommendations concerning pregnant women differ: while in some countries nitrofurantoin and trimethoprim are considered appropriate,89,90 drug formularies in other countries (e.g. Germany) warn against their use. Cephalosporins (see below) can be used alternatively.

Pivmecillinam or mecillinam are recommended in some countries (e.g. Norway),91 though in others they are not on the market. In older trials, pivmecillinam performed well in ambulatory patients;92 these findings were confirmed by a recent trial and a retrospective survey.93 A hospital-based Canadian study reports low resistance among UTI pathogens.94 A recent review article demands the role of pivmecillinam to be reassessed in comparative trials and studies of resistance in general practice patients.95

**Second-choice drugs**

According to older trials and recommendations, the combination of trimethoprim and sulfamethoxazole (co-trimoxazole) offers no advantages when compared with trimethoprim alone.96-99 Instead, there is a higher risk of adverse effects — particularly allergies caused by the sulfonamide component — and there may be increased selection pressure for resistant bacteria. In a recent retrospective survey, Lawrenson found a slightly lower risk of recurrence in patients who had received co-trimoxazole instead of trimethoprim; however, owing to the small differences, trimethoprim is still being recommended as first-line treatment.5

Fluoroquinolones, though effective (except against *Staphylococcus saprophyticus*) offer no advantage over first-choice drugs76 (recommendation grade A). They are contraindicated in pregnancy. Adverse effects, such as phototoxic skin reactions and cerebral dysfunction (mainly in patients aged over 70 years) are potentially serious, though rare in UTI treatment.100,101 As fluoroquinolones are used for serious infections in hospitals, they should not be widely used in general practice, as resistance levels are rising in countries where they are frequently prescribed in primary care.102,103 In addition, fluoroquinolones are expensive.

Fosfomycine-trometamol as single-dose therapy seems to be safe and effective, but is expensive.104,105 However, its effectiveness, compliance, adverse effects, and relapse rate have not been compared with short courses of other drugs. Studies on its effectiveness have been performed in countries (e.g. the United States) where fosfomycin is not used.

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### Table 2. Diagnostic value of dipsticks for nitrite and leucocytes (based on Verest 2000)6.

<table>
<thead>
<tr>
<th>Test result</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Positive predictive valuea (%)</th>
<th>Negative predictive valuea (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Both tests positive (n = 63) versus at least one negative</td>
<td>46</td>
<td>94</td>
<td>90</td>
<td>58</td>
</tr>
<tr>
<td>Only nitrite positive (n = 6) versus all others</td>
<td>5</td>
<td>100</td>
<td>100</td>
<td>46</td>
</tr>
<tr>
<td>Only leucocyte-positive (n = 105) versus all others</td>
<td>41</td>
<td>45</td>
<td>49</td>
<td>38</td>
</tr>
<tr>
<td>At least one test positive (n = 174) versus both negative (n = 47)</td>
<td>93</td>
<td>39</td>
<td>65</td>
<td>81</td>
</tr>
</tbody>
</table>

*68% of the sample population (n = 221) had UTI confirmed by culture.*
Resistance against ampicillin and amoxycillin is common (23% to 30%\(^22,78,79\)) making its use for empirical therapy questionable in the presence of alternatives. However, depending on the local resistance pattern and patient profile, amoxycillin can be considered as a relatively inexpensive option.

Cephalosporins, including the older ones, such as cefadroxil and cephalaxin, are generally effective,\(^{106,107}\) although some experts, in addition to a study on selected American HMO patients, warn against resistance.\(^{22,57}\) Third-generation cephalosporins are effective, but expensive.\(^{108}\) It has been pointed out, however, that cephalosporins have higher rates of adverse effects (particularly vaginitis) than trimethoprim and clinical outcome is not always as positive as should be expected from antibiograms.\(^53\) Cephalosporins are reserve antibiotics for severe (non-UTI) infections and should not be used empirically for UTI in non-pregnant patients. In pregnant women, they can be used as first choice if nitrofurantoin or trimethoprim are not considered appropriate by local formularies. Adequacy of short-course therapy has not been proven for this indication.

Although their effectiveness in relieving UTI symptoms has not been studied, antispasmodics, such as trospiumchloride and flavoxate are frequently prescribed for this purpose in Germany.\(^7\)

Adjuvant measures

Adjuvant measures for treatment — or, rather, recurrence prophylaxis — are often asked for by patients\(^32\) or recommended by GPs, based on risk factor studies.\(^22,23\) Most have not been evaluated in randomised trials or prospective studies. Sufficient fluid intake (at least two litres per day) and regular voiding is commonly believed to have a ‘flushing’ effect on the urinary tract; bacterial proliferation might be hindered, owing to a shorter retention of urine in the patient’s bladder. However, no trials of the effect of high fluid intake on UTI could be found. Micturition after sexual intercourse is supposed to rinse bacteria from the bladder and thus prevent UTI.\(^109\) As cooling of the feet has been shown to promote an acute episode in patients prone to recurrent UTI, they should try to avoid getting cold (recommendation grade B).\(^112\) Since damage to the physiological vaginal flora facilitates UTI, exaggerated genital ‘hygiene’ (deodorant sprays, vaginal lotions or douching, etc) should be avoided\(^22\) (recommendation grade A). If possible, other methods of contraception should be used in preference to spermicides or diaphragms (recommendation grade A).\(^22\) Although acupuncture has been shown to be successful in preventing frequent UTI episodes in one randomised, single-blind controlled trial in 67 patients with recurrent UTI,\(^111\) further trials should be performed to refute or confirm these results. Drug preparations and teas based on various plant extracts are very popular with both patients and GPs in Germany; cranberry products have been advocated in America. Their effectiveness in the treatment of acute UTI, however, has never been tested in RCTs.\(^15\) The (prophylactic) consumption of cranberry juice or cranberry extracts has also been advocated to lower the rate of recurrent UTI,\(^112,113\) but a Cochrane review\(^14\) concluded that, owing to the high number of dropouts, the lack of an intention-to-treat analysis, and baseline differences between the randomisation and control groups, the evidence is insufficient to confirm the usefulness of cranberry products in UTI prevention thus far. A recent randomised trial\(^14\) indicates a reduction of UTI episodes, but has similar flaws to earlier trials: the number of eligible patients is not reported and it took several years to recruit the relatively few participants. At present, plant extracts do not satisfy the requirements of rational pharmacotherapy. This is equally true for methenamine hippurate as a preventive agent.\(^19\) Bacterial extracts, which are supposed to act as ‘oral vaccines’, to reduce susceptibility to UTI seem to be promising; however, properly designed RCTs are required to confirm these findings.\(^115-117\)

Duration of therapy

In women under the age of 65 years, a three-day course of trimethoprim has shown to be as effective as a longer course, but caused fewer adverse effects\(^118,119\) (recommendation grade A). This is equally the case for some second-choice drugs (co-trimoxazol, fluoroquinolones).\(^120\) Compliance is often better, and the risk of adverse effects and damage of the patient’s physiological flora is less than with longer treatment.\(^121\) In about 82% of all patients, a single-dose therapy with trimethoprim is also clinically effective\(^122\) and very cost effective.\(^123\) Nevertheless, bacteriuria is eradicated more effectively using a longer therapy (94%), and the likelihood of recurrence is lower (29% versus 13% after five weeks).\(^120,122,124,125\)

In elderly women who live in care homes and have limited mobility, complicating factors (such as residual urine, poor immunity response) are probably more common. As short-term therapies are not well studied in this group, treatment for seven days is recommended by experts.\(^29\) A recent Cochrane review stated that although single-dose is less effective than treatment for three to 14 days, no difference could be found between shorter (three to five days) and longer courses. However, the poor quality of the included studies was criticised and optimal treatment duration for UTI in elderly women could not be determined.\(^18\)

Recurrent UTI

In the case of recurrent UTI, relapses are traditionally distinguished\(^27,126,127\) from reinfection; however, no strong evidence supporting this approach could be found.

Recurrent UTI may be caused by persisting bacteria (e.g. having invaded the bladder epithelium), despite initial clinically successful therapy or even sterilisation of the urine.\(^128\) Two recent, large retrospective surveys showed that between 8% and 15% of women receiving (empiric) antibiotics treatment for UTI had symptoms requiring another course of antibiotics within four weeks, irrespective of the type of antibiotic and the duration of the treatment prescribed initially.\(^8,9\) A second course, longer than the stan-
dard three days, of a first-choice drug has been proposed (recommendation grade C) for treatment of UTI recurring shortly after an initial episode. Most recurrent UTIs, however, seem to be caused by reinfections from the bowel or vaginal bacterial flora, and should again be treated with short-term therapy (recommendation grade B). Use of second-choice drugs is, however, probably not necessary and should be avoided (see above).

Further routine diagnostic procedures are not indicated in patients with recurrent uncomplicated UTI, and subgroups for whom investigations would be beneficial have not yet been identified (recommendation C). For frequently recurring UTI, different therapeutic/prophylactic regimens can be useful; if UTI episodes occur frequently after sexual intercourse, and if postcoital voiding is not successful, 100 mg trimethoprim can be taken after sexual intercourse (recommendation grade A). Otherwise, therapy with 50 mg trimethoprim daily or 50 mg nitrofurantoin daily for six months is effective and well tolerated (recommendation grade A). Should frequent UTI still occur after six months, this treatment can be continued for several years if necessary.

Self-administration of antibiotics has no prophylactic effect, but seems to be safe and results in successful treatment (recommendation grade A). Should frequent UTI still occur after six months, this treatment can be continued for several years if necessary.

However, high quality trials using first-choice drugs for patient-initiated treatment are lacking.

In postmenopausal women, local substitution of oestrogen (for example, vaginal cream containing oestrogens) improves the trophic of the vaginal mucosa and has been shown to reduce the frequency of UTI (recommendation grade A).

**Asymptomatic bacteriuria**

Occasionally, asymptomatic bacteriuria is found in screening tests (though screening for bacteriuria is indicated only in pregnant women — see below). There is a prevalence in female adults under 60 years of age of about 5%; of these, only a few (8%) develop subsequent symptomatic UTI within one week (as do 15% of those presenting with asymptomatic bacteriuria and pyuria). In elderly people, asymptomatic bacteriuria is much more prevalent — up to 50% for demented, incontinent patients. Nearly 100% of those with indwelling catheters have bacteriuria after 30 days. Only in pregnancy does asymptomatic bacteriuria require therapy.

Other patients, including elderly patients and those with indwelling catheters, diabetes or spinal cord dysfunction, should not be treated, as there is no reduction in mortality, the rate of symptomatic UTI, or urinary incontinence. Rather, it promotes colonisation with resistant bacteria or fungi (recommendation grade A).

**Implications for future research**

There is much literature on urinary tract infections, though many studies are based on (selected) outpatient groups in hospital or community specialist practices, and many trials on diagnostic tools or drug therapy only use small samples. Nevertheless, diagnosis and treatment of uncomplicated infections in women are well documented, though recommendations are probably not always followed in daily practice.
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