Urinary Tract Infection

Patient population: Adult women with uncomplicated UTI

Objective: Implement a cost-effective strategy for uncomplicated UTI in women

Key Points

■ Diagnosis
  • History. Diagnosis is made primarily by history. In women with dysuria and frequency, in the absence of vaginitis, the diagnosis is UTI 80% of the time [evidence: C*].
  • Phone triage. In women with prior history of uncomplicated UTI's, consider phone triage [C*].
  • Urinalysis. Urinalysis for detection of pyuria by dipstick or microscope has a sensitivity of 80-90% and a specificity of 50% for predicting UTI [B*].
  • No urine culture. Urine culture is NOT indicated in the vast majority of UTI's. UC has a sensitivity of 50% (if threshold for positive is >10^5 organisms), sensitivity can be increased to >90% if threshold is >10^2 organisms [C*]. Consider urine culture only in recurrent UTI or in the presence of complicating factors.

■ Treatment
  • First line - three days of trimethoprim / sulfa [A*].
  • Second line - three days of quinolone (contraindicated in pregnancy) [A*].
  seven days of nitrofurantoin, amoxicillin, 1° cephalosporin [A*].

■ Follow-up
  • No tests if asymptomatic. No laboratory follow-up is necessary if asymptomatic [B*].
  • For recurrent UTI's. In patients with recurrent UTI's (>3 / year)
    – consider prophylaxis / self-initiated therapy [A*]
    – urologic structural evaluation rarely indicated [D*]

* Levels of evidence reflect the best available literature in support of an intervention or test:
  A=randomized controlled trials; B=controlled trials, no randomization; C=observational trials; D=opinion of expert panel.

Clinical Background

Clinical Problem and Clinical Dilemma

Incidence

Urinary tract infections (UTI) are estimated to account for over 7 million office visits per year, at a cost of over $1 billion. Up to 40% of women will develop UTI at least once during their lives, and a significant number of these women will have recurrent urinary tract infections.

Cost-Effective Strategy

Establishing a cost-effective strategy for the diagnosis and treatment of UTI is important because of its high incidence. Laboratory tests should be ordered only when the results are likely to alter the process or outcome of care.

Antibiotic treatment should be prescribed only for as long as necessary to be effective. Recurrent UTI’s may be managed better by self-initiated therapy or prophylaxis than by continuing to treat each case emergently. This guideline provides an approach to uncomplicated UTI that results in good clinical outcomes and utilizes clinical care resources appropriately.

Rationale for Recommendations

The rationale for recommendations addresses:

• Risk factors
• Complicating factors
• Uncomplicated UTI
• Recurrent UTI’s
• Asymptomatic bacteriuria
• Acute uncomplicated pyelonephritis
• UTI in pregnancy

(Continued on page 3)
**Figure 1. Diagnosis and Management of UTI**

1. **Adult female with UTI symptoms phones office**
   - **Previous history of uncomplicated UTIs?**
     - Yes: Schedule office visit
     - No: Proceed to next step.

2. **Vaginitis symptoms?**
   - Yes: Evaluate for gynecologic pathology
   - No: Proceed to next step.

3. **Urinalysis microscopic dipstick results**
   - Positive: Consider:
     - Pelvic exam
     - Urine culture
   - Negative: Proceed to next step.

4. **UTI uncomplicated?**
   - Yes: Treat with 3 days Trimethoprim/Sulfa.
     - If Sulfa-allergic, see Table 3.
     - (No urine culture necessary.) [A*]
   - No: Symptoms persist?
     - Yes: Follow-up PRN (No follow-up UA or UC necessary) [B*]
     - No: Proceed to next step.

5. **Empiric treatment [B*]**
   - (See Table 3)

6. **Asymptomatic after 3 days?**
   - Yes: Empiric treatment [B*]
   - No: Proceed to next step.

7. **Follow-up PRN**

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**Table 1. Laboratory Charges (M-Labs)**

<table>
<thead>
<tr>
<th>Test</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinalysis - dipstick</td>
<td>$19</td>
</tr>
<tr>
<td>Urinalysis - microscopic</td>
<td>$15</td>
</tr>
<tr>
<td>(complete)</td>
<td></td>
</tr>
<tr>
<td>Urine culture</td>
<td>$52</td>
</tr>
</tbody>
</table>

**Table 2. Complicating Factors**

- Diabetes Mellitus
- Immunosuppression
- Urologic Structural / Functional Abnormality
- Nephrolithiasis present
- Recent Hospitalization /
  Nursing home
- Catheter
- Symptoms for > 7 days

**Table 3. Treatment Regimens and Cost***

<table>
<thead>
<tr>
<th>First Line:</th>
<th>Brand Generic</th>
</tr>
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<tbody>
<tr>
<td>Trimethoprim / Sulfa DS BID x 3 days</td>
<td>$11 / $4</td>
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</table>

<table>
<thead>
<tr>
<th>Second Line (preferred order):</th>
<th>Brand Generic</th>
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</thead>
<tbody>
<tr>
<td>Ciprofloxacin 250 mg BID x 3 days</td>
<td>$27 / $4</td>
</tr>
<tr>
<td>Levofloxacin 250 mg daily x 3 days</td>
<td>$52 / N/A</td>
</tr>
<tr>
<td>Amoxicillin 500 TID x 7 days</td>
<td>$7 / $5</td>
</tr>
<tr>
<td>Nitrofurantoin 100 QID x 7 days</td>
<td>$59 / $31</td>
</tr>
<tr>
<td>Macrobid 100 mg BID x 7 days</td>
<td>$31 / $22</td>
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</table>

*Levels of Evidence:
A = randomized controlled trials
B = controlled trials, no randomization
C = observational trials
D = opinion of expert panel

*Cost = Average wholesale price based -10% for brand products and Maximum Allowable Cost (MAC) + $3 for generics on 30-day supply or less, Amerisource AWP 01/05 & Blue Cross Blue Shield of Michigan Mac List, 01/31/05.
Rationale for Recommendations (continued)

Risk Factors

The majority of UTIs occur in sexually active women. Risk increases by 3-5 times when diaphragms are used for contraception. Risk also increases slightly with not voiding after sexual intercourse and use of spermicide. Increased risk has not been demonstrated with oral contraceptives, not voiding before intercourse, non-cotton underwear, and use of condoms.

Microbial Etiology

Escherichia coli is the predominant pathogen in uncomplicated UTI in women, associated with more than 80% of cases. Staphylococcus saprophyticus is found in 15% of cases. Other members of the Enterobacteriaceae family, such as Klebsiella sp., Proteus sp., or Enterobacter sp. are associated with uncomplicated UTI. Group B streptococci are an uncommon pathogen in UTI in young healthy women, but requires treatment in pregnant women.

Complicating Factors and Medical Conditions

Patients with complicating factors and medical conditions are at increased risk of development of pyelonephritis or infection with resistant organisms. Complicating factors are listed in Table 2 and include underlying urologic structural abnormalities, diabetes, immunosuppression, pregnancy, recent hospitalization, or urologic tract manipulation. It is necessary to differentiate these women from those with uncomplicated UTI in terms of both work-up and treatment. Unlike women with uncomplicated UTI, care for women with complicating factors includes:

- **Culture.** Obtain pretreatment culture and sensitivity.
- **Treatment.** Initiate treatment with trimethoprim / sulfa or quinolone for 7-14 days (quinolones contraindicated in pregnancy).
- **Follow-up UA.** Obtain follow-up urinalysis to document clearing.
- **Possible structural evaluation.** Lower threshold for urologic structural evaluation with cysto / IVP.

Uncomplicated UTI

**Diagnosis.** A practical, time- and cost-effective approach to the diagnosis of uncomplicated UTI in women is limited by the lack of a "gold standard" for presence of UTI. At the heart of this problem lies a debate over what actually constitutes a UTI. Traditionally, $10^5$ cfu/mL in cultured urine was the threshold. More recently, however, it is apparent that low colony counts ($10^2$ to $10^4$) may simply represent early UTI; moreover, it appears that symptoms associated with low colony counts respond to antibiotic treatment, as well as symptoms with high counts.

Laboratory diagnosis. Common tests used are: urinalysis by dipstick and urine microscopy under 40x power, both generally readily available in the clinic setting. Urine culture is more expensive and requires 24 to 48 hours for results. None of these tests have been shown to be ideal screening tools.

Dipstick analysis for leukocyte esterase, an indirect test for the presence of pyuria, is the least expensive and time intensive test. It is estimated to have a sensitivity of 75-96% and specificity of 94-98%. Depending on the cut-off used for "abnormal" pyuria as detected by urine microscopy, the positive predictive value for pyuria is only 50%. No studies were found directly comparing dipstick for leukocyte esterase with urine culture. Sensitivity is less for lower thresholds for UTI (i.e., $10^2$-$10^4$ cfu/mL) and specificity correspondingly higher for the same thresholds. Nitrite testing by dipstick is considerably less useful, probably in large part because it is only positive in the presence of bacteria that produce nitrate reductase, and can be confounded by consumption of ascorbic acid.

Microscopic examination of unstained, centrifuged urine by a trained observer under 40x power has a sensitivity from 82-97% and a specificity of 84-95%, again varying depending on defined thresholds for UTI. Microscopic urinalysis showing pyuria has a widely variable predictive value for urinary tract infection, depending upon the pretest probability.

For urine culture, sensitivity varies from 50 to 95%, depending on threshold for UTI, and specificity varies from 85-99%. Because of the limited sensitivity of urine culture, and the delay required for results, urine culture is not recommended to diagnose or verify uncomplicated UTI. With short treatment courses, treatment is nearly complete before culture results are available.

Several factors also may affect the validity of diagnostic testing. Apparent pyuria in a "clean-catch" urine specimen in clinic may in fact represent contamination from vaginal discharge. Apparent bacteriuria may similarly represent perineal or vaginal contamination. Leukocyte esterase, an indirect test for the presence of WBCs, may be negative in early but significant infection.

Diagnosis based on symptoms. In the setting of uncertain validity of testing, the prior probability of infection (i.e., before diagnostic testing) helps to determine which patients will likely benefit from treatment. Available data indicate that dysuria with either urgency or frequency, in the absence of vaginal symptoms, yield a prior probability of UTI of at least 70-80%. Dysuria alone is less useful, yielding only a 25% probability of UTI. Similarly, the presence of vaginal symptoms in addition to urinary symptoms markedly decreases the likelihood of UTI (about 25% probability).
Back pain and previous history of UTI have also been shown to increase the likelihood of UTI. Other symptoms which probably increase likelihood of UTI (but about which no data were found) include urinary urgency, new urinary incontinence, voiding of small volumes, suprapubic pain, and nocturia. Generally, UTI symptoms are of abrupt onset (<3 days); a longer or intermittent course of symptoms increases the likelihood of other etiologies besides UTI.

Summary of diagnostic approach. The diagnostic evaluation for UTI therefore begins with an estimation of prior probability of UTI based on the patient's symptoms. From the preceding, it is clear that presence of vaginal symptoms necessitates pelvic examination; however, in the absence of vaginal symptoms, vaginitis is very uncommon and pelvic examination is unnecessary. One caveat: the physician, nurse practitioner or triage nurse should be wary of anything in the patient's history that would increase the risk for sexually transmitted infection, as this may call for pelvic examination as well.

Beyond performing a pelvic examination in patients for whom it is indicated, no formal physical exam is needed, unless the patient has complaints suggestive of pyelonephritis (see that section).

With a number of "classic" UTI symptoms, the prior probability of UTI very likely exceeds 80% and may in fact exceed the predictive usefulness of either dipstick urinalysis or urine microscopy. Therefore, it may be appropriate to simply treat a patient with classic UTI symptoms without any diagnostic testing.

If diagnostic testing is desired, dipstick UA (the cheapest and quickest test) should be performed first. If this confirms a high likelihood of UTI, no further testing need be done, and treatment can be initiated. If dipstick UA is equivocal, possible next steps would be to perform a pelvic exam, perform urine microscopy, and/or defer treatment and send urine for culture.

Treatment. Acute uncomplicated cystitis in women historically has been treated with longer (7-10 day) courses of antibiotics. More recent studies have found shorter courses (3-5 days) of oral antibiotics to be as effective as traditional courses. A review of 28 treatment trials of adult women with uncomplicated cystitis concluded that no benefit was achieved by increasing the length of therapy beyond 5 days. The advantages of shorter course therapy include decreased costs of antibiotics, improved patient compliance and decreased adverse effects of antibiotic treatment (e.g., amoxicillin associated vaginitis).

When comparing the different treatment strategies, single-dose regimens are less efficient at eradicating bacteruria, than 3-5 day regimens (23-81% versus 77-91% long-term cure, respectively). Beta-lactam antibiotics are more effective, with cure rates of 77 to 92%, if given greater than 5 days. Similarly longer courses of 7 days for nitrofurantoin are recommended. There appears to be no benefit in increasing the duration of trimethoprim/sulfamethoxazole (TMP/SMX) or trimethoprim (TMP) beyond 3 days; cure rates of 82 to 85% have been achieved with 3-day therapy. Adverse effects increase markedly if treatment is continued past 3 days.

Of the 3-day regimens, TMP/SMX is more effective and less expensive than nitrofurantoin, cefadroxil, or amoxicillin for treatment of uncomplicated cystitis in women. Quinolones have also been shown to be effective in 3-day courses, however cost is increased significantly over TMP combinations. Ciprofloxacin, 100 mg BID for 3 days, appears to be the most cost effective quinolone regimen/SMX. Therefore, the optimal treatment of uncomplicated UTI in patients who are not allergic or sensitive, is 3-days of TMP/SMX.

Longer courses of therapy should be used in women who are diabetic, pregnant (quinolones contraindicated), have had symptoms longer than 7 days, or have other evidence for complicated UTI (see Table 2). In general, older women with lifelong history UTI and no history complicating factors are managed as uncomplicated UTI. However, specific treatment algorithms in this age group have been rarely been assessed. While 3-days of TMP/SMX is the first line in older women (>65 years), consider 7-days of TMP/SMX or 3-days of ciprofloxacin for those whose health status increases risk of urological defects.

Since 1990, there has been a steadily increasing rate of resistance to TMP/SMX, reaching >30% in some areas. The average resistance rates to TMP/SMX for E. coli in the US is 18%. Since TMP/SMX is concentrated in the urine, in vitro resistance does not necessarily translate into therapeutic failures. Gupta et al (2001) have estimated clinical and bacteriologic outcomes for varying levels of TMP-SMX resistance for uncomplicated UTI:

<table>
<thead>
<tr>
<th>TMP/SMX resistance rates</th>
<th>Expected Bacteriologic Eradication Rate</th>
<th>Expected Clinical Success Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>0%</td>
<td>93%</td>
<td>95%</td>
</tr>
<tr>
<td>10%</td>
<td>89%</td>
<td>92%</td>
</tr>
<tr>
<td>20%</td>
<td>84%</td>
<td>88%</td>
</tr>
<tr>
<td>30%</td>
<td>80%</td>
<td>85%</td>
</tr>
</tbody>
</table>

Resistance rates to quinolones have been increasing worldwide at alarming rates, reaching >20% in Spain. Quinolone resistance in E. coli in the US remains less than 5%. Similarly, nitrofurantoin resistance remains less than 5%. Cost effectiveness analyses have shown cost savings for quinolones over TMP/SMX when resistance to TMP/SMX exceeds 22%. This does not take into account potential detrimental effects of antimicrobial resistance to quinolones.
When resistance rates are less than 10-20%, TMP/SMX remains the most cost-effective therapy. If resistance rates exceed this threshold, or if the patient has risk factors for TMP/SMX resistance, then alternative therapies with a quinolone or nitrofurantoin should be considered. Factors associated with increased likelihood of resistance to TMP/SMX include: recent hospitalization, recent antibiotic use of any kind in the last month or use of TMP/SMX in the last 3-6 months, or the presence of diabetes mellitus or other complicating factors.

Recommending alternative forms of contraception is not necessary when prescribing antibiotics for UTI in women using oral contraceptives. Theoretically, antibiotics can alter hormone levels, suggesting that backup contraception could be advisable when using antibiotics and oral contraception. However, in practice no cases of oral contraceptive failure have been definitely related to antibiotic use for UTI.

**Follow-up.** Follow up urinalysis and urine cultures (so called "test-of-cure") are not indicated for women with uncomplicated UTIs. Approximately 5-10% of women treated for uncomplicated UTI will have persistent bacteruria after therapy is completed. The vast majority of these women will by symptomatic and will therefore seek medical attention. Those who are asymptomatic do not require any treatment except in select cases (see section below on asymptomatic bacteruria). Follow up urinalysis and urine culture and sensitivity (UA/C & S) should be considered in women with recurrent UTI's or complicating factors.

**Phone triage - nurse managed evaluation.** The majority of UTI's in women are uncomplicated and resolve readily with brief courses of antibiotics. Therefore, many women can be assessed and safely managed without an office visit or laboratory evaluation. A recent study in Seattle, examined a phone triage guideline. Use of the guideline decreased cost and increased appropriate antibiotic use without any increase in adverse outcomes. A form for telephone triage and management of UTI is appended to this guideline. Women who have had previous UTI's that have responded to antibiotics can be considered for phone triage and treatment without an office visit or laboratory evaluation. Management without an office visit is not recommended for women with symptoms of pyelonephritis, with complicating factors, or for women who have never been treated for a UTI. Patients who do not respond promptly (2-3 days) should be evaluated in the office.

**Recurrent UTI's**

**Diagnosis.** Eighty to ninety percent of women who have a UTI will experience another one in their lifetime. A smaller subset of these women (5-10%) will experience recurrent urinary tract infection defined as greater than 3 UTI's per year. Most women with recurrent UTI's have reinfection, while a minority (5-10%) have relapse. Reinfeciton occurs when there is recurrent urinary colonization by different organisms at different times, each cured or resolved before the next one begins. In relapse, the bacteriuria often persists during therapy or reoccurs soon after completion (1-2 weeks). Symptomatic recurrent UTI due to relapse tends to occur much sooner than does reinfection. Bacteriologic and DNA typing shows identical bacteria in relapse.

**Treatment.** Most women with recurrent UTI's respond to recommended antibiotics regimens (see Table 3). Persistent bacteriuria or early clinical reoccurrence should raise the possibility of relapse. These patients can be identified by early positive post therapy cultures with sensitivities showing "sensitive" to the agent used to treat them. Patients with documented relapse should be treated with prolonged courses of antibiotics (2-6 weeks) with follow-up urine cultures to document sterility. Consideration should then be made for prophylactic therapy. One should also have a somewhat lower threshold for urologic structural evaluation.

The vast majority of women with uncomplicated recurrent UTI's experience reinfection. They will respond clinically and bacteriologically to three day courses of antibiotic therapy. These women rarely have any urologic structural abnormality causing the recurrent reinfections, and structural evaluation is therefore not indicated. Patients should be counseled about risk factors for UTI's (diaphragm use, spermicide use, atrophic vaginitis in postmenopausal women, not emptying the bladder after intercourse). Post therapy urine cultures should occasionally be checked in women with recurrent UTI's to differentiate relapse from reinfection, but in general are not necessary. In women with recurrent UTI's due to reinfection prophylactic or self-initiated therapy should be considered.

**Management summary.** For recurrent UTI's:
1. **Treat acute UTI** (see Table 3).
2. **Follow-up urine culture.** Check follow-up urine culture if necessary to distinguish relapse from reoccurrence, otherwise generally not necessary.
3. **Educate.** Counsel about reinfection:
   - use of diaphragm or spermicide - consider alternative
   - postcoital voiding
   - consider vaginal estrogen in postmenopausal women
4. **Prophylaxis.** Consider:
   - continuous or postcoital (trimethoprim / sulfas SS, Macrodantin 100 mg)
   - self initiated therapy (Table 3)
5. **No structural evaluation.** Structural evaluation is generally not indicated.

**Prophylaxis of Recurrent UTIs**
Recurrent UTI is defined as 3 or more episodes of UTI over the past 12 months, or 2 UTIs in the past 6 months. Prophylaxis may be possible using antibiotics or other methods. The decision to use prophylaxis or not, and which agent to use, should be made jointly by the physician and patient, taking into account the individual preferences of each woman.

Prophylactic antibiotic use, either daily or used only postcoitally, has been shown to reduce frequency of UTI in sexually active women. The benefits accrue only during active prophylaxis. Once antibiotics are discontinued, UTIs occur at the same rate as in placebo-treated sexually active women. Adverse events from antibiotic use are generally mild, although women vary in their evaluation of the impact of various side effects (i.e., oral or vaginal candidiasis may be seen as a severe side effect by some, mild by others.)

Commonly use prophylactic antibiotics include cotrimoxazole, nitrofurantoin, cephalexin, or a quinolone. Nitrofurantoin appears to have the highest withdrawal rate, followed by cephalexin. It appears that post-coital prophylaxis is as effective as daily intake. Quinolones should be avoided, given concerns about antibiotic resistance, as well as higher cost. When used, they may be considered for weekly dosing. They are contra-indicated in pregnancy.

In regards to the use of other prophylactic measures, some studies have shown that cranberry juice or cranberry tablets can significantly reduce the annual incidence of UTIs in sexually active women with a history of recurrent UTIs. Commonly used prophylactic antibiotics include cotrimoxazole, nitrofurantoin, cephalexin, or a quinolone. Nitrofurantoin appears to have the highest withdrawal rate, followed by cephalexin. It appears that post-coital prophylaxis is as effective as daily intake. Quinolones should be avoided, given concerns about antibiotic resistance, as well as higher cost. When used, they may be considered for weekly dosing. They are contra-indicated in pregnancy.

Asymptomatic Bacteriuria (ASB)

Diagnosis. Asymptomatic bacteriuria is the presence of "significant" numbers of bacteria in the urine without the presence of symptoms. Significant bacteriuria is defined as >10^5 CFU/ml of urine. The presence of one organism per high-powered field in a clean-catch, midstream, unspun urine sample represents significant bacteriuria (equivalent to >10^5 CFU/ml).

Patients with chronic indwelling catheters are at particular risk for developing bacteriuria. The risk of UTI can be decreased by using catheters only when necessary, insertion of the catheter under aseptic technique, use of a closed drainage system, avoidance of irrigation, and change of catheters every 2-3 weeks. Intermittent catheterization and external catheters are associated with fewer infections than are indwelling catheters.

Asymptomatic bacteriuria occurs in 40% of elderly adults, especially in nursing homes. In controlled studies that address issues of underlying illness, asymptomatic bacteriuria does not increase risk of death.

Treatment. Screening and/or treatment of asymptomatic bacteriuria in most settings is not recommended because of unproved efficacy, risk of side effects from antibiotics, development of antibiotic resistance, and cost issues.

Treatment of asymptomatic bacteriuria is recommended in the following conditions:

- Pregnancy. See pregnancy section.
- Before invasive procedures. Post-operative complications, including bacteremia, are reduced are decreased by treating bacteriuria prior to urologic procedures.
- Renal transplant recipients.
- Children.

Treatment of asymptomatic bacteriuria in women with diabetes does not reduce complications, and therefore diabetes is not an indication for screening or treatment of asymptomatic bacteriuria.

Acute Uncomplicated Pyelonephritis

Patients presenting with typical lower tract symptoms (dysuria, frequency, urgency, etc.) with associated flank pain, abdominal pain, nausea, vomiting, fever or chills should be suspected of having pyelonephritis. In fact, a significant percentage (up to 20% in some cases) of patients who present with seemingly uncomplicated UTI without typical pyelonephritis symptoms can be shown by bacteriologic localization studies to have involvement of the kidney. Many women with pyelonephritis can be safely managed on an outpatient basis with oral antibiotics. Hospital admission with intravenous antibiotics is indicated for acutely toxic patients, pregnant or immunocompromised women, women unable to take in oral fluids, or in those where compliance is a significant issue.
UTI is the most frequent medical complication of pregnancy. Physiologic changes, both hormonal and mechanical, predispose the bacteriuric woman to an increased risk for developing acute pyelonephritis, preterm birth, and unexplained perinatal death. Factors contributing to increased risk of disease include dilation of the ureters and renal pelvices, increased urinary pH, and glycosuria promoting bacterial growth and decrease in the ureteric muscle tone.

**Asymptomatic bacteria (ASB).** ASB occurs in 4-7% of pregnant patients. Unlike nonpregnant women with ASB, in whom intervention is not recommended, pregnant patients with ASB will go on to develop pyelonephritis in up to 40% of cases if left untreated. Pyelonephritis in the pregnant patient leads to septicemia in 10-20% of cases and ARDS in 2%. Screening for asymptomatic bacteriuria is recommended for pregnant women at the first prenatal visit. Urine culture is an appropriate screening tool. Clean catch urine analysis is recognized as an appropriate screening tool by the American College of Obstetricians and Gynecologists.

Treatment of ASB can be accomplished with a variety of FDA category B drugs (see definitions below) including amoxicillin, cephalosporins, nitrofurantoin and trimethoprim/sulfa. Quinolones should generally not be used during pregnancy (FDA Category C). A seven day course is recommended with follow-up urine cultures to document sterile urine. Persistent bacteruria requires retreatment guided by sensitivities and then consideration of suppressive therapy, usually with nitrofurantoin.

FDA pregnancy risk categories for drugs are:

- **Category A** = Controlled studies in women fail to demonstrate a risk to the fetus in the first trimester (and there is no evidence of a risk in later trimesters), and the possibility of fetal harm appears remote. The drug should be used during pregnancy only if clearly needed
- **Category B** = Animal-reproduction studies have not demonstrated a fetal risk but there are no controlled studies in pregnant women OR animal reproduction studies have shown an adverse effect that was not confirmed in controlled studies in women in the first trimester. The drug should be used in pregnancy only if clearly indicated
- **Category C** = Studies in animals have revealed adverse effects on the fetus and there are no controlled studies in women OR studies in women and animals are not available. The drug should be used only if the potential benefit justifies the potential risk
- **Category D** = There is evidence of human fetal risk, but the benefits from use in pregnant women may be acceptable despite the risk (e.g., if the drug is needed in a life-threatening situation or for a serious disease for which safer drugs cannot be used or are ineffective).

**Symptomatic cystitis in pregnancy.** Symptomatic cystitis, in pregnancy, although rare, should be treated and followed-up similarly to ASB. Acute pyelonephritis, which occurs in 1-2% of all pregnancies, should be treated with hospitalization and IV antibiotics.
Information the Patient Needs to Know

• **Cause.** UTI are caused by bacteria and require antibiotic treatment.

• **Complete treatment.** Antibiotic must be taken for the full prescribed duration, even if symptoms disappear.

• **Fluids.** You should drink at least 8 glasses of fluids per day to help flush the urinary system.

• **Possible side effects of treatment.** Side effects of antibiotics include rash, nausea, diarrhea, vaginitis. If your doctor prescribes a urinary analgesic, phenazopyridine (Pyridium), to help with pain, it may turn your urine an orange color.

• **Call for early follow-up.** Symptoms that require early follow-up included: persistent fever or discomfort persisting greater than 72 hours after starting therapy, inability to take antibiotic due to nausea or vomiting, development of any new symptoms.

• **Call if symptoms return.** If your symptoms of urinary tract infection return after completing your antibiotic, you should contact your physician.

Patient education information about UTI is available to provide more detail and reinforce instruction.

**Strategy for Literature Search**

The literature search for this update began with the results of the literature search performed for the earlier version of this guideline. A search for literature published since that time was performed. The search was conducted prospectively using the major keywords of: urinary tract infections (including bacteriuria, pyuria, or schistosomiasis haematobia), guidelines, controlled trials, published from 7/1/98 to 8/31/04 years, adult women on Medline. Specific searches were performed for: predictive value of tests, diagnosis (other than predictive value of tests), treatment, uncomplicated UTI – treatment, pregnancy, postmenopausal women – treatment, recurrent UTI, self initiated therapy, group B strep and non-pregnant women, telephone triage – nursing protocol, other treatment, other references to UTI.

The search was conducted in components each keyed to a specific causal link in a formal problem structure (available upon request). The search was supplemented with recent clinical trials known to expert members of the panel. Negative trials were specifically sought. The search was a single cycle. Conclusions were based on prospective randomized clinical trials if available, to the exclusion of other data; if RCTs were not available, observational studies were admitted to consideration. If no such data were available for a given link in the problem formulation, expert opinion was used to estimate effect size.

**Disclosures**

The University of Michigan Health System endorses the Guidelines of the Association of American Medical Colleges and the Standards of the Accreditation Council for Continuing Medical Education that the individuals who present educational activities disclose significant relationships with commercial companies whose products or services are discussed. Disclosure of a relationship is not intended to suggest bias in the information presented, but is made to provide readers with information that might be of potential importance to their evaluation of the information.

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<tr>
<td>Carol E. Chenoweth, MD</td>
<td>None</td>
<td>(None)</td>
</tr>
<tr>
<td>Karen R. Fonde, MD</td>
<td>None</td>
<td>(None)</td>
</tr>
<tr>
<td>Steven E. Gradwohl, MD</td>
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<td>R. Van Harrison, PhD</td>
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<tr>
<td>Lauren B. Zoschnick, MD</td>
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**Acknowledgments**

In addition to current team members on the front page, the following individual is acknowledged for her contributions to the 1999 version of this guideline: Kathy Munger, MS, BSN, RN, Ambulatory Care Nursing.

**Annotated References**

Cochrane Systematic Review, Antibiotics for preventing recurrent urinary tract infection in non-pregnant women, Volume 3 2004


Prospective randomized trial comparing the outcome of 3-day regimens of trimethoprim, sulfâ, nitrofurantoin, cefadroxil and amoxicillin in women with cystitis. Trimethoprim/sulfâ was shown to be more effective 80% (vs. < 67%) and less expensive than the other regimens.


Review of 28 trials on women with uncomplicated urinary tract infection comparing single dose therapy to
three day or greater than five day courses of therapy. Single dose therapy was less effective than 3-day or >5, trimethoprim/sulfa was felt to be optimum therapy and there was no increased benefit from extending therapy to >5 days. β lactams, however, were effective when treatment was extended past 5 days.


Before-and-after study with concurrent control groups at 24 primary care clinics to assess the effect of a telephone-based clinical practice guideline for managing presumed cystitis. Women 18 to 55 who met specific criteria were managed without a clinical visit or laboratory testing. Guideline use decreased laboratory utilization and overall costs while maintaining or improving the quality of care.


Prospective trial which showed none of the routine pretreatment tests (Urinalysis, UC, sensitivities) or follow-up tests were predicative of outcome. Most women (>90%) responded to empiric therapy with trimethoprim/sulfa.


Women with previous UTI were able to accurately self-diagnose and treat recurrent episodes of UIT. Clinical cure rates of 92%, microbiological cure rate of 96%.


Reviews rationale for empirical antimicrobial therapy for uncomplicated UTI based on local antimicrobial susceptibilities.


Excellent concise review.


Treatment guidelines endorsed by IDSA, American Urologic Association, the European Society of clinical Microbiology and Infectious Diseases.