Clinical Guideline

Urinary Tract Infection

By Dr. CJ Tseng

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 >105 organisms), sensitivity can be increased to >90% if threshold is >102 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.
GUIDELINE TITLE
Urinary tract infection.

MAJOR RECOMMENDATIONS

Note from National Guideline Clearinghouse (NGC): The following key points summarize the content of the guideline. Refer to the full text for additional information, including detailed information on diagnosis, treatment regimens and costs.

The levels of evidence [A-D] are defined at the end of the "Major Recommendations" field.

Diagnosis

- **History.** Diagnosis is made primarily by history. In women with dysuria and frequency, in the absence of vaginitis, the diagnosis is urinary tract infection (UTI) 80% of the time [C].

- **Phone triage.** In women with prior history of uncomplicated urinary tract infections (UTIs), 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 UTIs. Urine culture (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, first-generation cephalosporin [A].

Follow-up

- **No tests if asymptomatic.** No laboratory follow-up is necessary if asymptomatic [B].

- **For recurrent UTIs.** In patients with recurrent UTIs (>3/year):
  - consider prophylaxis/self-initiated therapy [A]
  - urologic structural evaluation rarely indicated [D]
GUIDELINE TITLE

Uncomplicated urinary tract infection in women.

MAJOR RECOMMENDATIONS

The recommendations for uncomplicated urinary tract infection in women are presented in the form of an algorithm with 13 components, accompanied by detailed annotations. An algorithm is provided for Uncomplicated Urinary Tract Infection in Women; clinical highlights and selected annotations (numbered to correspond with the algorithms) follow.

Class of evidence (A-D, M, R, X) ratings are defined at the end of the "Major Recommendations" field.

Clinical Highlights for Individual Clinicians

1. Assess all women ages 18 to 65 with symptoms of urinary tract infection (UTI) for the presence of complicating factors. The presence of complicating factors warrants provider evaluation and may require additional diagnostic work-up. (Annotations #2, 4)

2. Patients who have classic symptoms of UTI and no complicating factors can be offered the option of phone treatment, if preferred by both provider and patient. (Annotation #4)

3. If laboratory evaluation is preferred by the provider, symptomatic women without complicating factors can be appropriately evaluated by a urinalysis rather than a urine culture. (Annotation #3)

4. Symptomatic women without complicating factors can be effectively treated with the following recommended therapy: (Annotation #9)
   - Trimethoprim Sulfamethoxazole D.S. 1 twice a day (BID) x 3 days
   - Trimethoprim 100 mg 1 BID x 3 days

If allergic to Sulfa or Trimethoprim:
   - Nitrofurantoin (Macrobid) 100 mg BID x 7 days
   - Ciprofloxacin 250 mg BID x 3 days

Sulfa and ciprofloxacin may cause an increase in international normalized ratio (INR) values for patients taking warfarin.

If an individual's institution has over 20% resistance in Escherichia coli to trimethoprim-sulfamethoxazole, consider choosing an alternate first-line treatment such as nitrofurantoin or ciprofloxacin.

5. All patients should be provided patient education about the prescribed therapy and the need to return to clinic if the symptoms do not subside. (Annotation #1, 9)
Uncomplicated Urinary Tract Infection in Women Algorithm Annotations

1. Adult Female Presents or Calls with One or More of the Following Symptoms: Dysuria, Frequency, Urgency

The classic symptoms of urinary tract infection (UTI) in women are dysuria, frequency, and urgency. One or more of these symptoms can trigger the initiation of the UTI guideline. Hematuria alone is not a classic uncomplicated UTI symptom. There is concern the presence of hematuria may be a sign of more significant disease. Patients whose symptoms do not subside should return to the clinic for a full examination.

2. Complicating Factors Present?

History taking is essential in differentiating uncomplicated from complicated urinary infection. Women should be screened for the presence of complicating factors when presenting or calling with symptoms of UTI. Depending upon which complicating factor is present, short course therapy may or may not be appropriate.

Symptoms for which short course therapy with trimethoprim/sulfamethoxazole (TMP/SMX) is not appropriate:

- Symptoms suggest pyelonephritis or other more severe infection: long duration, rigors, flank pain, or temperature greater than 101 degrees F.
- Patient’s medical history suggests likelihood of complicated urinary tract infection or need for different investigation or therapy: diabetes, pregnancy, immunosuppression, underlying urinary tract disease or renal calculi, recent medical intervention (hospitalization or catheterization), or recurrent UTIs or failure of therapy.
- Resident of an extended care facility

Factors for which short course therapy may be appropriate at physician discretion:

- Potential sexually transmitted disease (STD): an infected partner, other genitourinary symptoms. The patient should be seen and STDs ruled out.
- Younger or older patients (less than 18 or greater than 65). There is little literature documentation of efficacy of short course therapy in these age groups.
- Recent pyelonephritis or failure of antibiotic treatment. These patients may be at higher risk of complicated infection.

Evidence supporting this recommendation is of classes: B, R

3. Urinalysis (UA)/Hold for Urine Culture (UC)/Patient Education

Instructions on collecting a clean-catch, midstream urine specimen should be given to the patient. Education should also be given to the patient regarding urinary tract infection.
The laboratory should be instructed to perform a urinalysis with microscopy and hold for possible urine culture. Urine specimens that are marked "Hold for UC" should be refrigerated.

The final decision about culturing should be left to the provider.

4. **Provider Evaluation**

Women with a complicated history should be evaluated by a health care provider. The provider (physician or paraprofessional) will determine if a UC is necessary.

Complicating factors are listed in detail on the algorithm page (floating box 2 of the original guideline document), and include the following categories:

- Those that would preclude use of short course therapy
- Those that would allow for discretionary use of short course therapy
- Those that would necessitate a pelvic exam to rule out genitourinary (GU) disease
GUIDELINE TITLE

Recurrent lower urinary tract infections in women.

MAJOR RECOMMENDATIONS

ACR Appropriateness Criteria™

Clinical Condition: Recurrent Lower Urinary Tract Infections (UTIs) in Women

<table>
<thead>
<tr>
<th>Radiologic Exam Procedure</th>
<th>Appropriateness Rating</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>X-ray, kidney, intravenous urography, IVP</td>
<td>6</td>
<td>Not cost effective in this group. May be useful if there is an uncertain history.</td>
</tr>
<tr>
<td>CT, abdomen and pelvis, with and without contrast</td>
<td>6</td>
<td>In recurrent and persistent infection, CT may be indicated to exclude structural abnormalities. MRI may be indicated if urethral diverticulum is suspected.</td>
</tr>
<tr>
<td>X-ray, abdomen, KUB</td>
<td>4</td>
<td>May be useful in patients when there is a suspicion of calculi.</td>
</tr>
<tr>
<td>CT, abdomen, helical, without contrast</td>
<td>3</td>
<td>May be useful in patients when there is a suspicion of calculi.</td>
</tr>
<tr>
<td>X-ray, bladder, cystography</td>
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<td></td>
</tr>
<tr>
<td>X-ray, bladder, voiding cystourethrography (VCUG)</td>
<td>2</td>
<td></td>
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<tr>
<td>X-ray, urethra, retrograde</td>
<td>2</td>
<td></td>
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<tr>
<td>X-ray, colon, barium enema</td>
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<td>US, bladder</td>
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<tr>
<td>US, urethra</td>
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</table>

Appropriateness Criteria Scale
1 2 3 4 5 6 7 8 9
It is estimated that 20 to 35% of all females have at least one urinary tract infection (UTI) at some time in their lives. Most occur in healthy, sexually active women with a normal urinary tract and normal renal function. These infections are usually limited to the lower urinary tract, are not recurrent, and respond to appropriate antimicrobial therapy. Lower UTIs are confined to the bladder and occasionally the urethra and result in irritative voiding symptoms such as frequency, dysuria, urgency, and hematuria in severe cases. There is usually no associated flank pain, fever, or other systemic symptoms.

Recurrent lower urinary tract infections (UTIs) are usually defined as two or more episodes of such infection occurring in the preceding 12 months. In most cases, such infections are the result of sexual habits and hygiene (e.g., women who are sexually active, especially those using diaphragms and/or spermaticides). In fact, such lower UTIs are commonly referred to as "honeymoon cystitis." A clean-catch or catheterized specimen for culture typically reveals greater than 100,000 organisms per milliliter of urine. The typical infecting organism is Escherichia coli. The route of infection is ascending from the perianal area and vagina via the urethra and into the bladder. In women, it is not at all uncommon for such infections to be severe enough to result in gross hematuria. However, in uncomplicated lower UTIs, there is complete clearing of bacteriuria and hematuria with appropriate antimicrobial therapy. In some cases, single-dose antimicrobial therapy after intercourse or at the onset of irritative voiding symptoms is adequate to control frequent recurrences of cystitis. In patients without underlying risk factors (see Table 1 in the original guideline document), and with lower urinary tract infections as defined above that do not exceed two episodes per year on average, and that respond promptly to appropriate therapy, imaging is usually not cost-effective.

Uncomplicated recurrent lower UTIs in women must be differentiated from "reinfection," which may indicate causes such as a vesicovaginal or vesicoenteric fistula or a paravesical abscess with fistula to the bladder. Furthermore, "bacterial persistence" is defined as an infection with the same organism, typically from a site within the urinary tract, after the bacteriuria has resolved for at least several days and antimicrobial therapy has ceased. Causes of bacterial persistence include calculi, foreign bodies, urethral or bladder diverticula, infected urachal cyst, and postoperative changes such as a remaining ureteral stump that retains urine and results in stasis. In such patients with frequent recurrences and reinfections with the same bacteria, imaging is indicated to detect a treatable condition and monitor its progress.

In support of the premise that imaging has little efficacy in uncomplicated lower UTIs in women, one study reported a series of 164 women with recurring UTIs who had excretory urography (IVP). Of the IVPs, 88% were completely normal, and there were no cases with abnormalities in which the findings altered the medical or surgical management. A second report studied 153 women with IVP and cystoscopy and found that 89% were entirely normal. None of the abnormalities discovered in the remaining 11% were judged to be related to recurrent infections or influenced subsequent therapy. A third report studied 78 women with recurrent UTIs and found 6% with "major structural urologic abnormalities requiring further therapy." All women with such abnormalities had risk factors (to be defined subsequently).
fourth report prospectively studied 126 women with UTIs. Most, but not all, had two or more UTIs. It was concluded that in this group radiographic and endoscopic examination would rarely uncover abnormalities that are important in the treatment of UTI. A fifth study reported on 201 young women with recurrent UTIs, of whom 121 had uncomplicated lower UTIs. The IVPs for all of the latter either were normal or showed insignificant abnormalities. They also concluded that a risk factor should be present to justify an imaging study.

Therefore, imaging studies should be reserved for women who do not respond promptly to appropriate antimicrobial therapy, those who suffer frequent reinfections (or bacterial persistence), and those with known risk factors. Documented risk factors associated with other than uncomplicated lower UTIs include persistent hematuria, history of pyelonephritis, history of childhood urinary tract infections, flank pain, fever more than 38.5 degrees C, history of urinary calculi or urinary tract obstruction, obstructive voiding symptoms (straining to urinate, feeling of incomplete bladder emptying, etc.), infection with a urea-splitting organism, abnormal renal function studies, neurogenic bladder dysfunction, history of genitourinary surgery, asymptomatic bacteriuria, diabetes mellitus, and analgesic abuse. It should be remembered in all cases of UTI that it is often difficult to distinguish between infections associated with pathology in the upper versus the lower urinary tract. As an example, in a series of 293 patients, the most common presenting symptom in women with reflux nephropathy was lower UTI (72% of cases). The following paragraphs discuss the various imaging examinations that may be useful in evaluating women with recurrent UTIs that fall outside the category of uncomplicated.

Plain film (KUB) of the abdomen has long been an important examination for detecting calculi, bladder wall calcifications, gas in the wall or lumen of the urinary bladder, and/or foreign bodies that may be the etiology of a UTI. When calcifications are seen in the bladder wall, it is often possible to make a correct clinical diagnosis if these findings are viewed in the context of the clinical history, physical examination, appropriate laboratory studies, and further imaging of the remainder of the urinary tract. Bladder wall calcification is typically due to prior infection with schistosomiasis (uncommon in the United States, but very common in other parts of the world), tuberculosis, Cytoxan cystitis, radiation cystitis, or urothelial neoplasm (found in less than 1% of transitional cell carcinomas).

Excretory urography remains a highly effective modality for evaluating the urinary tract. The study optimally includes thin-section nephrotomography, which will generally detect a renal parenchymal mass such as an abscess that may be a focus of recurrent infection. Ill-defined renal margins may suggest a perirenal inflammatory process best evaluated by CT. However, for evaluation of the collecting system, IVP is virtually unexcelled and will correctly detect the changes caused by chronic atrophic pyelonephritis, papillary necrosis and subtle urothelial neoplasms, and other changes associated with infections such as pyelitis cystica and leukoplakia. IVP is also useful for excluding congenital anomalies or obstruction of the urinary tract. The bladder phase of the IVP can usually identify contour abnormalities suggestive of inflammation or neoplasm. Further, the ability of the bladder to empty on voiding can be reasonably assessed. However, when questions remain regarding the integrity of the bladder wall, cystoscopy is always indicated to rule out neoplasm.

Although abdominal plain-film radiography is considered the most cost-effective imaging modality for detecting opaque calculi associated with recurrent urinary tract infection, it may prove inadequate in some cases (e.g., poor definition due to moderate overlying bowel). In such instances, unenhanced helical CT
may be used. In many locations, the cost of this examination has been reduced so that it is competitive with that of an IVP. Its benefits include increased accuracy in detecting calculi (spatial resolution and lack of overlying bowel and bone), increased speed of examination, and increased abdominal detail, allowing, in some cases, an alternate diagnosis to explain patients' signs, symptoms, and laboratory findings. As a result, unenhanced CT has been used predominantly for the emergency patient with "renal colic" and/or hematuria. It has also been used to define the severity and extent of upper-tract calculi, sometimes associated with recurrent UTIs. Additionally, CT without and with intravenous contrast has been very helpful and has been described as the "examination of choice" in evaluating complicated UTIs (e.g., abscess).

Some investigators have advocated the use of renal and pelvic US combined with KUB as a replacement for IVP. They conclude that young women with recurrent UTIs should have this combination of exams (i.e., US and KUB) as the investigation of choice because it is cost-effective, "non-invasive, inexpensive and acceptable to the patient." Others have supported the continued use of IVP by citing the level of experience required to perform accurate US as well as the operator dependence of this exam. Ultrasound has been shown to be equal to IVP for detecting bladder stones but less sensitive than abdominal x-ray for detecting bladder wall calcifications or distal ureteral stones. Bladder and urethral calcifications have also been detected by CT, but this examination is more costly and should not be used routinely.

Patients with suspected bladder diverticula may be imaged with IVP, cystography, or US. When a bladder diverticulum is at or near a ureteral orifice, voiding cystourethrography should be considered to evaluate the possibility of vesicoureteral reflux. Although used commonly in children to reduce the dose of radiation, nuclear cystography has not been used widely in adults.

Diverticula of the urethra can be evaluated by voiding cystourethrography (VCUG) or retrograde urethrogramy. Some have also advocated US and MRI for detection. Endovaginal and transperineal sonography has been suggested as a "noninvasive screening technique for female urethral diverticula." It is said to better demonstrate the "spatial relationship of the diverticula to the urethra." MRI is accurate but expensive and should be reserved for those patients in whom there is strong clinical suspicion of a diverticulum and when the more conventional modalities are equivocal.

When performing cystography and urethrography for evaluating the lower urinary tract, the use of digital radiography has been shown to decrease radiation dose by approximately 90% while maintaining diagnostic accuracy. This is particularly important in reducing the gonadal radiation dose during the examination of young women.

Enterovesical fistulae are usually caused by diverticulitis (cancer is the second most common cause). Clinical suspicion is frequently raised by the presence of UTI with pneumaturia and/or fecaluria. The diagnosis and localization usually require more than one examination. In one large series, cystoscopy and barium enema were used in 75% of the patients but were positive in only 36% of the patients and 34% of the patients, respectively. IVP was performed in 55% of the patients but was only 12.5% diagnostic; cystography was used 36% of the time and was 44% diagnostic; CT scan was used in 23% of patients and was 60% diagnostic. Colonoscopy, US, upper gastrointestinal/small bowel follow-through, sigmoidoscopy, MRI, and nuclear imaging have very low yields, making them even less cost-effective. The authors conclude that CT, cystoscopy, and oral charcoal are the most effective modalities for diagnosing the
presence of a fistula. Yet, after analysis of another large series, the authors conclude that a combination of cystoscopy, cystography, and barium enema "resulted in diagnosis of all patients."

When UTI accompanies neuropathic bladder, cystography or US may demonstrate the morphologic changes of the bladder wall, and VCUG or transrectal sonographic voiding cystourethrography may document neuromuscular dysfunction of the bladder and/or associated sphincters.

**Summary**

Women with recurrent urinary tract infections (UTIs) should have one or more additional risk factors to justify urologic or radiologic investigation. In such cases, the abdominal plain film, US, IVP, and cystoscopy are the most common and most rewarding examinations for achieving a cost-effective diagnosis, and they continue to be the core examinations for evaluating the lower urinary tract. Abnormalities of the bladder and the urethra can also be shown with cystography and urethrography, respectively. For the detection of fistulae, contrast enema and CT scan have also been shown to be diagnostic and may supplement cystoscopy and cystography. MRI and nuclear imaging have had a very limited role in the evaluation of women with recurrent lower UTIs.

**Anticipated Exceptions**

Exceptions to the above guidelines occur when there is clinical confusion regarding the source of recurrent UTI or when risk factors (enumerated above and in Table 1 in the original guideline document) are present. In such cases, appropriate imaging as previously described is indicated.

**Abbreviations**

- CT, computed tomography
- IVP, intravenous pyelogram
- KUB, kidneys, ureters, bladder
- MRI, magnetic resonance imaging
- NUC, nuclear medicine
- US, ultrasound