Dysuria: Evaluation and Differential Diagnosis in Adults

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The most common cause of acute dysuria is infection, especially cystitis. Other infectious causes include urethritis, sexually transmitted infections, and vaginitis. Noninfectious inflammatory causes include a foreign body in the urinary tract and dermatologic conditions. Noninflammatory causes of dysuria include medication use, urethral anatomic abnormalities, local trauma, and interstitial cystitis/bladder pain syndrome. An initial targeted history includes features of a local cause (e.g., vaginal or urethral irritation), risk factors for a complicated urinary tract infection (e.g., male sex, pregnancy, presence of urologic obstruction, recent procedure), and symptoms of pyelonephritis. Women with dysuria who have no complicating features can be treated for cystitis without further diagnostic evaluation. Women with vulvovaginal symptoms should be evaluated for vaginitis. Any complicating features or recurrent symptoms warrant a history, physical examination, urinalysis, and urine culture. Findings from the secondary evaluation and determine the cause of dysuria or make an appropriate referral. (*Am Fam Physician*. 2015;92(9):778-786. Copyright © 2015 American Academy of Family Physicians.)

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▶ Patient information: A handout on this topic, written by the authors of this article, is available at http://www.aafp.org/afp/ 2015/1101/p778-s1.html.

ysuria is burning, tingling, or stinging of the urethra and meatus associated with voiding. It should be distinguished from other forms of bladder discomfort, such as suprapubic or retropubic pain, pressure, or discomfort that usually increases with bladder volume.1-3 Dysuria is present at least occasionally in approximately 3% of adults older than 40 years, according to a survey of roughly 30,000 men and women.⁴ Acute cystitis is the most common cause in women, accounting for 8.6 million outpatient visits in 2007 and 2.3 million emergency department visits in 2011.5,6 This article describes an evidence-based approach to the evaluation of adult outpatients with dysuria, focusing on the history, physical examination, and selected tests.

Pathophysiology and Differential Diagnosis

Sensory nerves are located just beneath the urothelium. Chemical irritation and inflammatory conditions (e.g., acute bacterial infection) can alter the mucosal barrier and stimulate these nerves, causing pain. Chronic inflammation and other unknown factors can lead to altered nerve sensitivity and persistent pain. Inflammation from adjacent abdominal structures, such as the colon, can also affect function and sensation in the bladder.⁷

Inflammatory disorders of the bladder and urethra are the most common causes of dysuria. Among these, infections of the bladder, urethra, kidneys, and genital organs are the most prevalent, including uncomplicated cystitis, pyelonephritis, and urethritis. Distinguishing a complicated urinary tract infection (UTI) from cystitis is important, because misdiagnosis increases the risk of treatment failure. Risk factors for a complicated infection may include patient characteristics, medical conditions, and urologic conditions (Table 1).8-11 In women, dysuria is also a common presentation of vaginitis. In men, prostatitis can present with dysuria. Sexually transmitted infections (STIs) can also cause dysuria.

Inflammatory, noninfectious conditions that can lead to dysuria include the presence of a foreign body (e.g., stent, bladder stone), noninfectious urethritis (e.g., reactive arthritis, formerly Reiter syndrome), and dermatologic conditions. Noninflammatory conditions can be divided into the following categories: anatomic; endocrine; neoplastic; medication-, food-, or recreational drug–related; iatrogenic; and idiopathic. Any condition that causes hematuria with clots can cause dysuria, including renal neoplasms and nephrolithiasis. Interstitial cystitis (also known as bladder pain syndrome) refers to chronic bladder pain, often with voiding symptoms, lasting six weeks or more without an identifiable cause.¹² The differential diagnosis of dysuria is summarized in *Table 2.*^{2,4,8,11-19}

History and Physical Examination

The medical history should characterize the timing, persistence, severity, duration, and exact location of the dysuria. Pain occurring at the start of urination may indicate urethral pathology; pain occurring at the end of urination is usually of bladder origin.^{1,2,9} Physicians should ask about other bladder symptoms, such as frequency, urgency, incontinence, hematuria, malodorous urine, and nocturia. The history should include the presence of flank pain, nausea, fever, and other systemic symptoms. A history of dysuria, UTIs, STIs, and recent sexual activity are crucial. Additionally, medication use, family history, and procedural history can help identify the cause of dysuria. In women, the history should also include the presence of vaginal discharge or irritation, most recent menstrual period, and type of contraception used.^{2,8}

Specific localization of the discomfort varies between men and women. Women with vaginitis often describe external dysuria, as well as vaginal irritation

Table 1. Risk Factors for Complicated Urinary Tract Infections*		
Patient characteristics	Urologic conditions	
Male sex	History of childhood or recurrent	
Postmenopausal†	urinary tract infections†	
Pregnant Presence of hospital-acquired urinary tract infection	Neurogenic bladder Polycystic kidney disease	
Symptoms present for seven or	Recent urologic instrumentation	
more days before presentation	Renal transplant	
Medical conditions	Urolithiasis	
Diabetes mellitus†	Urologic obstruction	
Immunocompromised status	Urologic stents	

*—Increased chance of treatment failure.

+—Some experts consider the following groups to be uncomplicated: healthy postmenopausal women; patients with well-controlled diabetes; and patients with recurrent cystitis that responds to treatment.¹¹

Information from references 8 through 11.

or discharge. With cystitis, the dysuria is characteristically felt in the bladder or urethra.^{5,9} In addition to dysuria, men with prostatitis may have deep perineal pain and obstructive urinary symptoms, whereas those with epididymo-orchitis may have localized testicular pain. Lesions from herpes simplex virus of the vulvar or penile area may cause dysuria.^{2,13} Patients with interstitial cystitis may have suprapubic or abdominal pain related to bladder filling. These patients nearly always report urinary frequency and urgency, whereas dysuria is variable.^{3,12}

A meta-analysis in which approximately 50% of patients had a UTI found that the highest positive predictive value (PV+) of cystitis in women was selfdiagnosis of cystitis (86%), followed by the absence of vaginal discharge (82%), presence of hematuria (75%), and urinary frequency (73%). This review found that the combination of dysuria and urinary frequency without vaginal discharge or irritation yielded a very high likelihood of UTI (positive likelihood ratio [LR+] = 24.6). A woman with dysuria and frequency, no risk factors for complicated infection, and no vaginal discharge had a 90% probability of UTI; thus, treatment based on symptoms alone was advocated.9 A study of 196 symptomatic women found that 79% of patients with "considerable" dysuria, suspicion of a UTI, and absence of vaginal symptoms had a UTI.²⁰ In a prospective study of 490 men with symptoms of a UTI, symptoms of dysuria and urgency were significantly

associated with a positive urine culture.²¹ A suggested history for patients with dysuria is provided in *eTable A*.

The physical examination, especially when complicated UTI is a consideration, should include vital signs, evaluation for costovertebral angle pain, palpation for abdominal mass or tenderness, and inspection for dermatologic conditions and acute joint effusions. Often the most relevant findings on physical examination are sexspecific, including inspecting for infectious or atrophic vaginitis and STIs in women, and prostatitis and STIs in men.^{15,18} The presence of costovertebral angle tenderness on examination modestly increases the likelihood of having a UTI in women (LR + = 1.7).⁹ Key physical examination findings are discussed in eTable B. Risk factors for complicated UTI and failure to respond to initial treatment are indications for a more detailed history and physical examination.

Laboratory Tests URINALYSIS

Urinalysis is the most useful test in a patient with dysuria; most studies have used dipstick urinalysis. Multiple studies of women with symptoms suggestive of a UTI have demonstrated that the presence of nitrites is highly predictive of a positive culture (PV+ = 75% to 95%); dipstick showing more than trace leukocytes is nearly as predictive (PV+ = 65% to 85%); and the presence of both is almost conclusive (PV+ = 95%).^{9,20,22-24} Urinary nitrites may be falsely negative in women with a UTI.²⁵ Few studies specifically address the value of urinalysis in men with dysuria, but evidence suggests similar value

Table 2. Differential Diagnosis of Dysuria in Adults

Category	Sex	Causes*
Inflammatory		
Dermatologic	Both	Irritant or contact dermatitis, lichen sclerosus, lichen planus, psoriasis, Stevens- Johnson syndrome, Behçet syndrome
Infectious	Both	Cystitis, urethritis, pyelonephritis, other sexually transmitted infections
	Women	Vulvovaginitis, cervicitis
	Men	Prostatitis, epididymo-orchitis
Noninfectious	Both	Foreign body (e.g., stent, stone), urethritis (e.g., reactive arthritis)
Noninflammatory		
Anatomic	Both	Urethral stricture or diverticulum
	Men	Benign prostatic hyperplasia
Drug- or food- related	Both	Spermacides, topical deodorants, cyclophosphamide, opioids, ketamine (Ketalar), nifedipine, and others; bladder-irritating foods
Endocrine	Women	Atrophic vaginitis, endometriosis
Idiopathic	Both	Interstitial cystitis/bladder pain syndrome
Neoplastic	Both	Bladder or renal cancer, lymphoma, metastatic cancer†
	Women	Vaginal or vulvar cancer, paraurethral leiomyoma
	Men	Prostate or penile cancer
Trauma/iatrogenic	Both	Genitourinary instrumentation or surgery, pelvic irradiation, foreign body presence, horseback or bicycle riding

*—Infectious causes, particularly acute cystitis, are the most common. There are few data to rank other diagnoses by prevalence; specific causes are listed by estimated prevalence.

†—Some cancers (e.g., renal cell) present with dysuria primarily by causing hematuria, and others by bladder-wall irritation, which may be difficult to distinguish from true dysuria.

Information from references 2, 4, 8, and 11 through 19.

to the combination of leukocyte esterase, nitrites, and possibly blood.^{4,21,26,27} Leukocyte esterase or pyuria alone with isolated dysuria suggests urethritis.^{8,10,28}

CULTURES AND CYTOLOGY

Any patient with risk factors for a complicated UTI (*Table 1*⁸⁻¹¹) or whose symptoms do not respond to initial treatment should have a urine culture and sensitivity analysis. Patients with suspected pyelonephritis should have renal function assessed with serum creatinine measurement, and electrolyte levels should be measured if there is substantial nausea and vomiting. Blood cultures are usually not necessary, but can be obtained in

patients with high fever or risk of infectious complications.^{2,8}

In women with vaginal symptoms, secretions should be evaluated with wet mount and potassium hydroxide microscopy or a vaginal pathogens DNA probe. Urethritis should be suspected in younger, sexually active patients with dysuria and pyuria without bacteriuria; in men, urethral inflammation and discharge is typically present. In patients with suspected urethritis, a urethral, vaginal, endocervical, or urine nucleic acid amplification test for Neisseria gonorrhoeae and Chlamydia trachomatis is indicated. Genital ulcerations can be sampled for herpes simplex virus culture or polymerase chain reaction testing, as well as testing for other STIs.²⁸ In men with suspected chronic prostatitis, urine culture after gentle prostatic massage can yield the causative bacterial agent. Prostate-specific antigen level is transiently elevated during acute prostatitis and should not be measured in patients with acute inflammatory symptoms. Urine cytology is helpful if bladder cancer is suspected, such as in older patients with hematuria and a negative culture result.²⁹

IMAGING AND OTHER ADVANCED STUDIES

Imaging is not necessary in most patients with dysuria, although it may be indicated in patients with a complicated UTI, a suspected anatomic anomaly (e.g., abnormal voiding, positive family history of genitourinary anomalies), obstruction or abscess, relapsing infection, or hematuria. Ultrasonography is the preferred initial test for patients with obstruction, abscess, recurrent infection, or

Table 3. Diagnostic Tests for Select Patients with Dysuria

Test*	Indications
Ultrasonography	Initial imaging study for most patients when imaging is indicated; useful in patients who have iodinated contrast media allergy or pregnancy; measurement of the bladder residual volume helps evaluate benign prostatic hyperplasia; secondary study in recurrent UTIs, complicated pyelonephritis, or hematuria
Plain abdominal radiography (kidneys, ureters, bladder)	Most useful in known urolithiasis
CT of abdomen and pelvis with and without contrast media (CT urography)	Evaluation of hematuria, recurrent UTI (with risk factors or relapses), and complicated pyelonephritis
CT of abdomen and pelvis without contrast media	Suspected urolithiasis (ultrasonography is best initial study)
Cystoscopy	Voiding symptoms, hematuria, recurrent UTI, concern for urethral diverticula, bladder cance or interstitial cystitis/bladder pain syndrome
Intravenous urography	Useful for hematuria evaluation if CT urography is unavailable
Magnetic resonance imaging of abdomen and pelvis with and without contrast media (MR urography)	Most useful for complicated pyelonephritis; helpful, not preferred, for stones and hematuria

CT = computed tomography; *UTI* = urinary tract infection.

*—Depending on complicating features, tests are listed in order of preferred use.

Information from references 4, 8, 9, 11, 21, 23 through 26, 28 through 30, 33, and 34.

Table 4. Clinical Decision Rule for UTI in Women Without Signs of Complicated Disease

Clinical score*		Dipstick score*	
Symptom	Points	Dipstick result	Point
Urine cloudiness	1	Nitrites	2
Any burning dysuria	1	Leukocyte esterase	1.5
Nocturia of any degree	1	Blood	1
Total:		Total:	
0 points: LR = 0.23; prevalence = 19%		0 points: LR = 0.16; prevalence = 14%	
1 or 2 points: LR = 0.82; prevalence = 46%		1 to 2.5 points: LR = 1 prevalence = 53%	.1;
3 points: LR = 2.25; prevalence = 70%		\geq 3 points: LR = 5.4; prevalence = 85%	

NOTE: Stratum-specific likelihood ratios and prevalences are calculated from data in Tables 2 and 5 in reference 23.

LR = likelihood ratio; UTI = urinary tract infection.

*—Suggested use: First, calculate clinical score. If score equals 3, treat empirically. If less than 3, obtain urinalysis and treat if dipstick score is 2 or higher, or based on clinical judgment.²³

Information from reference 23.

suspected kidney stones, because it avoids radiation exposure.^{30,31} Helical computed tomography urography is used to view the kidneys and adjacent structures, and may be considered to further evaluate patients with possible abscess, obstruction, or suspected anomalies when ultrasonography is not diagnostic.^{8,30} If urinalysis is unrevealing, cystoscopy can be performed to evaluate for bladder cancer, hematuria, and chronic bladder symptoms. Urodynamic studies can be performed for persistent voiding symptoms with otherwise unrevealing workup,¹² although a recent Cochrane review found no evidence that these tests led to reduction in symptoms in men with such indications.³² Further investigation and urology referral should be considered in patients with recurrent UTI, urolithiasis, known urinary tract abnormality or cancer, history of urologic surgery, hematuria, persistent symptoms, or in men with abnormal postvoid residual urine level (greater than 100 mL)^{8,10,11,29,33} (Table 3^{4,8,9,11,21,23-26,28-30,33,34}).

Clinical Decision Rules

More than 400 patients were included in an English study to develop and validate a clinical decision rule for women presenting with dysuria and urinary frequency. The scoring system they developed can be used in a two-stage process, with some patients treated empirically based on symptoms alone (*Table 4*).²³ Negative predictive values are poor; many women with UTI will not have all three clinical symptoms that were found to be predictive of UTI (dysuria, nocturia, and offensive urine odor), and about one-fourth of patients with urinary symptoms and a normal dipstick result have UTI, so appropriate follow-up is important.

A Dutch study included 490 outpatient men with dysuria, frequency, or urgency, while excluding men with symptoms suggestive of an STI or a complicated UTI. The authors found that the combination of age (60 years or older) and either a positive leukocyte esterase or nitrite test result had the best positive and negative predictive values for UTI (83% and 60%, respectively).²¹

Another study developed a symptoms-

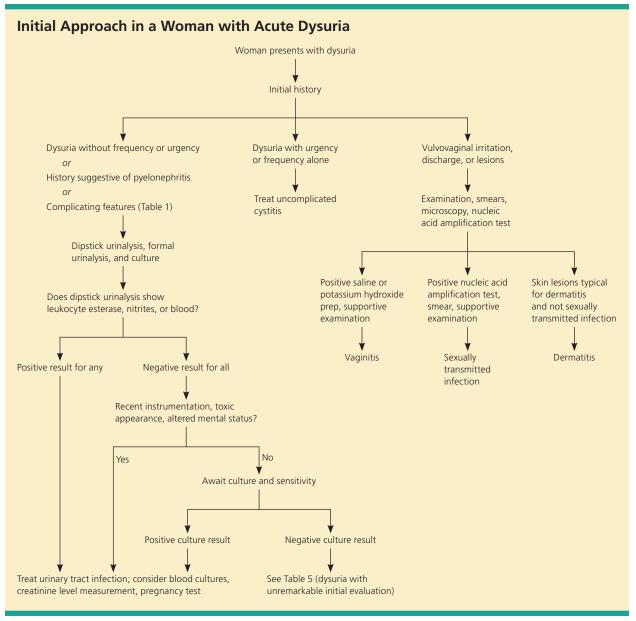


Figure 1. Algorithm for the initial approach in a woman with acute dysuria.

Information from references 2, 4, 5, 10, 20, 22, 24, 25, 31, 37, and 38.

history-urinalysis score that included symptoms of frequency, nocturia, dysuria, hematuria, and offensivesmelling urine; history of a previous UTI; and urinalysis results (protein, blood, and nitrites). The study found that a score of 0 or greater on the 13-item score sheet (range of possible scores from -19 to +31) identified 85% of women with infection; 25% of women without infection also had a score of 0 or greater.²⁶

All of the decision rules caution that in a patient with dysuria, these combinations of variables can reassure physicians that a UTI is likely present, but are not very useful in ruling out a UTI when they are absent. It is important to address the other clinical features discussed here to narrow the differential diagnosis.

Approach to the Patient

Many studies advise that, in the right clinical setting, symptoms alone can identify patients with a high likelihood of UTI who are candidates for empiric therapy. Women with an uncomplicated history who present with acute dysuria, urinary urgency or frequency, and no vaginal discharge can be treated for acute cystitis without other evaluation.^{9,23-25,31,35} Several studies suggest that this approach is effective in reducing costs while improving patient satisfaction, with no increase in adverse outcomes.^{5,35,36} This approach is reflected in the algorithms presented here for the evaluation and follow-up of dysuria. These algorithms are based on evaluation of the existing evidence. *Figure* 1^{2,4,5,10,20,22,24,25,31,37,38} addresses

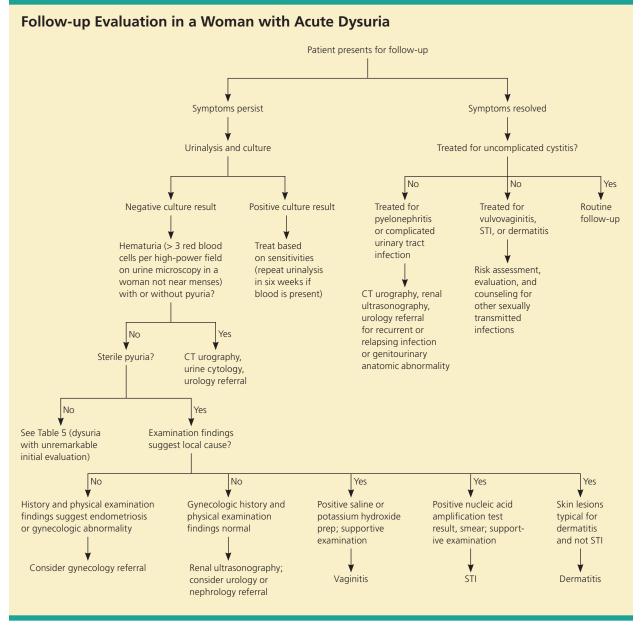
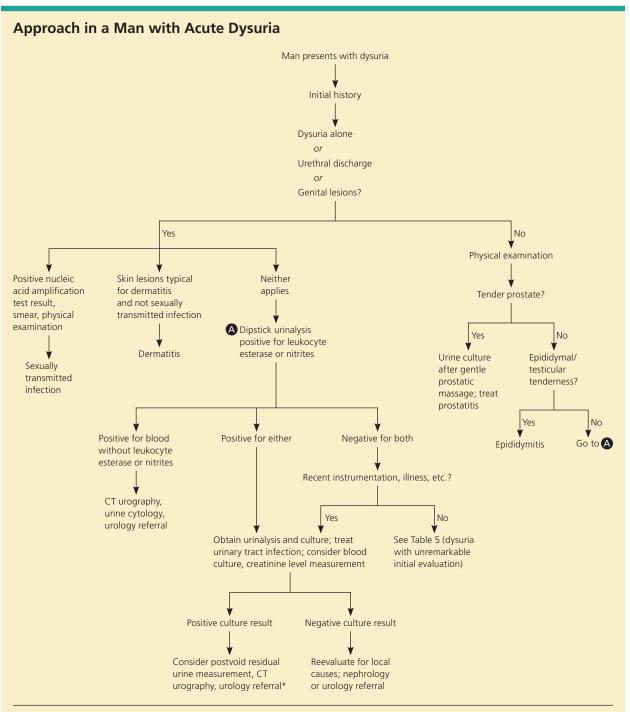


Figure 2. Algorithm for the follow-up evaluation in a woman with acute dysuria. (CT = computed tomography; STI = sexually transmitted infection.)

Information from references 2, 4, 8, 9, 12, 29, and 33.

the initial presentation of a woman with acute dysuria, and *Figure* $2^{2,4,8,9,12,29,33}$ addresses the follow-up evaluation. *Figure* 3 presents the approach to a man with dysuria.^{4,18,21,26-29,39} For patients with initially normal dipstick urinalysis and culture results, *Table* 5 lists common conditions that may be causing dysuria, the typical presentation, and management recommendations.^{4,12-19,28} It is important to use clinical judgment and to be aware of the inclusion and exclusion criteria for the studies on which these algorithms are based. For example, a sexually active adolescent with dysuria is more likely to have an STI than cystitis, and urinalysis results may be negative.⁴⁰⁻⁴² Similarly, an older patient who experiences dysuria shortly after having an indwelling catheter and who has a negative urinalysis result still has a high likelihood of having a UTI.³⁸



*—Men do not routinely need imaging, cystoscopy, and urinary flow measurement; some experts suggest that postvoid residual urine levels should be measured routinely. However, there are a number of features that should prompt further urologic evaluation: presence of fever, abnormal physical examination findings, history of recurrent urinary tract infections, history of urolithiasis, concern for renal impairment or urologic cancer, or postvoid residual urine volume greater than 100 mL.^{27,39}

Figure 3. Algorithm for the approach in a man with acute dysuria. (CT = computed tomography.)

Information from references 4, 18, 21, 26 through 29, and 39.

SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendation	Evidence rating	References	Comments
In low-risk women with dysuria and no vaginal symptoms or other typical UTI symptoms, physicians should obtain a dipstick urinalysis for nitrites and leukocyte esterase.	С	24, 25	Nitrites have higher predictive value for UTI but also higher false-negative rates than leukocyte esterase.
Patients with dysuria who are at risk of complications or whose symptoms do not respond to initial treatment should undergo a detailed history, directed physical examination, and urinalysis and culture.	С	8, 10	Clinical evaluation is useful to direct additional workup.
Further investigation and urology referral should be considered in patients with recurrent UTI, urolithiasis, known or suspected urinary tract abnormality or cancer, history of urologic surgery, hematuria, persistent symptoms, or in men with abnormal postvoid residual urine level (greater than 100 mL).	С	8, 10, 11, 29, 33	Some evaluations, such as postvoid residual urine, computed tomography urography, and symptom questionnaires, can be initiated by the family physician.
Women with an uncomplicated history who present with acute dysuria, urinary urgency or frequency, and no vaginal discharge can be treated for acute cystitis without other evaluation.	В	9, 23-25, 31, 35	Uncomplicated history includes 16 to 55 years of age, not pregnant, no history of recurrent or childhood UTI, not immunocompromised, no diabetes mellitus, and no anatomic urologic abnormality or recent urologic instrumentation

UTI = urinary tract infection.

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to http://www.aafp.org/afpsort.

Table 5. Considerations in Patients with Dysuria and Unremarkable Initial Evaluation

Condition suspected	Typical presentation	Recommendation
Interstitial cystitis/bladder pain syndrome	Variable dysuria; frequency and urgency as primary symptoms; pain with bladder filling and relief with emptying are most specific	Initiate conservative treatment (symptom diary to modify fluid intake, diet, and physical activity; bladder training)
Overactive bladder	Prominent urgency, frequency, possible urge incontinence	Fluid restriction, bladder training, pelvic floor muscle exercises, drug therapy as needed empirically
Potentially offending topical irritant	History of topical use with or without examination findings	Discontinue use of offending agent
Suspected bladder irritants	Based on review of medications and diet*	Dietary and medication modification*
Urethral diverticulum or endometriosis (women)	Localized symptoms with or without physical examination findings	Urology or gynecology referral
Urethritis	Localized symptoms; suspect based on exposures and physical examination	Examination, smears, microscopy, and/or nucleic acid amplification testing

*—For a detailed list of bladder-irritating foods, see http://my.clevelandclinic.org/disorders/overactive_bladder/hic_bladder_irritating_foods.aspx. Information from references 4, 12 through 19, and 28.

Data Sources: A PubMed search was completed in Clinical Queries using the key terms dysuria, urinary tract infection (acute, recurrent, elderly), and hematuria, as well as for the specific disease entities considered (e.g., gonococcal urethritis). The search included meta-analyses, randomized controlled trials, clinical trials, and reviews. The following databases and summaries were also used: Cochrane Database of Systematic Reviews, BMJ Clinical Evidence, National Guideline Clearinghouse, Essential Evidence Plus, and UpToDate. Search dates: January through August 2014, and May through July 2015.

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REFERENCES

- 1. Gerber GS, Brendler CB. Evaluation of the urologic patient: history, physical examination, and urinalysis. In: Wein AJ, et al.; eds. *Campbell-Walsh Urology*. 10th ed. Philadelphia, Pa.: Elsevier Saunders; 2012:75-76.
- Bremnor JD, Sadovsky R. Evaluation of dysuria in adults. Am Fam Physician. 2002;65(8):1589-1596.
- 3. Hanno P, Nordling J, Fall M. Bladder pain syndrome. *Med Clin North Am.* 2011;95(1):55-73.
- Guralnick ML, O'Connor RC, See WA. Assessment and management of irritative voiding symptoms. *Med Clin North Am.* 2011;95(1):121-127.
- Hooton TM. Clinical practice. Uncomplicated urinary tract infection. N Engl J Med. 2012;366(11):1028-1037.
- National Center for Health Statistics. National Hospital Ambulatory Medical Care Survey: 2010 Emergency Department Summary Tables. Hyattsville, Md.: Ambulatory and Hospital Care Statistics Branch; 2011. http://www.cdc.gov/nchs/data/ahcd/nhamcs_emergency/2011_ed_ web_tables.pdf. Accessed July 29, 2015.
- Wyndaele JJ, De Wachter S. The sensory bladder (1): an update on the different sensations described in the lower urinary tract and the physiological mechanisms behind them. *Neurourol Urodyn.* 2008;27(4):274-278.
- Gupta K, Trautner B. In the clinic. Urinary tract infection. Ann Intern Med. 2012;156(5):ITC3-1-ITC3-15.
- 9. Bent S, et al. Does this woman have an acute uncomplicated urinary tract infection? *JAMA*. 2002;287(20):2701-2710.
- Gupta K, Hooton TM, Naber KG, et al. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: a 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. *Clin Infect Dis.* 2011;52(5):e103-e120.
- Wells WG, et al. Treatment of complicated urinary tract infections in adults: combined analysis of two randomized, double-blind, multicentre trials comparing ertapenem and ceftriaxone followed by appropriate oral therapy. J Antimicrob Chemother. 2004;53(suppl 2):ii67-ii74.
- Hanno PM, Erickson D, Moldwin R, Faraday MM. Diagnosis and treatment of interstitial cystitis/bladder pain syndrome: AUA guideline amendment. J Urol. 2015;193(5):1545-1553.
- 13. Wise GJ, Schlegel PN. Sterile pyuria. N Engl J Med. 2015;372(11): 1048-1054.
- 14. Gabriel B, et al. Prevalence and management of urinary tract endometriosis: a clinical case series. *Urology*. 2011;78(6):1269-1274.
- Grady D. Clinical practice. Management of menopausal symptoms. N Engl J Med. 2006;355(22):2338-2347.
- Nuss GR, et al. Presenting symptoms of anterior urethral stricture disease: a disease specific, patient reported questionnaire to measure outcomes. J Urol. 2012; 187(2):559-562.
- Shephard EA, et al. Clinical features of bladder cancer in primary care [published correction appears in *Br J Gen Pract.* 2014;64(620):126]. *Br J Gen Pract.* 2012;62(602):e598-e604.
- Sarma AV, Wei JT. Clinical practice. Benign prostatic hyperplasia and lower urinary tract symptoms [published correction appears in N Engl J Med. 2012;367(7):681]. N Engl J Med. 2012;367(3):248-257.
- Cleveland Clinic. Diseases and conditions: bladder irritating foods. http://my.clevelandclinic.org/disorders/overactive_bladder/hic_ bladder_irritating_foods.aspx. Accessed January 14, 2015.
- 20. Knottnerus BJ, et al. Toward a simple diagnostic index for acute uncomplicated urinary tract infections. *Ann Fam Med.* 2013;11(5):442-451.
- den Heijer CD, van Dongen MC, Donker GA, Stobberingh EE. Diagnostic approach to urinary tract infections in male general practice patients: a national surveillance study. Br J Gen Pract. 2012;62(604):e780-e786.

- 22. Medina-Bombardó D, Jover-Palmer A. Does clinical examination aid in the diagnosis of urinary tract infections in women? A systematic review and meta-analysis. *BMC Fam Pract.* 2011;12:111.
- 23. Little P, et al. Validating the prediction of lower urinary tract infection in primary care: sensitivity and specificity of urinary dipsticks and clinical scores in women. *Br J Gen Pract*. 2010;60(576):495-500.
- 24. McIsaac WJ, Moineddin R, Ross S. Validation of a decision aid to assist physicians in reducing unnecessary antibiotic drug use for acute cystitis. *Arch Intern Med.* 2007;167(20):2201-2206.
- 25. Devillé WL, et al. The urine dipstick test useful to rule out infections. A meta-analysis of the accuracy. *BMC Urol.* 2004;4:4.
- 26. Dobbs FF, Fleming DM. A simple scoring system for evaluating symptoms, history and urine dipstick testing in the diagnosis of urinary tract infection. *J R Coll Gen Pract.* 1987;37(296):100-104.
- 27. Raynor MC, Carson CC III. Urinary infections in men. *Med Clin North Am*. 2011;95(1):43-54.
- Workowski KA, Berman S; Centers for Disease Control and Prevention (CDC). Sexually transmitted diseases treatment guidelines, 2010 [published correction appears in *MMWR Recomm Rep.* 2011;60(1):18]. *MMWR Recomm Rep.* 2010;59(RR-12):1-110.
- Lotan Y, Roehrborn CG. Sensitivity and specificity of commonly available bladder tumor markers versus cytology: results of a comprehensive literature review and meta-analyses. Urology. 2003;61(1):109-118.
- American College of Radiology. ACR Appropriateness Criteria. https:// acsearch.acr.org/list. Accessed January 14, 2015.
- Smith-Bindman R, Aubin C, Bailitz J, et al. Ultrasonography versus computed tomography for suspected nephrolithiasis. N Engl J Med. 2014; 371(12):1100-1110.
- 32. Clement KD, Burden H, Warren K, Lapitan MC, Omar MI, Drake MJ. Invasive urodynamic studies for the management of lower urinary tract symptoms (LUTS) in men and with voiding dysfunction. *Cochrane Database Syst Rev.* 2015;(4):CD011179.
- Colgan R, Williams M, Johnson JR. Diagnosis and treatment of acute pyelonephritis in women. *Am Fam Physician*. 2011;84(5):519-526.
- 34. Giesen LG, Cousins G, Dimitrov BD, van de Laar FA, Fahey T. Predicting acute uncomplicated urinary tract infection in women: a systematic review of the diagnostic accuracy of symptoms and signs. *BMC Fam Pract.* 2010;11:78.
- Booth JL, Mullen AB, Thomson DA, et al. Antibiotic treatment of urinary tract infection by community pharmacists: a cross-sectional study. Br J Gen Pract. 2013;63(609):e244-e249.
- Barry HC, Hickner J, Ebell MH, Ettenhofer T. A randomized controlled trial of telephone management of suspected urinary tract infections in women. J Fam Pract. 2001;50(7):589-594.
- 37. Fischer G, Bradford J. Persistent vaginitis. BMJ. 2011;343:d7314.
- D'Agata E, Loeb MB, Mitchell SL. Challenges in assessing nursing home residents with advanced dementia for suspected urinary tract infections. J Am Geriatr Soc. 2013;61(1):62-66.
- 39. National Clinical Guideline Centre for Acute and Chronic Conditions. Lower urinary tract symptoms. The management of lower urinary tract symptoms in men. Clinical guideline, no. 97. London, United Kingdom: National Institute for Health and Clinical Excellence (NICE); 2010:34. http://www.guideline.gov/content.aspx?id=23805&search=luts. Accessed July 29, 2015.
- Prentiss KA, Newby PK, Vinci RJ. Adolescent female with urinary symptoms: a diagnostic challenge for the pediatrician. *Pediatr Emerg Care*. 2011;27(9):789-794.
- 41. Shapiro T, Dalton M, Hammock J, Lavery R, Matjucha J, Salo DF. The prevalence of urinary tract infections and sexually transmitted disease in women with symptoms of a simple urinary tract infection stratified by low colony count criteria. *Acad Emerg Med.* 2005;12(1):38-44.
- Richards D, Toop L, Chambers S, Fletcher L. Response to antibiotics of women with symptoms of urinary tract infection but negative dipstick urine test results: double blind randomised controlled trial. *BMJ*. 2005;331(7509):143.

Category	Question or finding	Possible diagnoses
Dermatologic	Perineal rash or irritation; generalized dermatitis; mucosal symptoms or lesions	Sexually transmitted infection; atrophy; lichen sclerosus; dermatitis (psoriasis, lichen planus)
Exposures	Smoking/tobacco; occupational or environmental (benzene, aromatic amines); past pelvic irradiation	Genitourinary cancer
Family history	Autosomal dominant polycystic kidney disease; other renal disease	Autosomal dominant polycystic kidney disease; other causes or hematuria, pyuria, or abnormal urinalysis result
Gastrointestinal	Nausea; vomiting; diarrhea; constipation; rectal pain; relationship of symptoms to defecation	Pyelonephritis; adjacent abdominal inflammatory condition (inflammatory bowel disease, diverticulitis); interstitial cystitis/bladder pain syndrome
Genitourinary	Bladder outlet obstructive symptoms (hesitancy, decreased stream, dribbling); irritative symptoms (urgency, frequency); incontinence; pain with intercourse; urethral and testicular symptoms; pain with ejaculation; cyclic symptoms/relation to menses; postmenopausal; vaginal symptoms; rash	Vaginitis; sexually transmitted infection; prostatitis; urethritis epididymitis; stricture; interstitial cystitis/bladder pain syndrome; endometriosis; urethral diverticulum
Medical history	Neurologic disease or injury; systemic inflammatory disease; active cancer	Neurogenic bladder; interstitial nephritis or glomerulitis; metastatic disease
Medications	Current medication and supplement use; recreational drug use; prior treatment with cyclophosphamide	Can cause irritative bladder symptoms directly; interstitial nephritis or cystitis; bladder cancer
Surgical/trauma history	Remote or recent genitourinary or abdominal surgery or irradiation; history of stones; recent bladder catheterization or procedure	Nephrolithiasis; stricture; radiation cystitis; hematuria from instrumentation
Systemic symptoms	Fever; arthralgias; ocular symptoms	Pyelonephritis; transient glomerular injury due to febrile illness; spondyloarthropathy or autoimmune disease

eTable A. Elements of a Detailed History for Select Patients with Dysuria

Information from:

Bent S, Nallamothu BK, Simel DL, Fihn SD, Saint S. Does this woman have an acute uncomplicated urinary tract infection? JAMA. 2002;287(20): 2701-2710.

Bremnor JD, Sadovsky R. Evaluation of dysuria in adults. Am Fam Physician. 2002;65(8):1589-1596.

Colgan R, Williams M, Johnson JR. Diagnosis and treatment of acute pyelonephritis in women. Am Fam Physician. 2011;84(5):519-526.

Gerber GS, Brendler CB. Evaluation of the urologic patient: history, physical examination, and urinalysis. In: Wein AJ, et al.; eds. Campbell-Walsh Urology. 10th ed. Philadelphia, Pa.: Elsevier Saunders; 2012:75-76.

Giesen LG, Cousins G, Dimitrov BD, van de Laar FA, Fahey T. Predicting acute uncomplicated urinary tract infection in women: a systematic review of the diagnostic accuracy of symptoms and signs. BMC Fam Pract. 2010;11:78.

Hooton TM. Clinical practice. Uncomplicated urinary tract infection. N Engl J Med. 2012;366(11):1028-1037.

Wells WG, Woods GL, Jiang Q, Gesser RM. Treatment of complicated urinary tract infections in adults: combined analysis of two randomized, double-blind, multicentre trials comparing ertapenem and ceftriaxone followed by appropriate oral therapy. J Antimicrob Chemother. 2004;53 (suppl 2):ii67-ii74.

examination	Physical findings	Possible implications
Abdomen	Abdominal tenderness or mass	Suprapubic tenderness consistent with cystitis; other tenderness or mass suggests adjacent process, such as diverticulitis or malignancy; bladder distention suggests obstruction or retention
	Costovertebral angle tenderness	Pyelonephritis, stone, or obstruction with hydronephrosis
Dermatologic	Rash, generalized or local to genital area Isolated pustules of extremities	Psoriasis; lichen planus; Stevens-Johnson syndrome; other systemic dermatoses with genital manifestations causing local irritation; candidiasis Systemic gonococcal infection
General/vital signs	Hypertension Fever	Glomerulonephritis Pyelonephritis; systemic illness
Genitals (women)	Vulvar vesicles, ulcers, pustules; inguinal lymphadenopathy; cervical discharge Vaginal discharge and/or mucosal inflammation Cervical motion tenderness; mass or tenderness on bimanual examination Vulvovaginal atrophy Locally tender areas with otherwise normal findings Urethral mass or tenderness	 Herpes simplex virus infection; chancroid; other sexually transmitted infections Vaginitis Endometriosis; pelvic inflammatory disease; gynecologic mass; urethral diverticulum Atrophic vaginitis; lichen sclerosus Vulvodynia; tension myalgia; interstitial cystitis/bladder pain syndrome Urethral diverticulum or endometriosis
Genitals (men)	Penile discharge; urethral meatal inflammation; penile vesicles, ulcers, pustules; inguinal lymphadenopathy Swelling, tenderness of epididymis or testicle Prostate boggy swelling with tenderness Enlarged symmetric prostate Prostate with focal abnormality or hardness, asymmetry, nodule Locally tender areas with otherwise normal findings	Urethritis; herpes simplex virus infection; chancroid; other sexually transmitted infections Epididymo-orchitis Prostatitis Benign prostatic hyperplasia Prostate cancer Tension myalgia; interstitial cystitis/bladder pain syndrome
Other	Joint effusions; conjunctivitis Polyarticular tenosynovitis Neurologic disease	Reactive arthritis (conjunctivitis, arthritis, and urethritis/cervicitis) other systemic disease with local genital manifestations Systemic gonococcal infection Neurogenic bladder

Information from:

Bent S, Nallamothu BK, Simel DL, Fihn SD, Saint S. Does this woman have an acute uncomplicated urinary tract infection? JAMA. 2002;287(20): 2701-2710.

Grady D. Clinical practice. Management of menopausal symptoms. N Engl J Med. 2006;355(22):2338-2347.

Gupta K, Trautner B. In the clinic. Urinary tract infection. Ann Intern Med. 2012;156(5):ITC3-1-ITC3-15.

Sarma AV, Wei JT. Clinical practice. Benign prostatic hyperplasia and lower urinary tract symptoms [published correction appears in N Engl J Med. 2012;367(7):681]. N Engl J Med. 2012;367(3):248-257.