

# A CLINICAL APPROACH TO DYSURIA IN WOMEN

*Dysuria is a common presenting symptom among women and is not always associated with a urinary tract infection.*



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Dysuria is defined as pain, burning or discomfort on urination, which is commonly accompanied by frequency or urgency. Although many doctors equate dysuria with urinary tract infections (UTIs) and treat empirically without adequate evaluation, it is a symptom that is associated with many different clinical entities.

Dysuria is more frequent in young women. A comprehensive history and a step-wise diagnostic approach, accompanied by inexpensive office laboratory testing, are usually sufficient to determine the cause of dysuria. Table 1 lists disorders associated with symptoms of dysuria and their characteristic symptoms, laboratory and physical findings.

### **DIFFERENTIATION BY HISTORY**

Pain occurring at the start of urination may indicate urethral pathology, whereas pain occurring at the end of micturition (strangury) is usually of bladder origin. Dysuria with frequency and urgency with internal discomfort located in the urethra and bladder usually suggests cystitis, while dysuria with external discomfort suggests labial irritation or associated vaginitis. Sexual intercourse is associated with many causes of dysuria, but women with postcoital cystitis typically develop symptoms within a few days of intercourse.

Women are at risk of developing UTIs because of their short urethra, and certain behavioural factors which include delay in micturition, sexual activity and the use of diaphragms and spermicides which promote colonisation of the periurethral area with coliform bacteria. Haematuria is common with UTI, and is unlikely to occur with other potential causes. About 15 - 20% of women with acute cystitis have suprapubic pain.<sup>1</sup> Postmenopausal women not receiving hormone replacement therapy are prone to vaginitis and urinary tract infection.

Dysuria associated with a vaginal discharge suggests some type of vaginitis. Dyspareunia with the sensation of external dysuria is highly suggestive of vaginitis. Dysuria at the start of micturition with symptoms of pelvic inflammatory disease (PID) is suggestive of urethritis.<sup>2</sup>

Associated fever, myalgia and headaches suggest acute pyelonephritis or genital herpes as a cause of dysuria. The former usually has renal angle tenderness while the latter has tender vesicles in the vulva and vaginal area. Dysuria with post-micturition dribble, frequency, urgency and dyspareunia is highly suspicious of a urethral diverticulum and needs to be investigated. Questions should be asked about the use of medications and topical hygiene products since dysuria can be caused by penicillin G, cyclophosphamide, vaginal sprays, vaginal douches and bubble baths. Bladder irritation from compression by adnexal masses and radiation or chemical exposure also produces dysuria.

### **DIFFERENTIATION ON EXAMINATION**

The physical examination is usually not remarkable and special focus should be placed on the genito-urinary system. In patients with cystitis, only 15 - 20% have

Table 1. **Differential diagnosis of dysuria in females**

Diagnosis	Associated symptoms	Physical examination	Laboratory and other test results
Acute cystitis	Frequency, urgency with occasional haematuria	15 - 20% suprapubic tenderness	Usually positive for pyuria and occasionally positive for bacteriuria and nitrite
Subclinical pyelonephritis	Frequency, urgency with infrequent haematuria	May have suprapubic tenderness. No costovertebral angle tenderness	Positive for pyuria, sometimes positive for bacteriuria and nitrite, urine culture >10 <sup>5</sup> colony-forming units/ml
Acute pyelonephritis	Nausea, fever, emesis, back/flank pain. History of preceding cystitis	Costovertebral angle tenderness. Deep right or left upper quadrant tenderness	Pyuria with casts of WBC, urine culture >10 <sup>5</sup> colony-forming units/ml urine
Urethritis	Usually asymptomatic. If symptoms develop they are usually delayed (> 1 week)	No suprapubic pain, unless associated with PID, rarely visible urethral discharge	Urethral swab: positive for WBC, Gram stain for Gram-negative diplococci. Molecular techniques for chlamydia and gonorrhoea
Vaginitis	External irritation, vaginal discharge or pruritus, dyspareunia or premenstrual exaggeration of symptoms	Vaginal discharge, inflamed vaginal mucosa (absent in bacterial vaginosis), inflamed CX (trichomoniasis), vaginal atrophy (postmenopausal)	Positive KOH or vaginal saline preparation, elevated pH (bacterial vaginosis, trichomoniasis)
Genital herpes	Dysuria, fever, headaches, myalgia, vulval pain	Grouped vesicles usually on cervix or pubic area, tender inguinal lymphadenopathy	Viral culture (optional)
Interstitial cystitis	Frequency, urgency, haematuria (20%) with associated dysuria	Long-standing symptoms with negative cultures, may have suprapubic tenderness	Urinalysis negative for WBC or bacteria, positive for glomerulations on cystoscopy
Urethral diverticulum	Postmicturition dribble, dyspareunia and dysuria	Suburethral swelling, occasional pus expressed from urethra	Opening at cystourethroscopy, contrast in diverticulum at voiding cystourethrography
Burning vulvar syndrome	Dysuria is external, burning sensation on vulva	Exquisite tenderness by cotton swab palpation on vestibule, reddish spots at introitus	

KOH = potassium hydroxide.

suprapubic tenderness. Pyrexia, renal angle tenderness, or deep right or left upper quadrant tenderness to deep palpation, suggest acute pyelonephritis. Vaginal atrophy, especially in the elderly, will reflect the hypo-oestrogenic state.

A tender, reddish introitus may suggest vulvodynia and the presence of a tender suburethral swelling with a urethral discharge will be suspicious of a urethral diverticulum.

**DIFFERENTIATION WITH LABORATORY INVESTIGATIONS**

**Urine analysis**

Pyuria is the most sensitive laboratory indicator for UTI. A positive leucocyte esterase dipstick test is 75 - 95% sen-

sitive in detecting pyuria secondary to infection.<sup>3</sup> Bacteruria and urine nitrite are frequently present but are less sensitive as markers of UTI. Positive nitrite is over 90% specific for UTI, but the sensitivity is only 30%.<sup>4</sup> The sensitivity is increased to 60% if the first voided morning urine sample is tested. Therefore a dipstick test that is positive for nitrite suggests UTI. However a negative test does not rule out the diagnosis.

### Microscopic examination

Urine microscopic examination of a clean-catch, spun midstream urine sediment is regarded as the gold standard for evaluating dysuria. Pyuria is diagnosed by the presence of 3 - 5 white blood cells per high-power field and haematuria is diagnosed by the presence of 3 - 5 red blood cells per high-power field.<sup>5</sup>

### Urine culture

Non-pregnant women with uncomplicated cystitis do not usually require a urine culture. However, if it is performed, then more than 10<sup>3</sup> colony-forming units/ml is significant. Urine cultures are also deferred if dysuria is described as external and a probable urethral or vaginal cause is identified.

### Vaginal or urethral smears/pH

Increased vaginal pH is characteristic of trichomoniasis, bacterial vaginosis, and in conditions where *Lactobacillus* is replaced with coliform bacteria. Urethral smears with more than 5 white blood cells per high-power field are highly suggestive of a urethritis.

### Vaginal/urethral cultures

Although cultures for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* are the gold standard for identification of these organisms, they are not routinely done.

## CONDITIONS PRESENTING WITH DYSURIA

### Acute cystitis

Acute cystitis is the most common bacterial infection in young women. Approximately 40% of women will

experience at least one episode of cystitis in their lifetime, and 20% will have recurrent cystitis.

### Pathogenesis

The shorter urethra in women predisposes them to ascending infection of bacteria, especially during sexual intercourse. Naturally occurring defence mechanisms that tend to be protective are indicated below. When these defence mechanisms are disrupted, patients are prone to developing UTIs.

### Naturally occurring defence mechanisms

- Normal urine has a low pH, a high osmolality, and a urea content that makes it a natural bactericide.
- Normal urine flow and voiding expels bacteria.
- A protective mucous coating of the uroepithelial cells inhibits adherence of bacteria.
- Vaginal secretions have a low pH that inhibits growth of coliform bacteria.

### Conditions that cause an increased incidence of urinary tract infection

- Obstruction or alteration in urine flow secondary to tumours, stones, cystocele, pregnancy, and post-incontinence surgery.
- Disruption of the mucin layer following catheterisation with a Foley's catheter, or urinary tract instrumentation.
- Alteration in the normal vaginal lactobacillus colonisation, especially with usage of spermicides (nonoxynol-9), antibiotics, and postmenopausal women with oestrogen deficiency.

Table II lists the likely bacterial pathogens in uncomplicated and complicated UTIs.

### Treatment

Many episodes of bacterial cystitis resolve without treatment. Antibiotics hasten the reduction of symptoms and prevent the spread of infection into the upper urinary tract.<sup>6</sup>

Uncomplicated cystitis can be treated empirically with a single-dose antibiotic or a 3-day course (Table III). The use of single-dose antibiotic therapy has recently fallen into disfavour as there is a high risk of recurrence within 6 weeks of initial treatment.<sup>7</sup> This was attributed to failure to eradicate Gram-negative bacteria from the rectum which is a source or reservoir for ascending infections. It is now accepted that a 3-day regimen offers the optimal combination of convenience, low cost and efficacy comparable with that of a 7-day regimen with fewer side-effects.<sup>8</sup>

Recurrent infections are usually re-infections (infections with different organisms) separated by an asymptomatic interval of at least 1 month. Fortunately, most of these are uncomplicated and are generally not associated with underlying anatomical abnormalities. They are usually caused by vaginal and rectal colonisation with uropathogens.

Patients who have more than 3 UTI recurrences documented by urine culture within 1 year should be managed using one of the three preventive strategies:

- acute self-treatment with a 3-day course of standard therapy when symptoms of UTI develop
- postcoital prophylaxis with trimethoprim-sulfamethoxazole if UTI has been clearly related to intercourse
- continuous daily prophylaxis for a period of 6 months with nitrofurantoin 100 mg per day, or trimethoprim 100 mg per day.

The above regimens have been shown to decrease the morbidity of recurrent UTIs without concomitant increase in antibiotic resistance.<sup>9</sup>

### Complicated UTIs

Complicated UTIs are defined as those occurring in women with an anatomically or functionally abnormal urinary tract, or in women who are immunocompromised, which predisposes them to persistent infections, recurrent infections or treatment failure.

Although many doctors equate dysuria with urinary tract infections (UTIs) and treat empirically without adequate evaluation, it is a symptom that is associated with many different clinical entities.

Dysuria with frequency and urgency with internal discomfort located in the urethra and bladder usually suggests cystitis, while dysuria with external discomfort suggests labial irritation or associated vaginitis.

Aggressive clinical investigation is important since only 35% are *Escherichia coli* related and they are more likely to harbour resistant organisms.<sup>2</sup> Accurate urine culture and susceptibility tests are necessary to best target and eradicate the pathogens. Therapy consists of broad-spectrum agents such as quinolone derivatives for at least 10 - 14 days. Follow-up urine cultures should be performed after treatment to ensure complete cure.

### Subclinical pyelonephritis

This condition represents a diagnostic challenge since these patients have renal parenchymal involvement, but they experience only symptoms of cystitis. This clinical condition has important therapeutic sequelae, since infections are more difficult to eradicate and it requires a 2-week course of antibiotic therapy compared with the usual 3-day course for cystitis.

Identifiable factors that increase a patient's risk for subclinical pyelonephritis are listed below. Most patients with this condition tend to have bacterial counts greater than 10<sup>5</sup> units/ml on quantitative culture, but the specificity of this culture is not high enough to be clinically useful.

Accessory tests, such as antibody-coated bacteria assay, erythrocyte sedimentation rate (ESR) and renal cortical scintigraphy, have been used to identify patients with subclinical pyelonephritis but the specificity of these tests is too poor to make them useful.

Risk factors for subclinical pyelonephritis in women are:

- immunosuppression
- diabetes mellitus
- pregnancy
- anatomic anomaly of the urinary tract
- vesicoureteral reflux
- relapse of symptoms within 3 days of treatment for cystitis
- history of acute pyelonephritis within 1 year.

### Interstitial cystitis

Interstitial cystitis is a clinical syndrome of urinary frequency and pelvic pain in a patient in whom no other pathology can be established. It is significantly more common than was originally believed, affecting an estimated 450 000 people in the USA, 90% of whom are women.

The median age of diagnosis is 40 years. The diagnosis is difficult to make and a study showed that patients on an average have had their symptoms for 4.5 years before they were correctly diagnosed.<sup>10</sup> Of significance, patients with interstitial cystitis are more likely to have had UTIs both as children and adults.

The exact aetiology of interstitial cystitis remains unclear and the proposed theory is that there is an alteration in the glycosaminoglycan mucous layer, possibly in response to a previous bacterial urinary tract infection, allowing solutes in the urine to provide an inflammatory response.

Characteristic features of interstitial cystitis are:

- symptoms of suprapubic pain with frequency, urgency, dysuria, nocturia and dyspareunia for at least 9 months
- bladder capacity less than 350 ml and low first sensation and urge to void (usually less than 150 ml)
- no recent diagnosis of bacterial cystitis (within last 3 months)

Table II. Incidence of bacterial pathogens in lower urinary tract infections

Pathogens	Incidence (%)
<b>Uncomplicated infections</b>	
• <i>Escherichia coli</i>	80
• <i>Staphylococcus saprophyticus</i>	10
• <i>Proteus mirabilis</i>	5
• <i>Klebsiella pneumoniae</i>	4
• <i>Enterobacter</i> species	1
• β-haemolytic streptococcus	< 1
<b>Complicated infections</b>	
• <i>Escherichia coli</i>	35
• <i>Enterococcus faecalis</i>	16
• <i>Proteus mirabilis</i>	24
• <i>Staphylococcus epidermidis</i>	23
• <i>Klebsiella pneumoniae</i>	7
• <i>Pseudomonas aeruginosa</i>	5
• <i>Staphylococcus aureus</i>	4
• <i>Enterobacter</i> species	3
• Others	5

Table III. Empirical oral antibiotic therapy for uncomplicated cystitis in women

Drug	Dose	Active
Single dose <ul style="list-style-type: none"> <li>• Fosfomycin</li> <li>• Amoxicillin</li> <li>• Ciprofloxacin</li> </ul>	3 g sachet — stat 3 g 500 mg	<i>Citrobacter, Enterobacter, Klebsiella, Serratia</i> species
<b>3-day cover</b> <ul style="list-style-type: none"> <li>• Trimethoprim sulfa-methoxazole (Bactrim)</li> <li>• Nitrofurantoin</li> <li>• Ciprofloxacin</li> </ul>	2 tabs bd/3 days 100 mg 4x/3 days 250 mg bd/3 days	

- no alternative explanation for the symptoms, e.g. tuberculous cystitis, radiation cystitis, chemical cystitis
- characteristic cystoscopic appearance.

Definitive diagnosis is made with the identification of Hunner’s ulcers (mucosal ulceration on the bladder wall) or glomerulations (petechial-like haemorrhages on the bladder mucosa).

**Treatment**

There is no known curative therapy for interstitial cystitis. Hence management is directed towards alleviating symptoms and improving function. In general, treatment begins with dietary changes and oral medication. A combination of Taven-sp, Aterax and an antidepressant is usually first-line therapy. While these agents have been shown to improve symptoms relative to placebos, large double-blind, con-

trolled studies evaluating their efficacy are lacking. Intravesical therapy including hydrodistension of the bladder during cystoscopic evaluation, dimethyl sulfoxide (DMSO), intravesical capsaicin and resinferatoxin is usually used as second-line approach.<sup>11</sup> Surgery should be reserved as last choice for patients in whom other forms of management have failed.<sup>12</sup> Surgical procedures include supratrigonal cystectomy with formation of an enterovesical anastomosis.

**Management of interstitial cystitis**

- Dietary — avoid acidic, alcoholic or carbonated beverages, spicy foods, coffee, tea and chocolates.
- Bladder retraining — increasing time interval between voids.
- Medical therapy
  - pentosan polysulfate (Elmiron) — 300 mg/day
  - Taven-SP — 50 - 100 mg bd

- amitriptyline (Tryptanol) — start at 25 mg nocte, increasing by 25 mg every 2 - 4 weeks up to 100 mg
- imipramine (Tofranil) — 25 mg nocte
- hydroxyzine (Aterax) — 25 - 50 mg/day nocte
- nifedipine (Adalat) — 30 mg (extended release) daily
- cimetidine (Tagamet) — 200 mg 3 times/day

**CONCLUSION**

Dysuria is a common symptom that family care practitioners are faced with on a daily basis. Although many equate dysuria with UTIs it is a symptom with many causes. A detailed history and simple examination will identify most causes so that appropriate therapy can be instituted.

References available on request.

**IN A NUTSHELL**

Dysuria is defined as pain, burning or discomfort on urination.

It is commonly accompanied by frequency or urgency.

Pain at the start of urination suggests urethral pathology, while pain at the end of urination suggests bladder origin.

Haematuria is common with UTI. and is unlikely to occur with other potential causes.

Pyuria is the most sensitive laboratory indicator for UTI.

A positive nitrite test is suggestive of UTI, but a negative test does not rule out the diagnosis.

Other conditions which present with dysuria are cystitis, acute and subclinical pyelonephritis, urethritis, vaginitis, genital herpes, interstitial cystitis, urethral diverticulum and burning vulvar syndrome.