

leukocyturia

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Definition

- Leukocyturia or pyuria reflect presence of WBC more than 5-8 in high power field of centrifuged urine

leukocyturia

Urinary tract infection

Sterile leukocyturia

Urinary cancer

Urogenital tuberculosis

Sexually transmitted infection

Tubulointerstitial Nephritis

Urologic manipulation

Nephrolithiasis

Polycystic kidney disease

UTI

- Healthcare providers frequently struggle to differentiate UTI from asymptomatic bacteriuria, particularly in patients presenting with nonspecific symptoms.
- Urinary tract infections (UTIs) are responsible for 25% of all infections in geriatric patients

Molecular Pathogenesis of UTI

- **colonization of the periurethral** area by gastrointestinal tract flora
- UPEC (uropathogenic Escherichia coli) bind to superficial epithelial (facet) cells in bladder.

Pathogenesis of UTI

- After ascending the urethra, bacterial pathogens are challenged by **innate defenses** within the bladder
- promotes the expression of inflammatory cytokines and neutrophil chemoattractants
- This inflammatory milieu engenders **massive neutrophil influx** into the bladder tissue and lumen, **correlating with a diagnostic hallmark of UTI**

Clinical entities of UTI

- Asymptomatic bacteriuria(ASB)
- Acute uncomplicated cystitis
- Recurrent cystitis
- Catheter associated ASB
- Catheter associated UTI (CAUTI)
- Prostatitis
- Pyelonephritis

- **Premenopausal women** are at especially high risk for acute cystitis
- Incidence is **0.5–0.7 case per person-year** among sexually active women

- Hooton TM, et al. A prospective study of risk factors for symptomatic urinary tract infection in young women. N Engl J Med. 1996;335:468-74. [PMID: 8672152]

- Other **populations at risk for UTI:**
- **voiding abnormalities** related to diabetes;
- Neurogenic bladder
- Spinal cord injury
- Pregnancy
- prostatic hypertrophy
- Urinary tract instrumentation, including long-term (≥ 30 days) indwelling catheters
- Urinary stones
- Prostate hypertrophy

- **Diabetes** increases risk for all urinary infectious disorders, from ASB to perirenal abscess and emphysematous pyelonephritis

- Hooton TM. Pathogenesis of urinary tract infections: an update. J Antimicrob Chemother. 2000;46

screening for UTI or ASB

- In men and nonpregnant women, screening for ASB is generally **not recommended** because treatment does not improve clinical outcomes
- ASB does not lead to hypertension, chronic kidney disease, or decreased duration of survival
- Nicolle LE, Infectious Diseases Society of America. Infectious Diseases Society of America guidelines for the diagnosis and treatment of asymptomatic bacteriuria in adults. Clin Infect Dis. 2005;40:643-54

- ASB during **pregnancy** (4%–7% of pregnant women) is associated with progression to symptomatic UTI, including pyelonephritis
- Acute **pyelonephritis** occurs in up to 2% of pregnancies in the United States and is the most common non obstetric cause of hospitalization during pregnancy

- Wing DA, Fassett MJ, Getahun D. Acute pyelonephritis in pregnancy: an 18-year retrospective analysis. Am J Obstet Gynecol.2014;210:219.e1-6.

- **ASB during pregnancy** is also associated with **low birthweight** and **preterm labor not abortion**

- Antibiotic treatment of ASB was associated with significantly decreased risk for pyelonephritis, premature birth, and low birthweight compared with no treatment

- Smaill FM, Vazquez JC. Antibiotics for asymptomatic bacteriuria in pregnancy. Cochrane Database Syst Rev. 2015

- Screening for and treatment of ASB are also recommended before transurethral resection of the prostate (**TURP**) or other **urinary tract instrumentation** resulting in mucosal bleeding

- TURP in bacteriuric men can precipitate **bacteremia** with associated sepsis and that antimicrobial treatment of the bacteriuria can prevent these complications.
- Simple catheter placement and **cystoscopy without biopsy** do not warrant screening for ASB

- **Renal transplant** recipients who have ASB are at higher risk for pyelonephritis, but whether pyelonephritis affects graft function is controversial
- The relationship of ASB to UTI and sepsis in patients with **neutropenia** has not been well-studied.
- Fiorante S, Lo'pez-Medrano F, Lizasoain M, Lalueza A, Juan RS, Andre's A, et al. Systematic screening and treatment of asymptomatic bacteriuria in renal transplant recipients. *Kidney Int.* 2010;78:774-81

Signs and symptoms

- The most common symptoms of UTI in noncatheterized persons include **dysuria**, **urinary frequency**, and **urgency**.
- In pyelonephritis fever and chills and flank pain
- Symptoms that increased the probability were **dysuria**, **hematuria**, and **costovertebral angle tenderness**.
- A history of vaginal discharge or irritation decreased the probability of UTI

- In **catheterized patients**, signs and symptoms suggestive of CAUTI include new onset or worsening of **fever, rigors, altered mental status, malaise** or **lethargy** with no other identified cause, **flank pain**, costovertebral angle tenderness, acute **hematuria**, or pelvic discomfort

- In patients whose catheters have been removed within the past 48 hours, dysuria, urgent or frequent urination, or suprapubic pain or tenderness are also suggestive of **CAUTI**
- Guidelines also specify that **10^3 or more colony-forming units** per milliliter of urine is sufficient for diagnosis of CAUTI.

- Hooton TM, et al; Infectious Diseases Society of America. Diagnosis, prevention, and treatment of catheter associated urinary tract infection in adults: 2009

- CAUTI can occur with indwelling urethral (Foley) catheters, suprapubic catheters, or condom catheters.
- **other infections** and potential causes should be considered before attributing the symptoms to catheter-associated bacteriuria.
- Distinguishing between CAUTI and catheter-associated ASB is challenging.

- In **men** with urinary symptoms and fever, both acute infectious **prostatitis** and pyelonephritis should be considered in the differential diagnosis which needs **prolong duration** of treatment.
- In pyelonephritis 10-14 days
- In acute prostatitis more than 14 days to 28 days

Diagnostic tools

- **Women** presenting with classic symptoms of cystitis (dysuria or urinary frequency) without symptoms suggesting alternative diagnoses or underlying complications may be treated for UTI **without further testing**
- A dipstick test is not necessary if the history is clearly diagnostic of UTI

- In women with **acute dysuria**, pyuria is a highly sensitive
- indicator of bacteriuria and can be used as a surrogate for urine culture

- Performing a **culture** (with susceptibility testing) on a pretreatment urine sample is appropriate for women with suspected **cystitis** if :
 - The diagnosis is not clear,
 - An unusual or antimicrobial-resistant organism is suspected
 - A suspected relapse or treatment failure,
 - The patient's therapeutic options are limited by medication intolerance.

- *Escherichia coli* is isolated in more than 90% of patients with uncomplicated cystitis and pyelonephritis.
- Other coliforms, including *Klebsiella* and *Proteus*, are less common. *Staphylococcus saprophyticus* causes uncomplicated cystitis and pyelonephritis in a small proportion (5%–10%) of otherwise healthy women.

- *E coli* is a predominant pathogen in **complicated UTI**, but other coliforms and **enterococci** are also common.
- CAUTI in patients with **short-term** catheters can be caused by *E coli* as well as by a spectrum of typical hospital acquired pathogens, including ***Klebsiella*, *Citrobacter*, *Enterobacter*, *Pseudomonas***, coagulase negative **staphylococci**, **enterococci**, and ***Candida***.

- Patients with **long-term catheters** typically have **polymicrobial** infections; in addition to the aforementioned pathogens, *Proteus*, *Morganella*, and *Providencia* are common

- Nicolle LE. Catheterrelated urinary tract infection. Drugs Aging. 2005;22:627-39.

- Interpretation of urine culture results depends on the clinical context and the urinalysis findings; the threshold of bacteriuria required for the diagnosis of acute cystitis is **not absolute**.
- Even a low concentration (10^2 colony-forming units per milliliter) of coliform bacteria in a urine sample from a woman with acute dysuria and pyuria often represents true bacteriuria.

- Even high concentrations ($>10^5$ colony-forming units per milliliter) of nonpathogens may not reflect true bacteriuria if the urine specimen was **not collected properly** or was allowed to **stand at room temperature** before processing.

- Organisms other than coliform bacilli, *S saprophyticus*, and *Enterococcus* (for example, lactobacilli, -streptococci, and coagulase-negative staphylococci other than *S saprophyticus*) are usually considered **contaminants** in urine cultures from women with uncomplicated cystitis, whereas **in complicated UTI almost any organism can be causative** and must be seriously considered if the patient is symptomatic.

Diagnostic imaging

- For **uncomplicated bladder infections**, imaging studies (abdominal radiography, ultrasonography, computed tomography, and excretory urography) add little or no benefit but increase cost.
- Such studies should be done **only** if pretest suspicion is high for an **alternative diagnosis** or an **anatomical problem** (such as a bladder obstruction or stone) that requires intervention.

- Although men with acute cystitis should be considered **for further evaluation for urologic abnormalities**, imaging studies for acute cystitis in men younger than 45 years or in older men without symptoms of voiding difficulties or hematuria may not be useful. The evidence base for male cystitis is limited

- Ulleryd P, Zackrisson B, Aus G, Bergdahl S, Hugosson J, Sandberg T. Selective urological evaluation in men with febrile urinary tract infection. BJU Int. 2001;88:15-20.

Treatment

- Treatment of UTI depends on **host factors** (such as sex, compromised immune system, or urologic abnormalities), severity of illness, and risk for multidrug resistance.
- The prevalence of resistance in community populations has increased and must be considered, even in outpatients

- In women with symptoms of **cystitis** without fever or signs of systemic infection, outpatient **oral antibiotic** therapy is recommended.
- Clinicians should ask about factors that may influence the **choice of antimicrobial agent**:
 - Pregnancy and breastfeeding,
 - Use of other medications,
 - Drug allergy history,
 - Recent antibiotic therapy,
 - Other recent infections or positive culture results,
 - Recent travel

- **Previous microbiology** should also be reviewed because it can be useful in predicting multidrug resistance of the current pathogen

- Linsenmeyer KT
Two simple rules for improving the accuracy of empiric treatment of multidrug-resistant urinary tract infections.
Antimicrob Agents Chemother. 2015;59:7593-6.

- In patients admitted for **intravenous therapy**, a **broad-spectrum agent** should be given until susceptibilities are known.
- A carbapenem agent, an extended spectrum -lactam with or without an aminoglycoside, or another regimen chosen on the basis of local resistance patterns is appropriate.

- However, **resistance to fluoroquinolones** among uropathogens is increasing worldwide.
- If the local prevalence of fluoroquinolone resistance exceeds **10%**, another broadspectrum antimicrobial should be considered, including an extended-spectrum **cephalosporin** with or without an aminoglycoside or a carbapenem.

- For **CAUTI**, the recommended duration of antimicrobial treatment is 7 days for patients who have prompt resolution of symptoms and 10–14 days for those with a delayed response.
- In patients with CAUTI who have had a catheter in place for 2 weeks or longer, the catheter should be removed or replaced

- **In pregnant women** with symptomatic UTI, urine culture and susceptibility testing should be performed.
- Empirical therapy with an oral antimicrobial agent that is safe for use in pregnant women should be given for 3–7 days, depending on which drug is used.
- Antibiotic therapy should be adjusted on the basis of culture results.

Indication of hospital admission

- Complicated cystitis or pyelonephritis may require inpatient management
- Factors that may warrant hospitalization include:
- Serious **comorbid conditions** and
- **Pregnancy**, Patients with **high fever**,
- **Dehydration**, **High leukocyte count**, **Sepsis**, as do those who are **vomiting** and thus unable to take oral therapy.

- The patient has an upper urinary tract condition that **requires drainage** or surgical Intervention
- A patient may have a **multidrug resistant organism** in the urine that is susceptible only to parenterally administered antimicrobial agents
- patient is **intolerant** of agents that can be given orally

- In particular, patients with CAUTI who do not respond promptly to appropriate antibiotic therapy may have **obstruction** or **stones** in the upper urinary tract.
- Effective urine drainage reduces intraluminal pressure and restores the flow of antibiotic-containing urine.

Patients follow up

- In **uncomplicated cystitis**, **no follow-up** is needed if symptoms resolve.
- In pregnant women, urine culture should be done after treatment to confirm eradication of bacteriuria, and repeated urinalyses or urine cultures should be done at intervals to confirm sterility of the urine through the time of delivery

Pathophysiology, Treatment, and Prevention of Catheter-Associated Urinary Tract Infection

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- catheter-associated UTI (**CAUTI**) accounts for **40% of all nosocomial infections** worldwide
- In CAUTI, **duration of catheterization** is the most important determinant of bacteriuria, and CAUTI risk increases by **3% to 7% each day** after placement of an indwelling urinary catheter

- **Even short-term urinary catheterization** increases the risk of developing CAUTI and other complications up to 80%, and prolonged catheterization can increase the risk to nearly 100%
- Patients with catheter-associated bacteriuria have a 3% risk of developing **bacteremia**
- Delnay KM, Stonehill WH, Goldman H, Jukkola AF, Dmochowski RR. Bladder histological changes associated with chronic indwelling urinary catheter. *J Urol.* 1999;161(4):1106-1108; discussion 1108-1109.

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Prevalence and Clinical Characteristics of Asymptomatic Pyuria in Chronic Kidney Disease

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- Urine examination was performed for all stable hemodialysis (HD) and non-dialysis CKD patients of the outpatient clinic (total N=298).
- Urine culture and WBC analysis were performed when urinalysis revealed pyuria
- The prevalence of **ASP** was 30.5% (24.1% in non-dialysis CKD and 51.4% in HD patients).

- Over 70% of the pyuria cases were sterile.
- The majority of urinary WBCs were neutrophils, even in sterile pyuria. However, the percentage of neutrophils was significantly lower in sterile pyuria.
- In multivariate logistic regression analysis, the degree of pyuria, percentage of neutrophils, and presence of urinary nitrites remained independently associated with sterile pyuria.

Urinary Calprotectin loses specificity as tumour marker due to sterile leukocyturia associated with bladder cancer

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- Urinary Calprotectin, a **mediator of the innate immune system**, has been identified as a biomarker in bladder cancer.
- Our aim was to investigate the association between sterile leukocyturia and urinary Calprotectin in low-grade and high-grade bladder cancer

- a prospective cross-sectional study including 52 patients with bladder cancer and 40 healthy controls.
- Definition of sterile leukocyturia was > 5.0 leukocytes per visual field in absence of bacteriuria

- The rate of **sterile leukocyturia** in low-grade (60.0%) and high-grade (62.0%) bladder cancer was comparable ($p = 0.87$).
- a significant correlation between urinary Calprotectin and leucocyte concentration ($R = 0.4$, $p < 0.001$).
- Urinary Calprotectin cannot be regarded as a specific tumour marker for bladder cancer, but rather as a surrogate parameter for tumour inflammation

Urogenital Tuberculosis

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Affiliations + expand

PMID: 28087922 DOI: [10.1128/microbiolspec.TNMI7-0015-2016](https://doi.org/10.1128/microbiolspec.TNMI7-0015-2016)

- Urogenital tuberculosis is the second most frequent form of extrapulmonary tuberculosis
- Starting with a pulmonary focus, 2 to 20% of patients develop urogenital tuberculosis through hematogenous spread to the kidneys, prostate, and epididymis
- Hematuria, **sterile pyuria**, and recurrent urinary infections are the most symptoms

Urinary Tract Infection and Asymptomatic Bacteriuria in Older Adults

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- Urinary tract infections (UTIs) are a significant cause of morbidity among older adults; however, antibiotic prescriptions for clinically suspected UTIs are often inappropriate.

Healthcare providers frequently struggle to differentiate UTI from asymptomatic bacteriuria, particularly in patients presenting with nonspecific symptoms

- **Urinary tract infections** (UTIs) are responsible for 25% of all infections in geriatric patients .
- Colonization with multidrug resistant organisms is high in nursing home settings

Challenges in elderly

Poorly defined clinical criteria to diagnose UTIs

Reliance on laboratory criteria rather than clinical symptoms to define infection

Limited guidance regarding the use and interpretation of diagnostic tests

Challenges for selecting empiric antimicrobial therapy

Difficulty distinguishing ASB from UTI, particularly in older adults with dementia

Increased risk of adverse events and drug interactions related to antibiotic use

High Prevalence of Sterile Pyuria in the Setting of Sexually Transmitted Infection in Women Presenting to an Emergency Department

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- The clinical presentations for **sexually transmitted infections** (STI) and urinary tract infections (UTI) often overlap, and symptoms of dysuria and urinary frequency/urgency occur with both STIs and UTIs.
- Abnormal urinalysis (UA) findings and pyuria are common in both UTIs and STIs, and confirmatory **urine cultures** are not available to emergency clinicians to aid in decision-making regarding prescribing antibiotics for UTIs.

- **Neisseria gonorrhoeae**, **Chlamydia trachomatis**, and/or **Trichomonas vaginalis**
- Our results suggest that reliance on pyuria or positive nitrite for the decision to add antimicrobial therapy empirically for a presumed urinary tract infection in cases in which an STI is confirmed or highly suspected is likely to result in substantial over-treatment

Pyuria, urinary tract infection and renal outcome in patients with chronic kidney disease stage 3–5

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Shang-Jyh Hwang^{1,3,4}, Hung-Chun Chen^{1,3} & Chi-Chih Hung¹✉

- Pyuria is common in **chronic kidney disease** (CKD), which could be due to either urinary tract infection (UTI) or renal parenchymal inflammation
- was correlated to **old age, female, diabetes, hypoalbuminemia, lower eGFR, and higher inflammation status.**

- Recurrent and persistent **pyuria** may contribute to the decline of kidney function in patients with **autosomal dominant polycystic kidney disease** (ADPKD)
- In conclusion, CKD stage 3-5 patients with frequent pyuria or UTI episodes have increased risks of renal outcomes

Acute interstitial nephritis

- Inflammation in kidney mainly due to drugs specially cephalosporine and NSAIDS
- Other causes are **Infections**, **systemic disease** ,**idiopathic**
- 15-27 % of renal biopsies
- Acute deterioration in renal function
- Subnephrotic proteinuria
- leukocyturia

- The characteristic interstitial infiltrates, mostly composed of **lymphocytes, macrophages, eosinophils, and plasma cells**, experience a rapid transformation into areas of interstitial fibrosis

Steroid treatment

- The role of steroids in the treatment of drug-induced AIN remains controversial.
- Steroids are the mainstay of treatment in idiopathic AIN, TINU, and AIN associated with systemic diseases

- Kidney International (2010) 77, 956–961

THANK YOU