



UTI Myths



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Objectives

- ▶ Epidemiology
- ▶ Pathogenesis
- ▶ Risk factors
- ▶ Diagnosis
- ▶ Special Scenario
- ▶ Asymptomatic Bacteriuria
- ▶ Treatment
- ▶ Prophylaxis



Epidemiology

- ▶ Most common outpatient infection in United states
- ▶ UTI results in 8.6 billion health care visits and estimated costs of 1.6 billion dollars each year.
- ▶ 11% women report at least one physician diagnosed UTI per year and 20-30% report multiple recurrences
- ▶ Prevalence increases up to 20% after age 65 in women



Pathogenesis

- ▶ Ascending spread of bacteria through urethra
- ▶ Rarely hematogenous or lymphatic spread
- ▶ Pathogens originate in the rectal flora and colonization of the perineum and periurethral area precedes the development of infection.
- ▶ Colonization is inhibited by normal bacterial flora including *Staphylococcus epidermis*, *Lactobacilli*, *Corynebacteria* (Which are disrupted by antibiotics and estrogen deficiency)



Pathogenesis

- ▶ Normal Host Defense mechanisms
 - ▶ Complete voiding removes bacteria from bladder
 - ▶ Urinary acidification from concentrated urea and other excreted organic acids
 - ▶ Vesicoureteral valves prevents reflux of bacteria to urinary tract
 - ▶ Leukocyte phagocytosis
 - ▶ IgA production



Definitions

- ▶ **Classification: Complicated and Uncomplicated (Without any anatomical or functional abnormality)**
- ▶ **Recurrent UTIs (rUTIs) can be defined as at least three episodes of UTI in 1 year or two episodes in 6 months**



Complicated UTI

- ▶ **Presence of factors which makes UTI complicated :**
- ▶ **Diabetes**
 - ▶ Immunological impairment
 - ▶ Inadequate bladder emptying
 - ▶ Higher glucose concentration in the urine act as a culture medium for bacteria
- ▶ **Pregnancy**
- ▶ **Renal failure**
- ▶ **Urinary tract obstruction**
 - ▶ Prostate enlargement
 - ▶ Urethral stricture
 - ▶ Bladder neck obstruction



Complicated UTI

- ▶ Recent urinary tract procedure or instrumentation
- ▶ Functional or anatomical abnormality of urinary tract
- ▶ Neuropathic bladder
 - ▶ Multiple sclerosis
 - ▶ Spina bifida
 - ▶ Spinal cord trauma
- ▶ Renal transplant
- ▶ Immunosuppression
- ▶ Renal calculi



Risk factors

- ▶ **Female sex**
 - ▶ Shorter urethral length
 - ▶ Frequent vaginal colonization
 - ▶ Incomplete bladder emptying from prolapse and urinary retention
 - ▶ **Sexual intercourse**
 - ▶ Use of spermicidal promotes adherence of bacteria to uroepithelium
 - ▶ Use of Diaphragm
 - ▶ **Vesicoureteral reflux**
 - ▶ **Post menopause**
 - ▶ Lack of estrogen causes lack of lactobacilli and increases colonization by pathogenic bacteria spp
 - ▶ **Indwelling foley catheter, stent, nephrostomy tube, urinary diversion**
 - ▶ **Recent urinary tract instrumentation**
 - ▶ **Urinary tract obstruction**
 - ▶ **Functional or anatomical abnormality**
 - ▶ **Bladder prolapse**
 - ▶ **Blood group secretor status and IL-8 (Genetic factors) Not fully understood.**
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Diagnosis

- ▶ **3 main tests**
- ▶ Dipstick Urinalysis
- ▶ Microscopic analysis
- ▶ Urine cultures
- ▶ Bacteria multiply rapidly if urine left standing for long time at room temperature
- ▶ Positive Nitrites, Leukocyte esterase and presence of bacteria is highly suggestive of UTI
- ▶ If $> 15-20$ squamous epithelial cells are present per HPF – suggestive of contamination.



Diagnosis

- ▶ **Five symptoms significantly predicted the diagnosis of UTI**
 - ▶ Dysuria , frequency, hematuria, nocturia, urgency
 - ▶ Vaginal discharge decrease the risk of UTI
 - ▶ Hematuria most useful symptom to rule in UTI
 - ▶ (Sensitivity 25% but specificity 85%)
 - ▶ Absence of Dysuria, frequency and urgency are most useful to rule out UTI



Diagnosis

- ▶ **Urine Dipstick**
- ▶ Readily available outpatient
- ▶ Takes minutes for interpretation
- ▶ Sensitivity ~ 75% and specificity 82% with high probability of UTI
- ▶ Older population who has higher rates of asymptomatic bacteriuria has less sensitivity (~65%) and specificity (~70%).
- ▶ Negative dipstick does not rule out the possibility of UTI
- ▶ Does not distinguish between symptomatic and asymptomatic UTI.
- ▶ Symptomatic and asymptomatic patients > 65 years age showed similar specificity.
- ▶ 61 % of patients who had positive dipstick had negative cultures



Diagnosis

- ▶ Most important component to detect is Leukocyte esterase, Nitrite and red blood cells
- ▶ **Leukocyte esterase** : Enzyme present in WBC which is released due to lysis of WBC
- ▶ Fairly sensitive to leukocyte esterase in urine and turns positive with presence of $> 5-15$ WBC/hpf
- ▶ Normally presence of WBC in urine not high enough to result in positive leukocyte esterase.
- ▶ In presence of Pyuria, it will become positive
- ▶ Red blood cells can be detected in urine $> 1-4$



Diagnosis

- ▶ **Nitrite** : Positive nitrite due to presence of gram negative bacteria (E.coli, Klebsiella, proteus, enterobacter) convert urinary nitrates to nitrite.
- ▶ Urine dipsticks are able to detect Nitrites in the presence of bacteria $>100,000$ colonies
- ▶ It will not turn positive if gram positive bacteria
- ▶ (Staphylococcus or Streptococcus) are causing infection.
- ▶ Nitrites have high positive predictive value in the elderly.
- ▶ Nitrite alone and combination with Leukocyte esterase are more sensitive in >65 years than those < 65 years



Microscopic UA

- ▶ Pyuria > 5-10 leukocyte/hpf
- ▶ Bacteriuria > 15 bacteria/hpf
- ▶ Absence of Pyuria with Bacteriuria suggests colonization or contamination rather than active infection.
- ▶ Bacteriuria has high sensitivity and specificity than pyuria.
- ▶ Pyuria is misleading in chronic incontinence and asymptomatic bacteriuria.
- ▶ age > 70 – Sensitivity is lower but specificity is higher for Bacteriuria
- ▶ Absence of Bacteriuria reduces probability of UTI but can not rule out completely.



TABLE 2

Summary of diagnostic performance of dipstick urinalysis and microscopic urinalysis

Study	Test	Sensitivity	Specificity	PPV	NPV	LR+	LR-	DOR
Testing								
Dipstick urinalysis								
Bent et al ¹¹	Nitrite ± LE	75%	82%	79%	76%	4.2	0.3	
Meister et al ²⁴	Nitrite	34–42%	94–98%			7.5–24.6	0.6–0.7	
	LE (>0)	75–91%	41–87%			1.5–5.6	0.2–0.4	
	LE (>0) or nitrite	91–92%	39–41%			1.5–1.6	0.2	
Medina-Bombardó and Jover-Palmer ¹³	Nitrite					6.51	0.58	11.3
	LE					1.42	0.44	3.58
Population specific								
Older population								
Ducharme et al, ²⁵ Deville et al, ²⁶ Juthani-Mehta et al ²⁷	Nitrite ± LE (except for Juthani-Mehta et al ²⁷ : nitrite + LE)	64.3–100%	20–76.7%	31–45%	92–100%			
Pregnancy—asymptomatic bacteriuria								
Rogozínska et al ³⁰	Nitrite	55%	99%			54.08	0.46	
	Nitrite ± LE	73%	89%			6.36	0.31	
Deville et al ²⁶	Nitrite	46%	98%					165
	Nitrite ± LE	68%	87%					17
Microscopic urinalysis								
Kayalp et al ³¹	Pyuria	68.2%	87.8%	11.7%	99.2%	5.6	0.36	15.5
	Bacteriuria	78.8%	97.8%	45.4%	99.5%	35.3	0.22	162.6
Lammers et al ³²	Pyuria (≥5 WBC)	90–92%	43–47%	58–59%	83–85%			
	Pyuria (≥3 WBC)	99%	17%	50%	93%			
Population specific								
Older population								
Kupelian et al ³⁷	Pyuria	42%	73%	40%	75%			
Kayalp et al ³¹	Bacteriuria	86.4%	84.4%	65.4%	94.8%	5.5	0.16	34.4
	Pyuria	84.4%	72–76%	54.6%	93.5%	3.5	0.21	17.7
Pregnancy—asymptomatic bacteriuria								
Rogozínska et al ³⁰	Bacteriuria	78%	92%			9.4	2.4	
Bachman et al ³⁹	Bacteriuria	75%	59.7%	4.2%				
	Pyuria (>10 WBC)	25%	99%	37.5%				
	Bacteriuria ± pyuria	83.3%	58.9%	4.5%				

DOR, diagnostic odds ratio; LE, leukocyte esterase; LR, likelihood ratio; NPV, negative predictive value; PPV, positive predictive value; WBC, white blood cell.

Chu. UTI across age groups. Am J Obstet Gynecol 2018.

Urine cultures

- ▶ **Urine culture** : > 100,000 colony forming units of single bacteria with symptoms confirms diagnosis of UTI
- ▶ Culture with single pathogen with >100,000 colonies (high rate of false negativity) are considered positive cultures
- ▶ Cultures with multiple bacteria or mixed flora are usually contamination.
- ▶ 30-50% women with symptomatic UTI have low colony counts (~100 colonies)
- ▶ Low colony counts also results of women with UTI on already antibiotics or infection with pathogens like
 - ▶ Pseudomonas , Klebsiella, Enterobacter, Serratia, Moraxella



Pathogens

- ▶ Most common bacteria is E.coli (70% of time)
- ▶ Enterobacter
- ▶ Proteus
- ▶ Klebsiella
- ▶ Pseudomonas
- ▶ Enterococcus fecalis
- ▶ Staphylococcus saprophyticus
- ▶ Streptococcus agalactiae
- ▶ Gardnella vaginalis , Ureaplasma - Pregnant female
- ▶ Increasing rate of ESBL E.coli



Clinical symptoms

Asymptomatic Bacteriuria	No urinary symptoms	> 10 WBC/mm³ ≥ 100,000 Colony in 2 consecutive cultures > 24 hours apart
Uncomplicated UTI Uncomplicated Cystitis	Dysuria , Urgency, Frequency, Suprapubic pain	> 10 WBC/mm ³ > 1000 Colony
Acute uncomplicated Pyelonephritis	Fever, chills, flank pain, No H/o urological abnormalities	> 10 WBC/mm ³ ≥ 100,000 colonies
Complicated UTI	Symptoms of UTI with presence of any factors which makes it complicated	> 10 WBC/mm ³ ≥ 100,000 colonies in women ≥ 10000 colonies in men or straight cath urine in women
Recurrent UTI	At least 3 episodes of infection in last 12 months, women only , No structural abnormality	< 1000 colonies (between episode)

Catheter associated UTI

- ▶ Presence of indwelling Foley catheter
- ▶ Most common health care associated infection.
- ▶ Usually preventable by avoiding inappropriate use of Foley catheters
- ▶ Most effective means to decrease incidence of CAUTI is to reduce use of Foley catheter or to discontinue them as soon as possible.
- ▶ Symptoms:
 - ▶ Costovertebral angle tenderness
 - ▶ Rigors and chills
 - ▶ Delirium
 - ▶ Encephalopathy
 - ▶ Polymicrobial etiology



Diagnosis of CAUTI

- ▶ >1000 cfu/ml and more than one bacteria
- ▶ CAUTI patients lack signs of fever, urgency, pain or dysuria
- ▶ Foul smelling urine does not warrant the diagnosis of CAUTI
- ▶ Foley catheter should be first replaced followed by UA
- ▶ Treatment duration: CAUTI 7 day but if delayed response 10-14 days



Complicated UTI with Urolithiasis

- ▶ Stone obstruction leads to urinary stasis which promotes bacteria to adhere to uroepithelial and multiply and cause UTI.
- ▶ Primary infection by Urea splitting organisms can lead to struvite stone formation and in turn start vicious cycle
- ▶ Stones > Obstruction > stasis > Infection > Stones



Complicated UTI with Urolithiasis Management

- ▶ Urgent decompression of collecting system
 - ▶ Percutaneous drainage
 - ▶ Ureter stents
- ▶ Definitive treatment of stone should be delayed until sepsis resolved.
- ▶ Surgical removal of complete stone
- ▶ Either short or long course of antibiotics
- ▶ Acidification of urine :
 - ▶ Ammonium chloride 1 gm BID or TID
 - ▶ Methionine 200-500 mg BID or TID
- ▶ Urease inhibition



Complicated UTI with BPH

- ▶ No clear evidence about UTI related to high post void residual or bladder outlet obstruction.
- ▶ Antibiotics prophylaxis is not indicated.
- ▶ Lower urinary tract symptoms can be secondary to BPH itself.
- ▶ Medical treatment for BPH can not reduce incidence of UTI.
- ▶ Recurrent or persistent UTI in men with bladder outlet obstruction and BPH is indication for Prostatectomy.
- ▶ Screen and Treat Asymptomatic Bacteriuria before TURP.
- ▶ Discontinue antibiotics after procedure unless foley catheter remained in place.



Complicated UTI with Neurogenic Bladder

- ▶ Atypical symptoms
- ▶ Cloudy urine
- ▶ Foul smelling urine
- ▶ Fever
- ▶ Malaise
- ▶ Lethargy
- ▶ New or increased leak of urine
- ▶ Increased spasticity
- ▶ Autonomic dysreflexia
- ▶ Pelvic floor pain
- ▶ Supra pubic pain
- ▶ Dysuria



Complicated UTI with Neurogenic bladder

- ▶ Optimal duration is not established.
- ▶ 7 days are sufficient but duration can be 5 to 14 days
- ▶ Asymptomatic bacteriuria should not be treated even in cases of intermittent catheterization (Not beneficial and lead to emergence of MDR bacteria)
- ▶ Antibiotics prophylaxis is not recommended
- ▶ Scheduled time for urination/catheterization



Elderly population

- ▶ Symptoms and signs can present differently in older adults.
- ▶ Older patients has symptoms of Urgency and frequency unrelated to UTI
- ▶ Atypical symptoms thought to be associated with UTI in elderly population are not associated with positive urine culture.
 - ▶ Falls
 - ▶ Worsening incontinence
 - ▶ Functional and cognitive decline
 - ▶ Malodorous urine



Delirium, a Symptom of UTI in the Elderly: Fact or Fable? A Systematic Review*



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DOI:<http://dx.doi.org/10.5770/cgj.17.90>

5 Studies from 1988 to 2011

No randomized controlled study, cross sectional observational studies and one case series

Delirium patients had UTI ranges from 25% to 32% compared to 13% without delirium.

UTI patients had delirium from 30% - 35% compared to 8% without UTI

Conclusion: Studies have concluded there is association between UTI and Delirium.

All of studies has significant methodological flaws which lead to biased results.

Difficult to prove how much delirium UTI causes.

More research needed.



Asymptomatic Bacteriuria

- ▶ 2 consecutive clean catch mid stream bacterial cultures with colony counts $> 100,000$ in female consisting of the same bacteria.
- ▶ Single clean –catch specimen in men or single catheterized specimen in all patients.
- ▶ Catheterized sample – bacterial cultures with colony counts > 1000 is bacteriuria
- ▶ Prevalence of Bacteriuria
 - ▶ 5% of healthy, pre menopausal women
 - ▶ 30-50% of older women residing in ECF
 - ▶ 10.8 – 15% older women residing in community
 - ▶ 2-10% of pregnant women



When do you treat ASB

- ▶ Pregnant women
- ▶ Women undergoing invasive genitourinary procedures
- ▶ Men undergoing urological procedure that includes mucosal bleeding
- ▶ All renal transplant patient



Treatment

- ▶ **IDSA Guidelines (2011)**
- ▶ Nitrofurantoin 100 mg BID – 5-7 days
- ▶ Trimethoprim-sulfamethoxazole – 160/800 mg BID – 3 days
- ▶ Fosfomycin 3 gm – Single dose sachet
- ▶ Ciprofloxacin 250 mg BID – 3 days
- ▶ B lactams : Inferior to other medications.
 - ▶ Cefpodoxime 100 mg BID – 3 Days
 - ▶ Augmentin 500/125 mg BID
 - ▶ Cefdinir 100 mg BID – 5 days
 - ▶ Cefaclor 250 mg TID – 5 days



Empiric treatment of uncomplicated cystitis.

Drug	Dosing	Duration
First line		
Nitrofurantoin	100 mg twice daily	5 days
Trimethoprim–Sulfamethoxazole ^a	160/800 mg twice daily	3 days ^a
Fosfomicin	3 g	1 dose
Second line		
Ciprofloxacin ^a	250 mg twice daily	3 days ^a
Levofloxacin	250 mg daily	3 days
Third line		
Amoxicillin–Clavulanate	875-125 mg twice daily	3–7 days
Cefdinir	300 mg twice daily	3–7 days

Empiric treatment of complicated cystitis.^a

Drug	Dosing	Duration (days)
First line		
Ciprofloxacin	500 mg twice daily	7
Levofloxacin	750 mg daily	7
Narrowing of antibiotics (based on cultures)		
Nitrofurantoin (macrocrystals)	100 mg twice daily	7
Trimethoprim–Sulfamethoxazole	160/800 mg twice daily	7
Cannot tolerate orals		
Ceftriaxone	1 g daily IVPB	7
Piperacillin–Tazobactam	3.375 g every 6 h IVPB	7
Cannot tolerate orals and Penicillin allergy		
Aztreonam	1 g every 8 h IVPB	7

Effect of 5-Day Nitrofurantoin vs Single-Dose Fosfomycin on Clinical Resolution of Uncomplicated Lower Urinary Tract Infection in Women

A Randomized Clinical Trial

Angela Huttner, MD^{1,2}; Anna Kowalczyk, MS³; Adi Turjeman, MSc⁴; [et al](#)

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JAMA. 2018;319(17):1781-1789. doi:10.1001/jama.2018.3627

Randomized double blind controlled trial

513 Hospitalized and ambulatory women > 18 years of age who had > 1 symptom of acute lower UTI, positive Nitrites or LE

Exclusion – Suspected Upper UTI, Renal insufficiency, Immunosuppression, use of antibiotics or symptoms consistent with UTI in past 4 weeks

Intervention: Oral Nitrofurantoin 100 mg three times a day for 5 days vs Single dose Fosfomycin 3 gm

Outcomes : Clinical resolution at 28 days

Secondary outcomes : Clinical resolution at 14 days, duration of symptoms, pyelonephritis, bacteriological success in patients with positive results on baseline cultures

Main results: Clinical resolution and bacteriological success results did not differ for duration of symptoms or occurrence of Pyelonephritis.

Fosfomycin

- ▶ Option for outpatient antibiotics for MDR bacteria
- ▶ (ESBL producing organisms)
- ▶ Single dose
- ▶ Genes encoding Fosfomycin are wide spread across many gram negative bacteria.
- ▶ Widespread use can lead to emergent resistance
- ▶ Should not be first line agent for uncomplicated UTI
- ▶ Less effective compared to other agents but relatively safer profile and less side effects



Antibiotic Prophylaxis

- ▶ Women with more than 3 recurrent UTI per year should be considered for more aggressive regimen
 - ▶ **Women with recurrent UTI related to sexual intercourse :
Post coital prophylaxis**
 - ▶ (Single dose of postcoital Nitrofurantoin 100 mg, Bactrim 40/200 mg, Cephalexin 500 mg.
 - ▶ **Alternative regimen :**
 - ▶ Bactrim 40/200 every night or three times a week
 - ▶ Nitrofurantoin 50-100 mg every night or Three times a week
 - ▶ Safe and effective regimen even after 5 years or use
 - ▶ However after 6-12 months, antibiotic holiday is needed because 30% women can be UTI free for prolong time.
 - ▶ Prophylaxis can be started if patient develops recurrent UTI again.
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Other suggested strategies

- ▶ Probiotics
- ▶ Cranberry Juice
- ▶ Hippurate + Vitamin C
- ▶ Estrogen cream



Long-term antibiotics for prevention of recurrent urinary tract infection in older adults: systematic review and meta-analysis of randomised trials

Haroon Ahmed,¹ Freya Davies,¹ Nick Francis,¹ Daniel Farewell,¹ Christopher Butler,² Shantini Paranjothy¹

- 3 randomized controlled trials compared long term antibiotics with vaginal estrogen, oral probiotics and D-mannose powder in post menopausal women
- Follow up period from 6 to 15 months
- Study 1 - Nitrofurantoin 100 mg daily vs Estrogen vaginal pessary
- Study 2 – Bactrim 480 mg daily vs Lactobacillus rhamnosus BID
- Study 3 – Nitrofurantoin 50 mg daily vs D mannose powder
- **Long term antibiotics reduced the risk of UTI recurrence by 24%**
- One trial suggested 90% of E.coli isolates becomes resistant to Bactrim after 1 month



Effect of Cranberry Capsules on Bacteriuria Plus Pyuria among Older Women in Nursing Homes: A Randomized Clinical Trial

Manisha Juthani-Mehta, MD¹, Peter H. Van Ness, PhD, MPH², Luann Bianco, BA², Andrea Rink, RN², Sabina Rubeck, MPH², Sandra Ginter, BSN², Stephanie Argraves, MS², Peter Charpentier, MPH², Denise Acampora, MPH², Mark Trentalange, MD, MPH², Vincent Quagliarello, MD¹, and Peter Peduzzi, PhD³


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- Double blind , randomized , Placebo controlled trial (Nursing home adults 1 year surveillance)
- 2 Cranberry capsules (76 mg total – 20 Oz of cranberry juice) vs placebo in 92 treatment
- 147 completed treatment
- No significant difference between number of symptomatic UTI, presence of bacteriuria or pyuria , rate of deaths, hospitalizations, antibiotics days
- **Conclusion: Older women residing in ECF, Cranberry capsules compared with placebo has no significant difference in pyuria over 1 year.**

A systematic review of non-antibiotic measures for the prevention of urinary tract infections in pregnancy

Flavia Ghouri, Amelia Hollywood*  and Kath Ryan

- 8 studies were selected after reviewing 57
- 5 approaches (Hygiene, Cranberry juice, Vitamin C, Canephron N, Immunisation)
- Conclusion: Quality of evidence varies
- **Only Hygiene measures were supported by evidence and recommended in practice.**
- 2 Observations studies
- Increased sexual activity of more than 2-3 times a week is linked to higher incidence of UTI
- Washing pelvic area and voiding bladder after sexual activity has protective effect
- Direction of wiping after voiding bladder is important. Wiping from back to front had higher incidence of UTI



Lactobacilli vs Antibiotics to Prevent Urinary Tract Infections

A Randomized, Double-blind, Noninferiority Trial in Postmenopausal Women

- Randomized , double blind trial
- 12 months trial of Bactrim 480 mg daily vs Lactobacillus BID
- Conclusion: Do not meet non inferiority criteria for prevention of recurrent UTI



Learning points

- ▶ Not every positive Urine cultures means UTI. Be familiar with Asymptomatic Bacteriuria.
- ▶ Know when to treat Asymptomatic Bacteriuria.
- ▶ Help with preventing CAUTI
- ▶ Fosfomycin use for outpatient treatment
- ▶ Prophylaxis



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