Uncomplicated Urinary Tract Infections

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Objectives

Upon completion of this lecture, the participant will be able to:
• Differentiate uncomplicated UTI from complicated UTI
• Delineate female vs male uUTI
• Diagnose an uncomplicated UTI
• Discuss empiric therapy for uUTI
• Outline antibiotic choices for uUTI
• State follow up care for uUTI

Georgia, 31 year old single female
Tired, increased frequency of urination, back pain
Georgia

- 2 day sudden onset of urinary frequency
  - Less volume, more often
  - Back pain
  - Inappropriate fatigue
  - Absence:
    - Burning, urgency of urine
    - Sexual intercourse in last 2 months
    - Vaginal symptoms

Georgia

- PMH
  - Gravida 1, para 1
- Surgical History
  - None
- Medications
  - ASA, daily multivitamin (no changes)
- Urine
  - Leukocyte esterase +
  - Nitrate negative
  - WBC 11 per HPF
  - RBC 2 per HPF
  - 12 bacteria per HPF

Georgia.... Exam

- Normal vital signs
- Afebrile
- Negative CVA tenderness
- Looks well
- Blood sugar random 98
u UTI...What is it...

- Significant bacteriuria in the presence of symptoms
- Uncomplicated UTI’s are one of the most common diagnosis in the US
- Over 6 million patient visits to medical clinics due to acute cystitis.
- One half of all women will have a UTI in their lifetimes
  - ¼ will have recurrent UTI’s

2. Mehndiratta SK. Diagnosis and Management of Uncomplicated UTI. American Family Physician 72(4)451. Aug 2005

uUTI in women

- Incidence increases with age and sexual activity
- Postmenopausal women
  - Bladder or uterine prolapse
  - Incomplete emptying
  - Loss of estrogen with attendant changes in vaginal flora
  - Loss of lactobacilli
  - Allows periurethral colonization with gram negative aerobes (e.coli being most frequent organism)

UTI in Men...

- UTI in men much less frequent and age related secondary to longer urethra
  - Early peak during first three months of life
  - Symptomatic UTI in boys up to 10 years old is 1.1-1.6%
  - Adult male < 50 years – 5-8 per year per 10,000
  - Dysuria and urinary frequency – STD related infections of the urethra and prostate
  - Gonococcal and nongonococcal

**UTI in Men...**

- UTI in men much less frequent and age related
  - Men older than 50 years incidence rises dramatically – 20-50% prevalence
  - Enlargement of prostate
  - Prostatism
  - Debilitation
  - Subsequent instrumentation of the urinary tract

**Complicated vs Uncomplicated**

- Cystitis
  - Uncomplicated
    - Young women, non pregnant, normal anatomy, nonresistant organism, not recurrent
  - Complicated
    - Pregnant, very young or old, diabetic, immunocompromised, anatomically abnormal, catheter related, etc

**Complicated vs Uncomplicated**

- Pyelonephritis
  - Uncomplicated
    - Upper urinary tract infection
  - Complicated
    - Progression to involve corticomedullary abscess, perinephric abscess, emphysematous pyelonephritis or papillary necrosis
**Urine a great culture media**

- Unfavorable environment for bacterial growth
  - Low pH (5.5 or less)
  - High concentration of urea
  - Presence of organic acids derived from a diet that includes fruit and protein
  - Frequent and complete voiding
  - Voiding after intercourse

**Progression of Uncomplicated UTI**

- Pyelonephritis is associated with substantial mortality and systemic effects
  - Fever, vomiting, dehydration, loss of vasomotor tone resulting in hypotension
- Complications
  - Acute papillary necrosis
  - Development of urethral obstruction
  - Septic shock
  - Perinephric abscess
  - Scarring and decreased renal function

**Urinary Tract Infections in Females**
Pathophysiology

- Urinary tract is sterile
- Uncomplicated UTI – Cystitis
  - Bladder mucosal invasion by enteric coliform bacteria (e.g., *Escherichia coli*)
  - Inhabits the periurethral vaginal introitus
  - Ascend into the bladder via the urethra
  - Enhanced by sexual intercourse

Clinical History

- Classical, adult symptoms reported
  - Dysuria with urgency and frequency
  - Sensation of bladder fullness or lower abdominal discomfort
  - Hematuria reported 10% of cases of UTI in otherwise healthy women
  - Fevers, chills and malaise
    - Associated with pyelonephritis more commonly

- Flank pain and costovertebral angle tenderness
  - Referred pain pathways make this possible in simple lower UTI
- History of vaginal discharge
  - Vaginitis, cervicitis, PID can cause similar symptoms and pelvic exam is needed
- Important Information to obtain
  - History of STD
  - Multiple current sexual partners
**Clinical History in Elderly**

- Altered mental status, frequent falls, confusion, incontinence
- Refer to family for sudden changes in mentation or gait

**Physical Exam**

- Suprapubic tenderness
  - No evidence of vaginitis, cervicitis or pelvic tenderness
- Patient uncomfortable, not toxic
- Patient with Pyelonephritis
  - Usually appears ill
  - In addition to fever, sweating and prostration has CVA (flank) tenderness.

**Differential Diagnoses**

- Chancroid
- Constipation
- Dysfunctional uterine bleeding
- Dysmenorrhea
- Endometriosis
- Gonorrhea
- Ovarian cysts
- Ovarian torsion
- Pelvic inflammatory disease
- Other Issues to consider
  - Cervicitis
  - Chlamydia
  - Pregnancy, UTI
  - Renal calculi
  - Sexual assault
  - Toxic shock syndrome
  - Vaginitis
  - Vulvovaginitis

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*Howes DS. Urinary Tract Infection, female. Assessed 9-4-09.*

http://emedicine.medscape.com/article/778670-overview
Laboratory Studies

- Initial test urinalysis
- Midstream voided is as accurate as cath specimen if proper technique is used\(^1\)
- Pyuria - + leukocyte esterase dip test\(^1\)
  - Found in vast majority of patients with UTI\(^1\)
  - Specific 94-98\%\(^2\)
  - Sensitive 75-98\%\(^2\)


What if - leukocyte esterase dip is negative but you think that symptoms are convincing?

- Low level pyuria (6-20 WBC's) per HPF microscopy may be associated with an unacceptable level of false negative results with leukocyte esterase dip test\(^1\)
- Current emphasis in the diagnosis of UTI rests in the detection of pyuria\(^1\)
  - 2-5 WBC's per HPF in a female with symptoms may be significant\(^1\)
  - Positive nitrate test is highly specific for UTI
    - Typically urease-splitting organisms (proteus and occasionally E. coli)
    - Nitrate negative for enterococci, S. saprophyticus, Acinetobacter
  - Sensitivity varies from 35-95\%\(^2\)

**Caution!**

- **Hematuria**
  - Low level or occasionally frank hematuria may be seen in a UTI¹
  - Poor positive predictive value¹
  - May be seen microscopically as only component
  - Think renal cell cancer in asymptomatic hematuria patient with no signs or symptoms of UTI other than hematuria – get ultrasound of kidneys!


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**Laboratory Studies**

- **Visual inspection not helpful**
  - Cloudy urine could be crystal or protein
  - Malodorous urine could be due to medications or diet

- **Culture**
  - Historically 100,000 colonies/mL of single organism = UTI
  - Misses up to 50% of symptomatic infections
  - Lower colony count of 1,000 colonies is accepted now.


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**Laboratory Studies**

- CBC not helpful in differentiating upper from lower UTI
- Renal function testing not indicated in most episodes of UTI
  - May be helpful in older, particularly ill appearing individuals

For clinical signs and symptoms for uUTI empiric antimicrobial therapy initiated as soon as possible after the onset of the uUTI is recommended.

- Without waiting for results of culture
- Targeted to *E coli*
  - Isolated in 85-90% of episodes

**Gram negative organisms**

**uUTI, Female, Toronto, Ontario**

<table>
<thead>
<tr>
<th>Bacterial Species</th>
<th>Number of isolates</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>E. coli</em></td>
<td>91.8%</td>
</tr>
<tr>
<td>Klebsiella species</td>
<td>3.9%</td>
</tr>
<tr>
<td>Enterobacter species</td>
<td>0.9%</td>
</tr>
<tr>
<td>Proteus mirabilis</td>
<td>2%</td>
</tr>
<tr>
<td>Citrobacter species</td>
<td>0.7%</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>0.3%</td>
</tr>
<tr>
<td>Other</td>
<td>0.5%</td>
</tr>
</tbody>
</table>


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**Current options for first line antimicrobial therapy for uUTI Prior to 2005**

<table>
<thead>
<tr>
<th>Treatment Effects</th>
<th>Trimethoprim Sulfamethoxazole</th>
<th>Fluoroquinolones</th>
<th>Nitrofurantoin</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cure Rate</strong></td>
<td>95%</td>
<td>96%</td>
<td>85-95%</td>
</tr>
<tr>
<td><strong>Spectrum</strong></td>
<td>Broad-spectrum effective</td>
<td>Broad-spectrum effective</td>
<td>Narrow spectrum effective against <em>E. coli</em> and <em>S. saprophyticus</em></td>
</tr>
<tr>
<td><strong>Effect on Flora</strong></td>
<td>Eradicates uropathogens in gut and vaginal flora</td>
<td>Eradicates uropathogens in fecal and vaginal flora</td>
<td>No effect on fecal or vaginal flora</td>
</tr>
<tr>
<td><strong>Side Effects</strong></td>
<td>Severe side effects particularly rash</td>
<td>Excellent side effect profile</td>
<td>Few side effects if duration is short; serious adverse event profile with long term use at full dose</td>
</tr>
<tr>
<td><strong>Resistance</strong></td>
<td>Increasing resistance</td>
<td>Limited, but increasing</td>
<td>Limited, resistance over 50 years, not increasing</td>
</tr>
<tr>
<td><strong>Duration of Rx</strong></td>
<td>3 days</td>
<td>3 days</td>
<td>7 days</td>
</tr>
</tbody>
</table>


Nicolle LE. Urinary tract infection: traditional pharmacologic therapies. Am J Public Health 2002;113(suppl 1A):1-4S.

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**Clinical Recommendations 2009**

**uUTI in women**

- TMP/SMX – 3 day course
  - Areas where the rate of resistance to *E coli* is < 15-20%  
- Fluoroquinolones are NOT recommended as first line treatment
  - Preserve effectiveness for complicated UTI
- Use of beta-lactam antibiotics is not recommended for routine treatment of uUTI
  - Limited effectiveness


Sulfamethoxazole and trimethoprim

- Inhibits bacterial synthesis, therefore growth; useful except with *P. aeruginosa*
- Dosing
  - 160 mg TMP/800mg SMX po q 12 hours
  - uUTI 3 days
  - Uncomplicated pyelonephritis 10-14 days
- Interactions
  - Warfarin may increase PT
  - Diuretics increase incidence of TTP in elderly
  - May increase phenytoin levels
  - May increase hypoglycemic effect of SU
- Contraindications
  - Hypersensitivity; megaloblastic anemia due to folate deficiency
- Precautions
  - Fetal risk C; history of Stephens Johnson Syndrome

Ciprofloxacin

- Indicated for pseudomonal and infections due to multidrug-resistant gram negative organisms
- Dosing
  - 250-500 po bid for uUTI
  - Pyelonephritis 10-14 days
- Interactions
  - Antacids, iron salts, interfere with GI absorption; cimetidine may interfere with metabolism; may reduce therapeutic effects of phenytoin; may increase digoxin levels; may increase effects of anticoagulants
  - Contraindications - hypersensitivity
- Precautions
  - Fetal risk C

Cephalexin

- Inhibits bacterial growth by inhibiting bacterial cell wall synthesis; bactericidal (mostly gram + coverage only)
- Dosing
  - Adults 250-1000 po q 6hrs for 10-14 days
- Interactions
  - Aminoglycosides increase nephrotoxic effects
  - Contraindications
  - Fetal risk B
- Precautions
  - Adjust dose in renal impairment
Amoxicillin and clavulanic acid

- **Drug combination that treats bacteria normally resistant to beta lactam antibiotics**
- **Dosing**
  - 500 mg po q 12 hrs or 250 po q 8 hrs 10 days
- **Interactions**
  - Warfarin and heparin increase risk of bleeding
- **Contraindications**
  - Hypersensitivity
- **Precautions**
  - Fetal risk B

Nitrofurantoin

- **Interferes with bacterial carbohydrate metabolism; at low doses bacteriostatic; high doses bactericidal.**
- **Dosage**
  - 50-100 mg po q 6 hrs 7 days
  - Sustained release 100 mg po bid 7 days
- **Interactions**
  - Anticholinergics may delay gastric emptying and may increase absorption and bioavailability; antacids (magnesium salts) may decrease effects by decreasing absorption
- **Contraindications**
  - Renal insufficiency, anuria, oliguria; pregnant patients at term (38-42 weeks)

Phenazopyridine (Pyridium)

- **Urinary topical analgesic on urinary tract mucosa; compatible with antibacterial therapy**
- **Dosing**
  - 200mg po tid for 2 days or prn for relief of symptoms
- **Interactions**
  - None reported
- **Contraindications**
  - Renal insufficiency
- **Precautions**
  - Fetal risk B; adjust dosage for renal insufficiency
Complications to uUTI

- Rare in healthy individuals
- Resistant organisms
- Re-infection with the same organism
- Relapse of symptoms after a brief 3 day course of antibiotics may suggest presence of clinically unsuspected upper UTI and requires 10-14 day therapy


Serious complications of uUTI

- Acute papillary necrosis with potential for ureteric obstruction
- Overwhelming sepsis syndrome with septic shock due to loss of vasomotor tone, capillary leak and impaired myocardial performance
- Perinephric abscess


Patient Education Essential

- Adherence to medical plan
- Follow up appointments
- Fluid intake to enhance diuresis
- Frequent and complete voiding
- Drinking fruit juices to acidify the urine
- Post-intercourse voiding

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Georgia

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  - Less volume, more often
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  - Surgical History
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- Urine
  - Leukocyte esterase +
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  - WBC 11 per HPF
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  - 12 bacteria per HPF
**Georgia.... Exam**
- Normal vital signs
- Afebrile
- Negative CVA tenderness
- Looks well
- Blood sugar random 98

**Georgia... Diagnosis and Rx**
- Acute cystitis, uncomplicated
- Rx: TMP/SMX – 3 day course
- Urine culture and sensitivity
- Follow up call on day 4
  - Final CS report
  - Follow up on symptoms
  - If symptoms negative, and CS sensitive to agent chosen, no follow up needed.

**Georgia, Complicated UTI**
Fever of 101 F, chills, Moderate to severe CVA tenderness on Right.
**Georgia, complicated UTI**

- Clinical History
  - Fever for 5 days, increasing to 101.6°F at night
  - Can’t lie on right side due to pain in back
  - Really tired, can’t go to work
  - Nausea, vomiting last night
  - No vaginal itching, drainage, discomfort

- Clinical Exam
  - Looks “sick”
  - Skin flushed
  - Significant CVA tenderness
  - Pelvic tenderness and fullness
  - Urine
    - Leukocyte esterase +
    - Nitrate +
    - WBC 40+ per HPF
    - RBC 16 per HPF
    - TNTC bacteria per HPF

- Treatment
  - Urine CS
  - Transport patient to an acute care facility
    - IV Hydration
    - IV Antibiotics
    - Pain control
Consideration that this may be termed reproductive tract infections
Need to consider urethritis, epididymitis, prostatitis or orchitis

Usual routes of inoculation in males is with gram negative aerobic bacilli from the gut
Escherichia coli most common offending organism
Bacterial cystitis is uncommon in the absence of anatomical abnormalities
Males aged 3 months to 50 years, incidence of UTI is low and anatomical abnormality needs to be considered
May occur due to infection in prostate
Older males with BPH – incomplete bladder emptying predisposing them based on urinary stasis.
**Clinical History**

- **Most frequent complaint is dysuria**
- **Inquire about**
  - Urgency, frequency, nocturia, gross hematuria, fever, chills, back/flank pain, suprabubic pain, nausea and vomiting
  - **Elderly men: inquire about BPH, urinary dribbling, hesitancy or difficulty initiating the urinary stream, urinary tract manipulation, history of catheterizations**

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**Clinical History**

- **Urethritis**
  - Dysuria with or without a discharge
  - Much more common disease than UTI in men
    - Careful history, sexual history, genital tract symptoms
    - Testing or urethral swab
    - Testing of urine
    - Help with determination of UTI vs urethritis

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**Clinical History**

- **Pyelonephritis**
  - Fever, chills, shaking chills, CVA tenderness
  - 30-50% of pyelonephritis causes may be silent, without clinical signs or symptoms
  - In older men, prostate enlargement along with delayed presentation are the primary causes of pyelonephritis
Clinical History in Elderly

- Altered mental status, frequent falls, confusion
- Refer to family for sudden changes in mentation or gait

Physical Exam

- Fever, tachycardia, CVA tenderness, abnormal tenderness in the subpubic area and guarding
- Scrotal hematoma, hydrocele, masses or tenderness
- Meatal discharge
- Rectal lesions or abscesses
- Prostatic tenderness or hypertrophy
- Inguinal adenopathy

Causes

- Bacterial colonization of the urinary tract
- Can be caused by fungal or other organisms
- Routes of infection
  - Direct ascension up the urinary tract via the urethra
  - Hematogenous spread, as with bacteremia
  - Spreading from contiguous structures (prostate)
Differential Diagnoses

- Aneurysm, abdominal
- Appendicitis, acute
- Back Pain, mechanical
- Chlamydia
- Constipation
- Diverticular disease
- Epididymitis
- Gastritis and Peptic ulcer disease
- Gastroenteritis
- Gonorrhea
- Inflammatory Bowel Disease
- Obstruction, large bowel
- Obstruction, small bowel
- Orchitis
- Prostatitis
- Renal calculi
- Testicular torsion
- Urethritis
- Trauma of upper or lower genitourinary system

Laboratory Studies

- Urinalysis
  - Greater than or equal to 2-5 WBC’s per HPF
  - 15 bacteria per HPF
  - Positive nitrate test is poorly sensitive but highly specific for UTI; false positives are uncommon
  - In younger men – differentiation of UTI and urethritis may take
    - Urethral smear and culture or
    - Urinary antigen testing for chlamydia or Neisseria gonorrhoeae

Laboratory Studies

- Urine Culture in Men (all should have)
  - Controversial cut points
  - Cut off for positive culture is >1000 colony forming units/mL
    - Much lower than the standard for women
      - (10,000 colony forming units/mL)


Treatment of Male uUTI

Treatment – Male UTI

- All urinary tract infections in men are considered “complicated.”
  - Possibility that infection has ascended to the kidneys must be assumed
  - Outpatient treatment with 48 - 72 hour follow up
    - Well appearing, have stable vital signs, able to maintain oral hydration, no significant co-morbid conditions

Treatment – Male UTI

- Inpatient treatment
  - Appears toxic, unable to tolerate fluids by mouth, significant co-morbid disease

All antimicrobial therapy should be driven by antibiotic resistance data from the local health department or local hospital laboratory

Treatment – Male UTI

- Adult males should receive 10-14 day treatment
- Medications same as with the female
- Treat dysuria with phenazopyridine
- TMP-SMX resistance overall is approximately 25%
- Resistance to nitrofurantoin is slightly higher
- Resistance to fluoroquinolones remains below 5%
- Fluoroquinolones have become the preferred initial agent

**Enrique 56 year old male**

1 day onset of burning, urgency, frequency of urine and one occasion of incontinence of urine. Feels tired.

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**Enrique**

- Clinical History
  - 1 day onset of burning, urgency, low volume voiding, frequency
  - 1 episode of incontinence
  - Tired > baseline
  - Low grade temperature
  - No shaking chills
  - No orthostasis or hypotension by description

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**Enrique.. History**

- PMH
  - ASHD, stable with medical therapy
  - Hypertension
  - Dyslipidemia
- PSH : none
- Meds
  - Metoprolol 50 mg po bid
  - ASA 81mg po daily
  - Simvastatin 40 mg po q HS
  - Lisinopril 20 mg po q am
Enrique... Exam

- Urine
  - + nitrates
  - 2 RBC per HPF
  - 6 WBC per HPF
  - Negative leukocyte esterase
  - 20 bacteria per HPF

Enrique... Exam

- Vital signs stable
- Looks well
- Afebrile
- No CVA tenderness
- Scrotal Exam negative
  - Epididymitis absent
  - Orchitis absent
- Prostate
  - Firm, not tender or boggy

Enrique... Diagnosis and Rx

- Diagnosis: Acute Cystitis
- Urine Culture and Sensitivity
- Ciprofloxacin 500 mg ER po q 24 hours – 10 days
- Recall on day 4
  - Verify clinical history/presentation
  - Verify culture and sensitivity is appropriate
  - Return visit 14 days for repeat UA and exam
Enrique 56 year old male
Brought in by wife, a little confused, difficulty walking, temperature elevation, and incontinence.

Enrique – is sick
- Clinical History
  - Onset of some inappropriate statements reported from his wife concerned he is confused and disoriented
  - Shaking chills last night
  - Temperature 101.2 F
  - Weak and tired
  - Back pain

Clinical Exam
- Oriented, but “not at his baseline”
- Vital Signs are stable; Temp 100.6 F
- CVA tenderness is very +
- Looks sick
- Urine
  - Leukocyte esterase +
  - Nitrates +
  - 30 RBC per HPF
  - 40 WBC per HPF
  - 40 Bacterial per HPF
Enrique - ? Pylonephritis

- Treatment
  - Refer to an acute care facility
    - I V antibiotics
    - I V hydration
    - Close vital sign monitoring
    - Urology consult

Summary Uncomplicated UTI

- Significant bacteriuria in the presence of symptoms

Summary

- Female u UTI
  - Clinically "not ill"
  - Treat initially with trimethoprim-sulfamethoxazole
  - 3 days
  - Call back when CS ready
Male UTI
- Really not considered uncomplicated
- Starts asymptomatic - care that you are not missing pyelonephritis
- Initial drug fluoroquinolones
- Duration 10-14 days
- Must have call back with CS completed
- Must have clinical follow up at end of treatment