Case Studies in Urinary Tract Infections

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Objectives
After hearing this presentation, the participant should:
- Know the symptoms and bacteriology of uncomplicated and complicated urinary tract infections
- Be aware of the diagnostic criteria, office testing and treatment of UTI's
- Know the signs and symptoms of urosepsis
- Understand proper care of indwelling catheters

Disclosure Statement
Neither myself nor any member of my family have a financial arrangement related to the content of this activity or any supporters of this program.
Urinary Tract Infection (UTI)

- Account for 7 million doctor visits annually, 100,000 hospitalizations
- UTI cost to society >1.5 billion annually
- Most common bacterial infection in women
- UTI No. 1 cause of infection in hospitalized patients
- UTI’s 14 times more common in women than men
- 50% of women have at least one UTI in their lifetime
- Following initial episode of acute cystitis in young women, recurrent UTI’s occur in approximately 20%, usually due to exogenous reinfection

Symptoms of Urinary Tract Infection

- Lower Tract (bladder, urethra)
  - Dysuria
  - Frequency
  - Urgency
  - Hematuria
  - Suprapubic discomfort
  - Incontinence-urge
  - Nocturia
- Upper Tract (kidneys ie pyelonephritis)
  - Flank pain
  - Fever
  - Chills
  - Malaise
  - Nausea, vomiting
  - Costovertebral angle tenderness

Asymptomatic Bacteruria

- Definition: growth of ≥100,000 CFU/mL on urine culture without symptoms
- Prevalence increases with age:
  - 1 year = 1 – 2%
  - 15-24 years = 2 – 3% due to sexual activity, pregnancy
  - 60 years = 15%
  - 80 years = 25 – 50% due to pelvic organ prolapse, chronic illness, hospitalization
**Asymptomatic Bacteruria in Pregnancy**
- Present in approximately 5% of pregnant women
- Women with ASB have 20 to 30 fold ↑ risk of acute pyelonephritis
- Untreated ASB associated with ↑ risk of preterm delivery
- Incidence of ASB and prematurity increase inversely with socioeconomic status

**Bacteriology of Urinary Tract Infections (UTI's)**

**Uncomplicated UTI's**
- Majority (> 80%) caused by E. coli and other gram-negative bacilli (Proteus, Enterobacter, Klebsiella, Pseudomonas)
- Staphylococcus saprophyticus is no. 2 most common cause of uncomplicated UTI (10%)
- Also see group B Strep, Enterococcus

**Complicated UTI's**
- Most common species Proteus, Klebsiella, Pseudomonas, Serratia and Enterococcus fecalis
- Streptococcus agalactiae especially associated with diabetes, immunosuppression, catheter use
- Anaerobic bacteria do not cause UTI's, probably due to oxygen tension in urine

**Complicated Urinary Tract Infection**
- Definition: A UTI that has a higher chance of failing standard therapy
- May include any of the following
  - Pregnancy
  - Elderly patient
  - Structural/functional abnormality of urinary tract
  - Multidrug-resistant infection
  - Indwelling catheter
  - Recent urinary tract instrumentation
  - Hospital acquired infection
  - Childhood UTI history
  - Diabetes
  - Immunosuppression
  - Recent antibiotic use
Case 1
A 26 yo female 1001 calls the office frequently requesting antibiotics for symptoms of a UTI. She comes in for a visit 4-6 times yearly for dysuria, urgency, frequency and receives treatment for a positive urine for infection. She uses a combination low-dose OCP for contraception. She and her husband have sexual intercourse 1-2 times most weeks. On close questioning the patient, she usually washes her perineum before and gets up and empties her bladder after intercourse. In spite of this, she has recurrent (≥ 3 per year or 2 or more in 6 months) UTI’s that always occurs within 12 hours of intercourse. Today, she calls complaining of UTI symptoms and asks, “What can I do to prevent this from happening?”

Why are Women at Risk for UTI’s?
- Anatomy – short urethra, approx 4 cm, close proximity to vagina and rectum
- Estrogen ↓ tissue estrogen levels → ↓ urethral mucosal and submucosal coaptation (closure) → increases ease of ascending bacterial contamination
- Sexual activity action of vaginal intercourse introduces genitorectal flora into urethra and bladder
- Spermicide use – kills lactobacilli

Normal Bladder Defense Mechanisms in Women
- Normal acidic vaginal environment (pH = 3.0 – 4.5) in premenopausal women inhibits growth of bacteria such as E. coli, promotes growth of lactobacilli, other gram positive bacteria: gram positives replicate poorly in urine
- High urea and organic acid concentrations of urine inhibit bacterial growth to a degree
- Efficient bladder emptying
- Glycosaminoglycans in the bladder lining and immunoglobulins in urine block bacterial adherence to urothelium

Walters, MD, Karram MM, Urogynecology and Reconstructive Surgery, 3rd edition, 2007
Diagnosis of UTI

- Traditional definition of UTI no longer used (ie ≥ 100,000 CFU/mL)
- Up to 50% of patients with symptoms of UTI have < 100,000 CFU/mL on culture of midstream urine
- Symptomatic woman + ≥ 100 CFU/mL has sensitivity of 95%, specificity of 85%, positive predictive value of 88% → treat
- Culture of a single organism + symptoms means UTI regardless of CFU/mL → treat

Office Testing for UTI

- Midstream clean catch with dipstick analysis (if done properly)
  - Nitrite + → for gram-negative bacterial which can convert nitrate to nitrite (sensitivity 92-100%, low specificity); false negative with bacteria that do not reduce nitrate, gram-positive bacteria, excess dietary Vitamin C, patient does not eat nitrate containing foods
  - Leukocyte esterase + → indicates presence of white blood cells, since leukocytes produce this enzyme (sensitivity 75-95%, specificity 94-98%)
  - Dipstick results may be affected by medications/dyes, ie pyridium, nitrofurantoin, metronidazole, bilirubin, methylene blue, Vitamin B complex

Office Testing for UTI (contd)

- In obese or demented patients, those with physical disabilities, perform sterile catheterization
- If midstream clean catch positive for pyuria, microscopic hematuria, with or without positive nitrites + UTI symptoms → high probability of UTI → treat
- Presence of pyuria without bacteria on culture, ie sterile pyuria, rule out:
  - Tuberculosis
  - Interstitial cystitis (IC)
  - Chlamydia urethritis
  - Kidney disease (stone, glomerulonephritis)
When is Culture Indicated?

- Patient suspected of complicated infection
- Atypical symptoms of UTI
- Patient with persistent symptoms following course of standard treatment
- UTI symptoms recur < 1 month after treatment
  - Pregnancy
  - Age > 65 years

Treatment of UTI

- Uncomplicated – adequate hydration plus 3 day antibiotic treatment, 7 day has no added benefit
  - First line treatment of uncomplicated community acquired UTI:
    - Trimethoprim – sulfamethoxazole (Bactrim – 160/800 mg bid)
  - Also may use:
    - Nitrofurantoin monohydrate macrocrystals (Macrobid 100mg bid)
    - Ciprofloxacin (Cipro 250 mg bid)
    - Levofloxacin (Levaquin 250 mg bid)
    - Trimethoprim (100mg bid, useful in sulfa allergy)
  - Test of cure (TOC) urine culture not necessary if patient symptoms resolve

- Complicated – treat with a fluoroquinolone as initial therapy until culture results available

Bacterial Resistance to UTI Antibiotics

- Nitrofurantoin (Macroductin, Macrobid)
  - E. coli <5%
  - Other uropathogens 15-20%
  - Not active against Proteus, some Enterobacter and Klebsiella strains
- TMP-SMX (Bactrim)
  - Uropathogens 10-22% varies geographically
- Fluoroquinolones (Cipro, Levaquin)
  - <5%
  - More expensive, not recommended as initial empirical therapy for acute uncomplicated cystitis
- Ampicillin
  - 30% of E. coli resistant in USA
Prophylaxis for “Sexually Associated” UTI's

- Pure cranberry juice can prevent adherence of bacteria to urothelium
- Vaginal estrogen for post-menopausal women
- No evidence for vaginal douching, washing perineal area before or after intercourse
- Empty bladder soon after intercourse
- My recommendation
  - Take one dose of antibiotic (Macrobid, Keflex or Bactrim) soon after intercourse with a glass of water; repeat in 8-12 hours regardless of symptoms; if symptomatic, take antibiotic BID x 3 days

UTI-like Symptoms

May be misdiagnosed and go untreated when caused by infectious agents such as:
- Chlamydia trachomatis
- Neisseria gonorrhoea
- Mycoplasma hominis, Ureaplasma urealyticum
- Candida albicans, Candida glabrata (esp in diabetics)
- Herpes simplex viral outbreak

Also:
- Overactive bladder (urgency, frequency)
- Interstitial cystitis (IC)
- Suburethral diverticulum, three D’s, dribbling, dysuria, dyspareunia

Case 2

An 88 year old woman resides at Happy Daze nursing home. She shows signs of mild dementia, sits in a chair most of the day due to arthritis and ambulates aided by a walker. She takes meds for hypertension, hyperlipidemia and edema and has used no form of estrogen in at least 30 years. She has confirmed urinary tract infections 4-6 times yearly. One morning, her caregiver is unable to coax patient out of her bed. She seems confused and disoriented. Vital signs reveal tachycardia in the 130’s, respirations 22/min and hypotension 80/50. She is taken to an ER for evaluation. A chest x-ray and CT of the abdomen are normal, cath urine very positive for infection, elevated WBC count with a marked left shift, and marked confusion compared to her baseline. Sepsis secondary to urinary tract infection is suspected. Urine and blood cultures are subsequently positive for E. coli and enterococcus. A central line is placed, antibiotics and fluid replacement are instituted. After 10 hospital days, recovering but in a much weakened state, the patient is returned to Happy Daze to complete 2 more weeks of antibiotics.
Risk Factors for UTI in Elderly, Institutionalized Women

- Urogenital atrophy due to aging, poor tissue estrogen effect, → poor urethral closure, ↓ mucosal immune function
- Sedentary, sitting most of day exposes urethra to genitorectal flora, especially with any degree of fecal incontinence
- Dementia, compromised mental status, difficult for care givers to assess change in overall condition, signs of sepsis

What Defines Sepsis?

- Clinical evidence of infection plus evidence of Systemic Inflammatory Response Syndrome (SIRS)
  - Temperature > 100.4 or < 96.8°F
  - Tachycardia > 90 beats/min
  - Tachypnea - respiratory rate >20/min
  - Altered WBC > 12,000 or < 4000/mL or >10% immature neutrophils (bands)
- In addition to above, often see:
  - Confusion, anxiety, disorientation
  - Flushing, peripheral vasodilatation
  - With gram negative endotoxin mediated sepsis, approximately 25% of patients develop ARDS (Adult Respiratory Distress Syndrome) with mortality rate of 50-90%
  - Decreased platelet count and fibrinogen, elevated fibrin degradation products → DIC

Bacteriology of Sepsis (2000)

- Gram positive organisms – 52% of cases
- Gram negative organisms – 38%
- Polymicrobial – 5%
- Anaerobes – 1%
- Fungi – 5%

**Modifiable Risk Factors for UTI**

- Abnormal vaginal pH due to ↓ tissue estrogen, ↓ lactic acid
- Inadequate hydration and regular voiding pattern
- High post-void residuals (pelvic organ prolapse, DM, MS, spinal injury)
- Recent anti-incontinence surgery
- ↓ functional status (dementia, stroke, MI)
- Sexual intercourse (↑ frequency, new partner(s))
- Catheterization, hospitalization
- Pregnancy
- Concomitant fecal incontinence
- Anticholinergic meds
- Spermicide use (kill lactobacilli, not E. coli)

**Treatment of Complicated UTI’s**

- **Mild to moderate in women without nausea and vomiting**
  - Ciprofloxacin 500mg q 12h
  - Ofloxacin 200mg q 12h
  - Levofloxacin 250mg q 24h
- **Severe complicated UTI’s requiring hospitalization**
  - Ampicillin 1g q 6h and gentamicin 1mg/Kg q 8h
  - Imipenem-cilastin 250-500mg q 6-8h
  - Ciprofloxacin 200-400mg q 12h
  - Ceftriaxone 1-2g q 24h
  - Levofloxacin 250mg q 24h

**Case 3**

A 52 year old woman underwent a TVT vaginal sling and prolapse repairs; the surgery was uneventful. On post-op day 1, a voiding trial was performed. The nurse disconnected the Foley catheter from the tubing, instilled 300cc into the bladder and had the patient void into a receptacle in the toilet. She voided only 50cc; the Foley catheter was replaced and the patient was sent home on Macrobid twice daily. Five days later the patient called the office reporting low grade fevers, suprapubic and low back pain. Office visit revealed cloudy urine positive on dipstick for leukocytes, nitrites; culture revealed Proteus sp., resistant to nitrofurantoin, sensitive to fluoroquinolones.
Catheter Associated UTI

- 10-15% of hospitalized patients have indwelling catheters; incidence of UTI directly related to duration of catheterization
- Incidence of bacteriuria: 5-10% per day of catheterization
- 10% of elderly patients with indwelling catheters develop bacteremia and gram-negative septicemia → mortality from sepsis in 80 year old → 60-90%

Catheter Associated UTI's

Bacteria gain access to the bladder by three routes

- Introduction of bacteria from external genitalia into the bladder at time of catheterization
- Development of bacterial biofilm on outside of catheter
- Once draining system contaminated, bacteria migrate up inside catheter lumen – most common, occurs during disconnecting catheter to obtain specimen, irrigation

Prevention of Indwelling Catheter Associated UTI's

Modifiable Factors

- Adequate fluid intake – very difficult in the elderly
- Avoid manipulating catheter
- Check urine often weekly at least
- Treat at first sign of infection; symptoms plus positive dipstick, hematuria, foul smelling urine
- Exchange catheter if infection diagnosed, change routinely at least monthly, sooner if indicated
- Frequently re-evaluate the patient's need for an indwelling catheter
- Asymptomatic bacteriuria does not need antibiotic treatment unless the patient has symptoms of UTI, systemic infection, or sepsis
**Intermittent Self Catheterization (ISC)**

- Viable alternative to indwelling catheter if patient is able/willing to learn. Most patients can be taught.
- Approximately 50% of patients will have asymptomatic bacteriuria; no difference in infection rate of clean versus sterile catheterization.
- Goal is to keep volume of bladder < 300 mL; if post void residual is < 20% of total voided volume, ISC can be stopped.
- Most patients catheterize every 3 to 4 hours during the day and as needed at night.

**Final Thought/Recommendations**

- Don’t stop having sex just to avoid bladder infections; always have supply of a urinary antibiotic, especially on vacation.
- If someone tries to put you in a nursing home, RUN! If you can’t run, hide. If you can’t hide…..
- Use vaginal estrogen cream post-menopause, it’s expensive, but like the cost of a divorce, it’s worth it.
- If you have an indwelling Foley catheter for as long as a week, take it out and figure out a way to pee. If you really can’t, learn intermittent self catheterization.