Urinary Tract Infections

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Objectives

- Identify the three factors that determine the progression to a UTI.
- Differentiate between the characteristic clinical, physical, and laboratory findings associated with UTIs.
- Identify the most common pathogens associated with the various UTIs.
- Suggest appropriate Rx and non-Rx treatment modalities for UTIs.

Definitions

- Urinary Tract Infection (UTI)
  - Micro-organisms present in the urine not accounted for by contamination
  - Infection anywhere within the urinary system
- Cystitis
  - Lower tract infections
- Pyelonephritis
  - Upper tract infections (kidneys, systemic)
Definitions (cont.)

• **Uncomplicated**
  – Typically in females of childbearing age
  – No structural/neurologic abnormalities interfering with urine flow
• **Complicated**
  – Flow impedance secondary to
  • Lesion
  • Congenital abnormality
  • Renal or prostate stones
  • Indwelling catheter
  • Prostatic hypertrophy
  • Physical obstruction
  • Neurologic deficit

Definitions (cont.)

• **Recurrent**
  – Reinfection or relapse with asymptomatic periods
  • Reinfection
  • Relapse
  – Same organism
• **Asymptomatic bacteriuria (ASB)**
  – Significant bacteriuria (>10^5) without symptoms
  – Always precedes symptoms of UTI
  – Lower tract infection
• **Symptomatic abacteriuria**
  – Symptoms without 10^5 CFU/ml

UTI: Epidemiology

• Approximately 8 million physician visits annually
  – By age 32, ___ of all women have at least 1 UTI
  – 1/5 of men > 70 y.o. have experienced a UTI
• Lead to > 1 million hospitalizations/year
• Most commonly occurring nosocomial infection
Pathogen reservoirs

- Females (urethra proximal)
  - Rectal
  - Vaginal
- Males (urethra distal)
  - Rectal

Pathogenesis

- Ascending
  - Rectal and/or vaginal reservoirs
  - Colonization of perianal area/migration to perivaginal area
- Colonization typically precedes UTI
  - Bacterial adhesive characteristics
  - Host receptor on epithelial surface
  - Surrounding fluids
- Hematogenous
- ? Lymphatic

Pathogenesis (cont.)

- Facilitating issues
  - Females
    - Reservoir(s) and urethra proximity
    - Urethra length
    - Sexual intercourse
      - Spermicide and diaphragm
      - Condoms
    - Pregnancy
  - Biofilm (slime) theory:
    - Bacteria interact $\rightarrow$ microcolonies
    - Small microcolonies coalesce $\rightarrow$ form bacterial biofilms
    - Glycocalyx
Pathogenesis (cont.)

- Facilitating issues (cont.)
  - Urinary Catheters
    - Can be traumatic
    - Biofilm adherence
    - Bacterial aggregates can block catheter
    - Catheter can shed bacteria
    - Antibiotics drained immediately
  - Aging
    - Bladder wall collagen content
    - Detrusor muscle thickens
    - Neurologic diseases
    - Vaginal flora

Predisposing factors

<table>
<thead>
<tr>
<th>Structural abnormalities</th>
<th>Residual urine</th>
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<tbody>
<tr>
<td>Obstruction</td>
<td>Prostatic hypertrophy</td>
</tr>
<tr>
<td>Vesicourethral reflex</td>
<td>Tumors</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>Anticholinergic agents</td>
</tr>
<tr>
<td>Catheterization</td>
<td>Calculi</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>Neurologic disease</td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
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</tbody>
</table>

Determining Factors

- Three factors determine the progression to infection
  - Inoculum size
  - Pathogen virulence
  - Competency of host defenses
Host defense mechanisms

- pH (normal range 5-8)
- Urea concentrations
- Organic acid concentrations
- Osmolality
- Urine flow
- Vaginal flora

Clinical presentation

- Common symptoms of lower UTIs
  - Dysuria
  - Frequency
  - Urgency
  - Hesitancy
  - Nocturia
  - Suprapubic pain/heaviness

Clinical presentation (cont.)

- Common symptoms of upper UTIs
  - Flank pain
  - Costovertebral tenderness
  - Abdominal pain
  - Fever
  - N/V
  - Malaise
Clinical presentation (cont.)

• Infants and children
  – Typically no specific UTI signs and symptoms
    • fever
• Elderly
  – Typically no specific UTI symptoms
    • Altered mental status
    • Altered dietary habits

Laboratory findings

• Urine analysis
  – Pyuria ( > 10 WBC/mm³ or leukocyte esterase)
  – Bacteria ( > 10⁵ CFU/ml urine)
    • microscopic or dipstick (NO₃ --> NO₂)
  – Hematuria (approximately 1/3 gross hematuria)
  – Elevated pH (6.5-8)
    • Proteus, K. pneumoniae, S. saprophyticus produce urease: catalyzes hydrolysis of urea in urine → ammonia and CO₂
    • Leukocyte esterase and nitrite dipsticks
• Urine culture
  – Gold standard
  – 1,000-100,000 CFU/ml

Differential diagnosis

• Uncomplicated UTI
  – Vaginitis
  – Urethritis
  – STD
    • Odor
    • Itching
    • Pain on intercourse
• Complicated UTI
  – Depends on contributing underlying diseases
Treatment

- Algorithms available
  - Complicating factors
- Appropriate antimicrobial consideration factors
  - Duration - Adverse Events
  - Spectrum - Resistance
  - Pharmacokinetics

Non-Rx treatment/prevention

- Acute uncomplicated UTIs spontaneously resolve in 50-70% of cases
- Behavior modification
  - Personal toilet hygiene
  - Patient’s choice of fabric and clothes
  - Frequent voiding
  - Voiding after intercourse
  - Method of contraception
- ? Vaccines

Non-Rx treatment/prevention (cont.)

- Cranberry juice
  - Believed to have preventative/treatment effects
    - Increases fluid intake and urine output
    - Acidifies urine (study pH = 6 vs. CTN pH = 5.5)
    - May interfere with bacterial attachment (fructose or polymeric cpd acts as lectin inhibitor)
    - Benzoic acid $\rightarrow$ hippuric acid which may have intrinsic antibacterial properties
  - Database review of literature conclusion
    - Small number/poor quality trials: no reliable evidence

Non-Rx treatment/prevention (cont.)

- Lactobacilli
  - Limited data
  - Restoration of normal vaginal flora
    - Prevent colonization by virulent pathogens
      - Acidic pH
      - Direct killing due to \( \text{H}_2\text{O}_2 \)
      - Interference with bacterial attachment
    - Must select appropriate probiotic strain
      - \textit{L. crispatus}
      - Intravaginal administration


ASB

- Controversy about clinical importance
  - ? Lead to complications of UTIs
  - ? Protective effects
- Diagnosis
  - 2 consecutive urine specimens with \( >10^5 \text{ CFU/ml} \) without symptoms
- Pathogenesis
  - Urethral ascension of bacteria into urinary tract/introduction by instrumentation persistence without host response
  - Persistence may be facilitated by host genetic predisposition, incomplete bladder emptying, or presence of a foreign body

ASB (cont.)

Etiology

- Predominantly \textit{E. coli}
- Others
  - Structural/functional abnormalities – \textit{Enterobacteriaceae, P. aeruginosa}
  - \textit{Enterococcus} spp., CoNS other than \textit{S. saprophyticus}
Screening/Treatment beneficial
- Pregnant women
- Prior to traumatic GU procedure
- ? Renal transplant recipient (1st 6 mos.)
- ? Females with persistent catheter-acquired bacteriuria after catheter removal

Screening/Treatment not beneficial
- Healthy individuals
- Elderly men and women in community and LTCFs
- Women with diabetes
- Pts. with HIV
- Pts. with catheters
- Pts. with neurologic impairment of bladder emptying
- Pts. with chronic urologic devices

Uncomplicated UTI: Etiology

<table>
<thead>
<tr>
<th>Young women</th>
<th>Women &gt;65 years</th>
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<tbody>
<tr>
<td>E. coli</td>
<td>E. coli</td>
</tr>
<tr>
<td>S. saprophyticus</td>
<td>P. mirabilis</td>
</tr>
<tr>
<td>Others (Klebsiella/Proteus)</td>
<td>Other Gram (-) (Pseudomonas)</td>
</tr>
</tbody>
</table>

Uncomplicated UTI: Treatment

- Current standard of therapy
  - TMP/SMX PO x 3 days
  - 3-Day therapy
    - Superior to single-dose
    - Optimal regimen for TMP/SMX
  - Resistance
TMP/SMX Resistance

- *E. coli* – ~20% resistant
  - Geographic variation
- Risk factors
  - Recent antibiotic use, especially TMP/SMX
  - Diabetes
  - Recent hospitalization
  - Current use of antibiotics

**Infect Dis Clin N Am. 2003;17:303-32.**

Recommendation

- Locations with resistance rates > 20%
  - Alternatives
    - 3-day fluoroquinolone
    - 7-day nitrofurantoin
      - Associated with lower cure rates than 1st line agents (85% vs. 95%)
      - Macrocystals better GI SE profile
    - Single dose fosfomycin
      - Phosphoric acid bactericidal agent
      - Can be used in pregnancy
      - 3 gm single dose
      - Comparable microbiologic cure as 5-day TMP (alone), but likely less effective than 3-day regimens of TMP/SMX or fluoroquinolones

**Infect Dis Clin N Am. 2003;17:303-32.**
Uncomplicated UTI: Treatment (cont.)

3 day treatment options

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
</tr>
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<tbody>
<tr>
<td>Ciprofloxacin</td>
<td>250 mg q12h</td>
</tr>
<tr>
<td>Ciprofloxacin XR</td>
<td>500 mg q24h</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>250 mg q24h</td>
</tr>
<tr>
<td>Gatifloxacin</td>
<td>200 mg q24h</td>
</tr>
<tr>
<td>Trimethoprim (Proloprim, Trimpe)</td>
<td>100 mg q12h</td>
</tr>
<tr>
<td>Trimethoprim/sulfamethoxazole (Bactrim, Cotrim, Septra, etc.)</td>
<td>160 mg TMP/800 mg SMX q12h</td>
</tr>
</tbody>
</table>

Uncomplicated UTI: Treatment (cont.)

• Single-dose therapy (SDT)
  – Gatifloxacin 400 mg
  – TMP/SMX 2 DS tablets
  – ? Fosfomycin 3 gm
  – NOT to be used in
    • Pregnant women
    • Males
    • Upper UTI infections
    • Renal failure
    • Indwelling catheter

• Other therapy options
  – Nitrofurantoin/ Macrobid 100mg BID X 7 days
  – Amoxicillin 250 mg TID x 7 days or 500 mg BID x 7 days
  – Amoxicillin/clavulanate 500/125 mg BID x 7 days
  – Cefixime 400 mg QD x 7 days
  – Cefpodoxime 100 mg BID x 7 days
Complicated UTI: Etiology

- E. coli 40%
- P. mirabilis 10%
- Other Gram (-) 40%
- Gram (+) 10%

Gram stain of urine culture should be performed.

Complicated UTI: Management

- Depending on status, may need to admit
  - Severely ill
    - Direct therapy towards bacteremia/sepsis
    - Hospitalize + IV abx.
  - Prompt initiation of broad-spectrum antibiotics
  - Immediate urinary tract decompression in pts. with evidence of obstruction

Complicated UTI: Treatment

- Empiric
  - Fluoroquinolones (PO or IV)
  - Gentamicin + Ampicillin IV
    - Preferred when suspect Enterococcus spp.
    - Alternatives to ampicillin
      - Amp/sulbactam
      - Piperacillin
      - 3rd generation cephalosporins (cefotaxime, ceftriaxone)
  - Nursing home resident or indwelling catheter (suspect Pseudomonas spp.)
    - Cefazidime or piperacillin + gentamicin
Complicated UTI: Treatment (cont.)

- Duration
  - PO
    - Single dose therapy not effective
    - Patients should be treated 10 to 14 days
    - Patients failing 10 to 14 day antibiotic course should then be treated for 4-6 weeks
  - IV
    - IV treatment maintained until afebrile for 24 hours
    - PO treatment continued for 10-14 days post IV

Case #1

- TJ – 28 y.o. female
- CC: three days of nocturnal frequency, dysuria, urgency
- U/A (per ml): >50 WBC, 35 RBC, > $10^5$ bacteria
- UC: G- bacilli, lactose fermenting

Case #1 Discussion

- What is the most likely diagnosis?
- What is the most likely organism?
- Suggest appropriate treatment.
Case #2

- MR – 72 y.o. female, nursing home resident; normally active and healthy
- U/A (per ml): (-) leukocyte esterase, 0 RBCs, (-) bacteria
- UC: >10^5 E. coli

Case #2 Discussion

- What is your assessment?
- Should we treat?

Catheter-related UTIs

Etiology
- Most caused by E. coli
- Nearly any organism is possible, especially in nosocomial infections
- Usually polymicrobial with rapid and constant changes
**Catheter-related UTIs (cont.)**

**Treatment**
- Asymptomatic + bacteriuria
  - REMOVE CATHETER
  - withhold systemic antibiotics
- Symptomatic
  - REMOVE CATHETER
  - Start antibiotics
  - complicated UTI

**Recurrent UTI**

- **Classification**
  - <2-3 episodes/year
  - >3 episodes/year
- Risk higher with *E. coli* vs. non-*E. coli* pathogens

**Recurrent UTI: Management**

- Post-coital single dose antibiotic (SMX/TMP SS)
- Continuous low-dose therapy (SMX/TMP SS qd x 6 mos., Nitrofurantoin 50 mg qd x 6 mos.)
- Self-initiated antibiotics
- Vaginal estradiol cream in post-menopausal women
- Cranberry juice
Case #3

- JS – 25 y.o. female, paraplegic, nursing home resident
- Hx: indwelling catheter
- CC: spiking fever, cough
- Chest X-ray: (+) pulmonary process
- Sputum culture: G- bacilli
- UC: >10^5 CFU/ml

Case #3 Discussion

- What is a predisposing factor to the development of a UTI?
- What is your assessment?
- What organism should we suspect due to this patient’s situation?
- Suggest appropriate action.

UTI in pregnancy

- 4-7% pregnant patients
  - Most common medical complication
- Pathogenesis
  - Decreased ureteral peristalsis
  - Urinary stasis
  - Reduced bladder tone
  - Hormonal changes
- Monitor
  - Quantitative urine Cx
- Management
  - Treat any significant bacteriuria, including ASB
  - Upper UTI – hospitalization + IV antibiotics
UTI in Pregnancy (cont.)

Etiology
• > 90% – E. coli, Klebsiella spp., Enterobacter spp.)
• Others – Proteus, Pseudomonas, Citrobacter, Staphylococcus, S. agalactiae

UTI in Pregnancy: ASB

• When left untreated…
  – Associated with pyelonephritis and hypertension in mother
  – Prematurity, low birth weight, mental retardation, and cerebral palsy in infants
• Thus, treat all pregnant women with ASB

UTI in Pregnancy: ASB (cont.)

Treatment of ASB
• Amoxicillin 500 mg TID x 3 days
• Ampicillin 250 mg BID x 3 days
• Cephalexin 250 mg BID x 3 days
• Nitrofurantoin* 100 mg BID x 7 days
• TMP/SMX* 1 DS BID x 3 days

* Not during 3rd trimester
UTI in Pregnancy: Treatment

Treatment
- Uncomplicated cystitis
  - Same as ASB
- Pyelonephritis
  - 14 – 21 days
  - 2nd or 3rd gen. cephalosporin IV
  - Gentamicin IV
  - Aztreonam IV
  - TMP/SMX IV (not in 3rd trimester)

Avoid
- Tetracyclines (teratogenic)
- Quinolones (cartilage development)
- Nitrofurantoin in G6PD deficiency

UTI in Infants and Children

Epidemiology
- Underestimated in the past
- Prevalence ranging from 1.7-7.5% febrile children
- Newborns
  - More prevalent in premature infants
  - More common in males
  - High recurrence rate
- Children
  - More common in females


UTI in Infants and Children (cont.)

Pathogenesis
- Migration of bacteria from GI tract to periurethral mucosa → ascend to bladder

Etiology
- E. coli – 70-90%
- Others – P. aeruginosa, Enterococcus spp., P. mirabilis
- Rarely – S. agalactiae, S. aureus, Candida spp.
UTI in Infants and Children (cont.)

Clinical findings
- Typically no specific urinary tract symptoms
- Limited value of physical examination
- Less than 2 y.o.
  - Failure to thrive, feeding problems, vomiting, and fever
- 2 – 5 y.o.
  - Fever, abdominal pain
- > 5 y.o.
  - Classic UTI symptoms more common

UTI in Infants and Children (cont.)

Management (cont.)
- Hospitalization
  - Infants <2 mos.
  - Consider for any child < 5 y.o.
  - Not necessary for children who are not severely ill, can tolerate oral fluids and oral abx, and follow-up is guaranteed
- Imaging studies
  - Any child < 5 y.o. with a positive urine culture
  - Consider for older girls with recurrent UTIs
  - Renal ultrasound and cystography

UTI in Infants and Children (cont.)

Treatment
- Need coverage for S. agalactiae and Enterobacteriaceae during first 8 weeks of life pending blood and CSF cultures
- Oral therapy for well-appearing children
  - TMP/SMX, cephalosporins, nitrofurantoin
- Failure of oral therapy
  - IV antibiotics
  - IM ceftriaxone or gentamicin
Prostatitis

Definitions and classification
• Prostatitis – Inflammation of the prostate & surrounding tissues
• Bacterial prostatitis – Inflammation in presence of bacteria and significant inflammatory cells
  • Acute: severe illness, sudden onset, fever
  • Chronic: recurrent infection with same organism
• Nonbacterial prostatitis – S+S in presence of inflammatory cells WITHOUT bacteria
• Prostatodynia – S+S with bacteria WITHOUT leukocytosis

Pathogenesis
• Reflux
• Ascending
• Hematogenous
• Lymphatic
• Other
  – Catheter, urethral instrumentation, transurethral prostatectomy
Host defense mechanisms

- Prostatic fluid
  - Antibacterial factor (PAF)
  - High concentrations of zinc
    - Note: concentrations of Zn decreased in elderly
  - pH
    - Normal: 6.6-7.6
    - Inflamed: 7-9

Etiology

<table>
<thead>
<tr>
<th>Acute Bacterial</th>
<th>Chronic bacterial</th>
<th>Chronic non-bacterial</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. coli</td>
<td>E. coli</td>
<td>Chlamydia</td>
</tr>
<tr>
<td>K. pneumoniae</td>
<td>K. pneumoniae</td>
<td>Trichomonas</td>
</tr>
<tr>
<td>P. mirabilis</td>
<td>P. mirabilis</td>
<td>Ureaplasma</td>
</tr>
<tr>
<td>P. aeruginosa</td>
<td>E. faecalis</td>
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</tr>
<tr>
<td>Serratia</td>
<td>S. aureus</td>
<td></td>
</tr>
<tr>
<td>Enterobacter</td>
<td>S. epidermidis</td>
<td></td>
</tr>
</tbody>
</table>

Clinical presentation

Acute
- Local
  - Uncomplicated UTI symptoms
- Systemic
  - High fever
  - Malaise
  - Chills
  - Myalgia
- Prostate
  - Swollen
  - Tender
  - Warm

Chronic
- Commonly asymptomatic
- Vague symptoms
  - Recurrent UTIs
  - Frequency
  - Urgency
  - Dysuria
  - Lower back pain
  - Suprapubic discomfort
  - Prostate
    - May appear normal
Treatment

- **Empiric**
  - **Acute**
    - Severely ill:
      - AG + β-lactam IV
    - Patient able to take PO
      - TMP/SMX
      - Fluoroquinolone
  - Duration
    - IV therapy until patient is afebrile for 48h (or 3 – 5 days of IV therapy)
    - Continue PO for 4 weeks total

- **Chronic**
  - Fluoroquinolone X 4-6 weeks
  - TMP/SMX X 4-6 weeks
  - Duration
    - May need to extend to 12 weeks

Questions???