Urinary Tract Infections

- Symptomatic and asymptomatic UTI’s are a common problem
- > 10 million office visits per year
- > 1 million hospital admissions per year
- Cause of significant nosocomial morbidity
- Affects women more than men throughout life

UTI’s in Adults

- Acute uncomplicated UTI in young women
- Acute uncomplicated pyelonephritis
- Recurrent UTI’s in women
- Complicated UTI’s in older women
- Catheter-associated bacteriuria
- Asymptomatic bacteriuria
- Candiduria

UTI - Definitions

- **Lower UTI**
  - cystitis
  - urethritis
  - prostatitis

- **Upper UTI**
  - pyelonephritis
  - intra-renal abscess
  - perinephric abscess

**Uncomplicated:** simple cystitis of short (1-5 days) duration

**Complicated:** long-duration or hemorrhagic cystitis, cystitis with anatomic or functional abnormalities, cystitis with progression to involve the the upper tract, or instrumentation-related cystitis

Asymptomatic Women

Voided vs. Catheterized Specimen

Adapted from Kass, et al.

Symptomatic Women

Suprapubic Tap

Midstream Voided Urine

Adapted from Kass, et al.
Urinary Tract Infections
Populations at Risk

- Newborn
- Prepubertal girls
- Young boys
- Sexually active young women
- Elderly males
- Elderly females

Epidemiology of Urinary Tract Infections by Age Group

<table>
<thead>
<tr>
<th>Age</th>
<th>Females Risk Factor</th>
<th>Prevalence</th>
<th>Males Risk Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1</td>
<td>Anatomic or functional urologic abnormalities</td>
<td>1%</td>
<td>Anatomic or functional urologic abnormalities</td>
</tr>
<tr>
<td>1-5</td>
<td>Congenital abnormalities, vesicoureteral reflux</td>
<td>4.5%</td>
<td>Congenital abnormalities, uncorrected penis</td>
</tr>
<tr>
<td>6-15</td>
<td>Vesicoureteral reflux</td>
<td>4.4%</td>
<td>None</td>
</tr>
<tr>
<td>16-35</td>
<td>Sexual activity, diaphragm use, spermicides</td>
<td>20%</td>
<td>Homosexual activity, anal intercourse</td>
</tr>
<tr>
<td>36-65</td>
<td>Gynecologic surgery, bladder prolapse</td>
<td>35%</td>
<td>BPH, obstruction, catheterization, surgery</td>
</tr>
<tr>
<td>&gt;65</td>
<td>All of above, incontinence, chronic catheterization</td>
<td>40%</td>
<td>All of above, incontinence, chronic catheterization, condom catheters</td>
</tr>
</tbody>
</table>

Urinary Tract Infections Infecting Organisms

- E. coli: 79%
- S. saprophyticus: 11%
- Klebsiella: 3%
- Mixed: 3%
- Proteus: 2%
- Enterococcus: 2%
- Other: 2%

Microbial Species Most Often Associated with Specific Types of UTI’s

<table>
<thead>
<tr>
<th>Organism</th>
<th>Acute uncomplicated cystitis</th>
<th>Acute uncomplicated pyelonephritis</th>
<th>Complicated UTI</th>
<th>Catheter-associated UTI</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. coli</td>
<td>79%</td>
<td>89%</td>
<td>32%</td>
<td>24%</td>
</tr>
<tr>
<td>S. saprophyticus</td>
<td>11%</td>
<td>0%</td>
<td>1%</td>
<td>0%</td>
</tr>
<tr>
<td>P. mirabilis</td>
<td>2%</td>
<td>4%</td>
<td>4%</td>
<td>6%</td>
</tr>
<tr>
<td>Klebsiella spp.</td>
<td>3%</td>
<td>4%</td>
<td>5%</td>
<td>8%</td>
</tr>
<tr>
<td>Enterococcus spp.</td>
<td>2%</td>
<td>0%</td>
<td>22%</td>
<td>7%</td>
</tr>
<tr>
<td>P. aeruginosa</td>
<td>0%</td>
<td>0%</td>
<td>20%</td>
<td>9%</td>
</tr>
<tr>
<td>Mixed</td>
<td>3%</td>
<td>5%</td>
<td>10%</td>
<td>11%</td>
</tr>
<tr>
<td>Other*</td>
<td>0%</td>
<td>2%</td>
<td>5%</td>
<td>10%</td>
</tr>
<tr>
<td>Candida spp.</td>
<td>0%</td>
<td>0%</td>
<td>1%</td>
<td>28%</td>
</tr>
<tr>
<td>S. epidermidis</td>
<td>0%</td>
<td>0%</td>
<td>13%</td>
<td>8%</td>
</tr>
</tbody>
</table>

*Genital, Perineal, Enteric bacterial colonization

Introital colonization
Gut flora
Sexual activity
UTI in Women - Host Factors

- Short urethra
- Vaginal colonization
- Diaphragm / vaginal spermicide
- Sexual intercourse
- Delayed post-coital voiding
- P$_1$ blood group - upper UTI

UTI - Other Host Factors

- Extra-renal obstruction
  - posterior urethral valves
  - urethral strictures
  - prostatic hypertrophy
- Neurogenic bladder
- Vesico-ureteral reflux
- Catheterization/instrumentation

Urinary Tract Infections

- The initial pathogenic event in UTI is an encounter between bacteria and host mucosa at the tissue surface
- Attachment, binding of bacteria to mucosal cells, is the result of multiple interactions between bacterial surface ligands (adhesins) and epithelial cells (receptors).

Anti-adherence Mechanisms in the Urinary Tract

- Normal bacterial flora of vaginal, introital, and periurethral region and urethra
- Uromucoid (Tamm-Horsfall protein)
- Urinary oligosaccharides
- Urinary immunoglobulins (IgG, IgA, S-IgA)
- Bladder mucopolysaccharide (glycosaminoglycan)
- Mechanical effects of flushing
UTI - Bacterial Factors - 1

- **Attachment**
  - Type 1 fimbrae (MS-adhesins) - attach to mannoses on urothelial cell
  - P fimbrae - attach to globoseries receptors on urothelial cell - these strains cause pyelonephritis
    - 97% of women with recurrent pyelo are P1 blood group (+)
    - women with pyelo due to VU reflux - same prevalence of P1 as gen. pop.
  - Afimbrial adhesins (AFA I, AFA III)

- **Toxins**
  - RTX hemolysins - protein toxins that contain a tandem duplication of 9 amino acids (cause pores in cell membrane, lysis)
    - *E. coli* that do not produce these toxins are less virulent

- **Phase variation**
  - Type I down-regulated, Type P upregulated in strains that cause upper-tract infections (PAP gene expression triggered by temperature, [glucose], concentration of certain amino acids.

UTI - Bacterial Factors - 2

- **Internalization**
  - enters bladder cells, protected from antibody, phagocytes
  - intracellular persisters - ?source of recurrent infection

- **Doubling time**
  - if <50 - 60 minutes, increased ability to cause cystitis
    - *E. coli* bowel strains that do not cause UTI’s generally have slower doubling times

- Serum-resistant capsules

- Anti-phagocytic mechanisms (e.g., P-fimbriae)

- Iron acquisition efficiency is a virulence factor
  - uropathogenic strains may have multiple sequestration systems

UTI - Clinical

- **Children**
  - < 2 years - enuresis, fever, poor weight gain
  - > 3 years - dysuria, lower abdominal pain

- **Adults**
  - urgency, frequency, dysuria, cloudy or malodorous urine, bladder or flank pain
  - Pyelo: fever >101 F, chills (bacteremia), flank pain and tenderness
### Urinary Catheters
- Foreign body
- Biofilm formation
  - bacteria, bacterial glycocalyces, host proteins, urinary salts (apatite and struvite)
- Sanctuary site for bacteria
- Condom catheters carry same risk of infection as indwelling (Foley) catheters
- 100% become infected in 7-10 days

### Bacteriuria in the Catheterized Patient
- Avoid use of antimicrobials, if possible
- Indications for treatment
  - symptomatic infection
  - suspected sepsis
  - renal transplant
  - immunocompromised patient
  - pre-operative patient
- Remove or change catheter during treatment

### UTI - Diagnostic Criteria
- U/A microscopic - quantitative
- Leukocyte esterase test
- Nitrate → nitrite test
- Leukocyte esterase / nitrate test
- Gram’s stain, unspun urine

### UTI - Diagnostic Criteria
- Collection: clean midstream specimen or straight-catheterized specimen
- >10 WBC/µL in symptomatic female
- (+) Gram’s stain of unspun urine
- Culture criteria
  - >10^5 CFU/mL = infection
  - symptomatic female: 10^2-10^4 CFU/mL of *E. coli*, *Proteus*, *S. saprophyticus* are significant

### UTI - Stamey Test
1. Sterilize instruments and culture medium
2. Use 2 mL syringe with 15 ga needle and 16 ga catheter
3. Remove the catheter rubber stopper to allow air to enter
4. Grasp the catheter and hold in hand to prevent movement
5. Grasp the needle and insert into the urethra
6. Insert the needle through the rubber stopper into the culture medium
7. Injection of urine in the culture medium (VB1)
8. The addition of the urine to the culture medium (VB2)
9. The addition of the urine to the culture medium (EPS)
10. The addition of the urine to the culture medium (VB3)
Indications for Evaluating the Urinary Tract

- Children
  - ultrasound, IVP, VCUG
- Bacteremic pyelonephritis
  - ultrasound, or IVP
- Nephrolithiasis or Neurogenic Bladder
  - ultrasound, or IVP with post-voiding films
- Men with 1st infection
  - careful prostate examination
- Men with 2nd infection
  - ultrasound or IVP with post-voiding films

General Principles of Treatment

- Quantitative cultures may be unnecessary before treatment of typical cases of acute uncomplicated cystitis.
- Susceptibility testing is necessary in all recurrent or complicated infections, perhaps not for uncomplicated cases.
- Identify or correct factors predisposing to infection (obstruction, calculi)
- Relief of symptoms may not indicate bacteriologic cure: follow-up cultures are indicated if symptoms recur.
- Duration of therapy depends on the site and duration of the infection.
- Classify recurrences as re-infection or relapse.

Treatment of Asymptomatic Bacteriuria

- Pregnancy
- Neurological or structural abnormality of the urinary tract with > 10^5 CFU/mL
- Pre-op for GU (and other?) surgery