URINARY TRACT INFECTIONS

Goals

To introduce one of the most common clinical syndromes in infectious diseases, including the epidemiology, pathophysiology, clinical presentation and evaluation and management of adults and children with urinary tract infection (UTI).

To review the microbial agents which are important in the microbiology of this clinical syndrome.

Lecture Outline

I. Definitions

A. Significant bacteriuria
   1. Defined as $> 10^5$ colony forming units (cfu)/ml of urine
   2. A lower cut-off is used in symptomatic patients ($10^2$ cfu/ml)

B. Asymptomatic bacteriuria
   The presence of significant amounts of bacteria in the urine is in the absence of any symptoms suggestive of UTI.

C. Cystitis (lower UTI)
   Infection that is confined to the superficial bladder surface

D. Pyelonephritis (upper tract UTI)
   Infection that involves the kidney

E. Uncomplicated UTI
   Cystitis or pyelonephritis that occurs in an otherwise healthy individual with no underlying structural or functional abnormality of the urinary tract.
F. Complicated UTI

UTI that is associated with:

1. Obstruction at any site in the urinary tract (bladder outlet obstruction due to an enlarged prostate, uterine or bladder prolapse, stones, tumor, urethral stricture, congenital abnormalities)

2. Foreign body (catheter, stent)

3. Incomplete voiding (detrusor muscle dysfunction due to neurologic disease, medications)

4. Vesicoureteral reflux

5. Recent history of instrumentation

6. Renal transplant recipient

7. UTIs in males (always considered potentially complicated)

G. Recurrence

1. May be due either to relapse (20%) or reinfection (80%)
   a. Relapse is recurrence due to the same microorganism (usually within 2 weeks)
   b. Reinfection is recurrence due to a different microorganism (usually greater than 2 weeks)

II. Epidemiology

A. UTIs account for more than 7 million physician visits and one million hospitalizations in the United States annually and are the second most common community-acquired infection.

B. UTI is the most common nosocomial infection in the United States.

C. UTIs are the most common source of bacteremia due to gram-negative organisms.
D. UTIs in early childhood may be responsible for chronic renal failure

E. Prevalence by age group

1. UTI occurs more frequently in males than females in early infancy (<3 months)
2. The overall period prevalence in infants (< 1 year) is 1%.
3. 1-15 years: 4-5% in females and 0.5% in males
4. 16-35 years: 20% in females and 0.5% in males
5. 36-65 years: 35% in females and 20% in males
6. over 65 years: 40% in females and 35% in males

F. Natural history of UTI

1. The presence of bacteriuria in school children defines a population at greater risk of bacteriuria in adulthood

2. Asymptomatic bacteriuria occurs in 5% of pregnant women (usual onset 9-17 weeks). 40% will develop pyelonephritis during the pregnancy if untreated.

3. Both symptomatic and asymptomatic UTIs can resolve without treatment; antimicrobial therapy increases the probability of cure and speeds resolution of symptoms.

III. Pathogenesis

A. Bacteria that originate from the intestinal flora normally colonize the vaginal introitus, periurethral and distal urethral meatus

B. Infection occurs by the ascending route

1. Major reason why UTI is much more common in women than men; the antibacterial effect of prostatic secretions also contributes to decreased incidence
2. In women, sexual intercourse facilitates the entry of organisms into the bladder

C. Once infection has been established in the bladder urine, the infection may ascend via the ureter to involve the kidney
IV. Clinical presentation

A. Cystitis
   1. Dysuria, urgency frequency; may also have hematuria
   2. Suprapubic or low back pain may be present; fever, chills, other signs of systemic infection are absent.
   3. Physical exam: suprapubic tenderness

B. Pyelonephritis
   1. May or may not have symptoms of cystitis
   2. Flank pain
   3. Symptoms/signs of systemic toxicity
      a. Fever, chills
      b. Nausea, vomiting
      c. Hypotension, other signs of sepsis
   4. Physical exam: fever, costovertebral angle tenderness
   5. In the frail elderly, unexplained fever, new onset incontinence and/or change in mental status may be presenting complaint. Since prevalence of bacteriuria is high, UTI is always a diagnosis of exclusion

C. UTI in the pediatric population
   1. In infants, presentation is relatively non-specific: poor feeding, failure to gain weight, GI symptoms, unexplained fever (including febrile seizures)
   2. Toddlers/preschoolers: lower tract symptoms, recurrence of daytime/nocturnal enuresis, fever
   3. School-age children: same as adults

V. Evaluation

A. Urine is collected as a “midstream, clean catch” specimen. Special “stick on” collection bags can be utilized in infants and toddlers. Occasionally, catheterization will be utilized to obtain a specimen.
   1. Can use a “dipstick” to detect presence of red blood cells, white blood cells and bacteria
B. In a patient with suggestive signs/symptoms the presence of pyuria (WBCs in the urine) is suggestive of UTI
   1. Specimen is spun for 5 min at 2000 rpm
   2. Greater than 5-10 leukocytes per high-power field is considered significant

C. One or more bacteria per high-power field in an unspun specimen correlates with growth of greater than $10^5$ cfu/ml in a urine culture.
   1. A Gram’s stain of urine is a fast and easy way to give information regarding presence of pyuria, significant bacteriuria and the morphology of the infecting organism

D. In clinical practice, an otherwise healthy young woman who presents with classic symptoms of lower UTI is generally managed empirically
   1. Urine dipstick or microscopy can confirm diagnostic impression
   2. Culture of urine is not recommended
      a. Microbiology is predictable
      b. “short course” therapy is utilized-results would not be available in a clinically meaningful time frame

E. All other patients and all patients with pyelonephritis should be cultured

F. Differentiating lower tract (cystitis) from upper tract (pyelonephritis) infection

   1. Usually done on clinical grounds
      a. Problem: up to 30% of women with symptoms/signs of cystitis may have unrecognized (subclinical) pyelonephritis
      b. A number of laboratory tests have been studied in an attempt to “localize” infection more accurately
         i. Antibody-coated bacteria
         ii. Glitter cells and WBC casts
      c. None of these non-invasive tests have been shown to be sufficiently sensitive or specific to be clinically useful
VI. Microbiology

A. Cystitis
   1. *Escherichia coli* up to 80%
   2. *Staphylococcus saprophyticus* 10-20%
   3. Rarely, *Proteus, Klebsiella, Enterococcus*

B. Pyelonephritis
   As above, although *S. saprophyticus* is rarely described

C. Complicated infections/nosocomial UTI
   1. *E. coli* still important
   2. *Proteus, Klebsiella, Enterobacter, Serratia, Citrobacter, Psuedomonas, Enterococcus*

D. Pediatric population
   1. Again, mainly *E. coli*
   2. *Klebsiella, Proteus*
   3. Rarely, coagulase negative *Staphylococci* (epidermidis, albus)

VII. Management

A. Uncomplicated cystitis in young otherwise healthy women
   1. Short course (3 day) oral therapy
      a. Trimethoprim-sulfamethoxazole (concerns regarding increasing resistance)
      b. Fluoroquinolones
   2. Nitrofurantoin can be used, but 7 day courses are needed
   3. High rates of resistance to ampicillin and first generation cephalosporins preclude their use

B. Cystitis in other patient groups
   7 day courses of therapy (TMP-SMX, fluoroquinolones, nitrofurantoin)
C. Pyelonephritis
   1. Decision regarding intravenous (need to hospitalize) versus oral therapy is based on overall severity of illness
      a. 14 days of total therapy based on culture/susceptibility testing
      b. longer courses of treatment (21-28 days) may be utilized for complicated infections

D. Asymptomatic bacteriuria
   1. Only treated in certain circumstances
      a. Pregnancy
      c. Prior to invasive instrumentation of the urinary tract or urologic surgery
      c. Renal transplant patient
      d. Children

E. Radiologic imaging
   1. Usually reserved for patients with complicated infections, recurrent pyelonephritis or pyelonephritis which fails to respond to appropriate antibiotic therapy
      a. Computerized axial tomography
      b. Ultrasound
      d. Specialized imaging procedures may be utilized in children with suspected vesico-ureteral reflux