Pyelonephritis

**Background**

1. Definition:
   - Urinary tract infection that has progressed from lower urinary tract to upper urinary tract
   - Mostly uncomplicated; must distinguish between acute uncomplicated and complicated or chronic pyelonephritis.
     - **Acute:** single episode of infection with bacterial invasion of the renal parenchyma
     - **Complicated:** associated with underlying condition that increases risk of failing therapy (e.g., urinary tract obstruction, anatomic anomaly, multiple antibiotic resistant pathogens and diabetes)
       - Progression to emphysematous pyelonephritis, renal corticomedullary abscess, perinephric abscess, or papillary necrosis.
     - **Uncomplicated:** no associated conditions that increase risk of failing therapy
     - **Chronic:** uncommon cause of chronic tubulointerstitial disease
       - Due to persistent/recurrent infection associated with underlying pathology (e.g., vesicoureteral reflux, chronically obstructing kidney stone)
       - Results in permanent renal injury and scarring; can lead to ESRD (end-stage renal disease)

2. See also urinary tract infections (UTIs)

**Pathophysiology**

1. Pathology
   - Ascending infection from lower urinary tract
   - E. coli most common pathogen in uncomplicated cases (70-80%)
     - Klebsiella spp. 6-10% (increased rate with >55 years old)
     - Enterococcus spp 3-7%
     - Staph saprophyticus: <3%
   - Microbiology may be significantly different in complicated pyelonephritis: E. coli still most common. Citrobacter, Enterobacter, Pseudomonas aeruginosa, Enterococci, Staph. Aureus and fungi more common than in uncomplicated pyelonephritis.
   - Life-threatening infection rare; patients can present with sepsis/bacteremia

2. Incidence/prevalence
   - Estimated 250,000 hospitalizations annually
   - Women > men (Ratio > 5:1)

3. Risk factors
   - Uncomplicated
     - Same as for uncomplicated lower tract infections
       - Sexual intercourse: Frequency (>= 3 times per week) of sexual intercourse in the previous 30 days
       - A new sexual partner in the previous 12 months
• Use of spermicidal products (foams, spermicide-coated condoms)
• History of UTI within the previous 12 months
• Diabetes
• Episodes of stress urinary incontinence within the previous 30 days

  o Complicated
    ▪ Age: infants, elderly >60 years of age
    ▪ Kidney stones
    ▪ Obstruction, diverticulae, fistulae, ileal conduits/urinary diversions, vesicoureteral reflex, indwelling catheter, ureteral stent, nephrostomy tube
    ▪ Neurogenic bladder, pregnancy, diabetes, renal failure, renal transplant, immunosuppression
    ▪ Multi-drug resistant uropathogens, hospital-acquired infection

4. Morbidity/mortality
  o No significant mortality in acute uncomplicated pyelonephritis
  o Higher mortality rates in males vs. females (16.5/1000 vs. 7.3/1000) in complicated pyelonephritis

Diagnostics
1. Clinical Manifestations:
  o Fever: >37.8 C. Strongly correlated with acute pyelonephritis; absence of fever warrants re-evaluation for alternate diagnoses
  o Flank pain, abdominal/pelvic pain
  o Nausea/Vomiting
  o And/or costovertebral angle tenderness
  o +/- symptoms of cystitis: frequency, dysuria and suprapubic pain
  o Pelvic exam if suspect PID/STD
2. Diagnostic testing
  o Urine: Recommended for routine diagnosis.
    ▪ Pyuria: present in almost all acute pyelonephritis cases (absence of pyuria suggests alternative diagnosis or presence of obstructing lesion
      • White-cell casts indicate renal origin
    ▪ Hematuria
    ▪ Nitrite test
      • Helpful only when positive
      • Detects only gram-negative bacteria
      • Will not detect enterococci or staphylococci (cannot reduce nitrate to nitrite)
    ▪ Culture
      • Should be performed routinely
    ▪ Gram stain may be useful in guiding empirical therapy
      • 80-95% of acute pyelonephritis: > 10(5) CFU/mL
      • Can have pyelo with only 10(3)-10(4) CFU/mL (SOR:C)
o Blood
  • Elevated WBC (nonspecific, does not distinguish between lower UTI and pyelonephritis)
  • ESR: nonspecific, >30mm/hr highly predictive of acute pyelonephritis
  • CRP: Sensitive but nonspecific markers of renal parenchymal involvement
  • Blood cultures positive in 10-20% pts. Should be obtained in patients with acute pyelonephritis only if diagnostic uncertainty, patient immunocompromised, or hematogenous source suspected. (SOR:C)\(^7,8\)
  • No evidence that positive blood cultures indicate more complicated course in otherwise healthy patients with pyelonephritis.

  o STD cultures if suspicion exists

  o Imaging studies
    • Not routinely required for acute uncomplicated pyelonephritis
    • Consider in patients with persistent fever or no improvement after 48-72 hours of antibiotics (SOR:C)\(^1\)
      - **Contrast enhanced helical/spiral CT**: study of choice to detect complication of pyelonephritis in adults (high sensitivity)
      - **Non-contrast helical/spiral CT**: less sensitive, standard study for gas forming infections
      - **Ultrasound**: low sensitivity, negative study does not exclude possibility of pyelonephritis
      - **99mTc- DMSA scintigraphy**: high sensitivity, preferred study in children due to less radiation exposure

Differential Diagnosis
1. Acute appendicitis (retrocecal appendix): can present with flank pain
2. Nephrolithiasis: pain usually much more prominent; patient constantly moves to get comfortable; in pyelonephritis, patient lies still
3. **PID**
4. Musculoskeletal pain in lumbosacral muscles or lower rib cage
5. Lower urinary tract infection

Therapeutics
1. Outpatient therapy safe for select pts.
   - Successful in 90% of appropriate Pts. (SOR:B)\(^9,10,11\)
     - Mild to moderate uncomplicated cases
     - Pts. able to tolerate PO fluids/meds
     - Compliant
2. Indications for hospitalization
   - Complicated pyelonephritis
   - Cannot tolerate PO/dehydration
   - Uncertainty regarding diagnosis
3.13.11

3. Antibiotic choices

- Start with empirical antibiotics then change based on culture results
- Knowledge of community profiles should guide empirical therapy (local antibiotigram)
- Culture/sensitivity results important when available

3.1 Oral

- Fluoroquinolones: (SOR:A)\textsuperscript{11}
  - Ciprofloxacin: 500 mg PO BID; levofloxacin: 500 - 750 mg PO QD\textsuperscript{11,12}
  - Moxifloxacin avoided due to ineffective concentrations in urine
  - For gram negative bacilli
- Bactrim DS: BID if pathogen is known to be susceptible (SOR:B)\textsuperscript{11}
- Amoxicillin: Less effective (SOR:B)\textsuperscript{11} 500 mg TID or 875mg bid
  (added to treatment regimen if gram positive cocci seen on gram stain: enterococcus or S. Saprophyticus)
- Ampicillin & sulfonamides
  - High rates of resistance
  - Do not use for empiric therapy
- Nitrofurantoin
  - Do not use; insufficient tissue levels

3.2 Parenteral

- Ceftriaxone: 1 gram IV QD (SOR:B)\textsuperscript{11}
  - If enterococcus not suspected
- Fluoroquinolones IV: excellent genitourinary penetration, used in areas where resistance is relatively low (SOR:B)\textsuperscript{11}
- Gentamicin
  - Add ampicillin 1-2 grams IV q6hr if enterococcus suspected
- Aztreonam 1g IV q8-12 hours (Pts with beta lactam hypersensitivity and Fluoroquinolone resistance)

4. Duration of therapy

- Not influenced by the presence of bacteremia\textsuperscript{13}
- Can usually switch from parenteral to oral after 24-48 hr if:
  - Pt. afebrile and demonstrating clear improvement
  - Tolerating po fluids/meds
- 14-day regimen of antibiotics recommended (SOR:A)\textsuperscript{11}
  - 7-10 days for mild illness and pts who have a rapid response to tx (SOR:B)\textsuperscript{11}
  - 7 day course of ciprofloxacin had more favorable outcome than 14 days course of trimethoprim-sulfamethoxazole\textsuperscript{6}
  - Levofloxacin FDA approved for five day course of 750 mg po daily for treating uncomplicated pyelonephritis only.
  - Beta lactam regimens < 14 days have high failure rates.
- 21 days treatment indicated for slow response to tx/severe illness
**Acute Complicated Pyelonephritis**

1. May be associated with nonspecific signs/symptoms
   - Malaise, fatigue, nausea, abdominal pain
2. Insidious onset
3. Pyuria/bacteriuria may be absent if infection does not communicate with collecting system, or with obstruction
4. Lower threshold for diagnosis of infection
   - $10^3$ CFU/mL ($10^2$ CFU/mL if sample from newly inserted catheter)
5. Wide range of pathogens (E. coli still most common)
   - Citrobacter, Enterobacter, Pseudomonas aeruginosa, enterococci, Staph aureus, fungi sp
   - S. saprophyticus uncommon
6. Generally treated as inpatients
   - Including pregnant women
7. Floroquinolones, aminoglycosides, cephalosporins can all be appropriate
8. 14-day course recommended (SOR:A)\(^1\)
9. Repeat culture after treatment
10. Suppressive antibiotics indicated in some cases
11. See also pregnancy and UTI

**Follow-Up**

1. Follow up in 2 days if treated as outpatient (by phone or secure messaging okay)
2. Post-treatment cultures
   - Not indicated in asymptomatic pt.
3. If symptoms recur within two weeks of apparent resolution
   - Repeat urine culture
   - Consider renal ultrasound or CT scan (SOR:C)\(^1\)
   - Additional 2 wks of treatment
4. If symptoms recur more than 2 wks after apparent resolution
   - Approach same as with sporadic episode
     - Persistent infection with original organism less likely
5. Consultation
   - Pt. febrile/no signs of clinical improvement after 72 hrs of appropriate tx (based on C&S)
   - History of complicating factors

**Prognosis**

1. Low risk of recurrence in uncomplicated cases

**Evidence Based Inquiries**

1. What is the minimum number of days of antibiotic treatment for patients hospitalized with acute uncomplicated pyelonephritis?
2. When are empiric antibiotics appropriate for urinary tract infection symptoms?
References
6. Talan, DA, Stamm, WE, Hooton, TM, et al. Comparison of ciprofloxacin (7 days) and trimethoprim-sulfamethoxazole (14 days) for acute uncomplicated pyelonephritis pyelonephritis in women: a randomized trial. JAMA 2000; 283:1583.

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