

# 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 (eg, 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 (eg, 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<sup>2</sup>

- Uncomplicated
  - Same as for uncomplicated lower tract infections
    - Sexual intercourse: Frequency ( $\geq 3$  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
  - 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
- No significant mortality in acute uncomplicated pyelonephritis
  - Higher mortality rates in males vs. females (16.5/1000 vs. 7.3/1000) in complicated pyelonephritis<sup>5</sup>

## Diagnosics

1. Clinical Manifestations:
  - Fever: >37.8 C. Strongly correlated with acute pyelonephritis; absence of fever warrants re-evaluation for alternate diagnoses<sup>3</sup>
  - Flank pain, abdominal/pelvic pain
  - Nausea/Vomiting
  - And/or costovertebral angle tenderness
  - +/- symptoms of cystitis: frequency, dysuria and suprapubic pain<sup>4</sup>
  - Pelvic exam if suspect PID/STD
2. Diagnostic testing
  - **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)<sup>1</sup>

- **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)<sup>7,8</sup>
  - No evidence that positive blood cultures indicate more complicated course in otherwise healthy patients with pyelonephritis.
- **STD cultures** if suspicion exists
- **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)<sup>1</sup>
    - **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
    - **<sup>99m</sup>Tc- 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)<sup>9,10,11</sup>
    - 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

- Severe illness
  - High fever, significant pain, markedly disabled
- Concerns regarding compliance
- 3. Antibiotic choices
  - Start with empirical antibiotics then change based on culture results
  - Knowledge of community profiles should guide empirical therapy (local antibiogram)
  - Culture/sensitivity results important when available
  - **Oral**
    - Fluoroquinolones: (SOR:A)<sup>11</sup>
      - Ciprofloxacin: 500 mg PO BID; levofloxacin: 500 -750 mg PO QD<sup>11,12</sup>
      - Moxifloxacin avoided due to ineffective concentrations in urine
      - For gram negative bacilli
    - Bactrim DS: BID if pathogen is known to be susceptible (SOR:B)<sup>11</sup>
    - Amoxicillin: Less effective (SOR:B)<sup>11</sup> 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
  - **Parenteral**
    - Ceftriaxone: 1 gram IV QD (SOR:B)<sup>11</sup>
      - If enterococcus not suspected
    - Fluoroquinolones IV: excellent genitourinary penetration, used in areas where resistance is relatively low (SOR:B)<sup>11</sup>
    - 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<sup>13</sup>
  - 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)<sup>11</sup>
    - 7-10 days for mild illness and pts who have a rapid response to tx (SOR:B)<sup>11</sup>
    - 7 day course of ciprofloxacin had more favorable outcome than 14 days course of trimethoprim-sulfamethoxazole<sup>6</sup>
    - 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. Fluoroquinolones, aminoglycosides, cephalosporins can all be appropriate
8. 14-day course recommended (SOR:A)<sup>11</sup>
9. Repeat culture after treatment
10. Suppressives 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)<sup>1</sup>
  - 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

1. Grabe M.: *Uncomplicated urinary tract infections in adults*. In: Grabe M., Bishop M.C., Bjerklund-Johansen T.E., et al ed. *Guidelines on the management of urinary and male genital tract infections*, European Association of Urology (EAU) Arnhem (The Netherlands) 2008: 11-40.
2. Scholes, D, Hooton, TM, Roberts, PL, et al. Risk factors associated with acute pyelonephritis in healthy women. *Ann Intern Med* 2005; 142:20.
3. Pinson, AG, Philbrick, JT, Lindbeck, GH, Schorling, JB. Fever in the clinical diagnosis of acute pyelonephritis. *Am J Emerg Med* 1997; 15:1
4. Fairley, KF, Carson, NE, Gutch, RC, et al. Site of infection in acute urinary-tract infection in general practice. *Lancet* 1971; 2:615.
5. Foxman B, Klemstine KL, Brown PD. Acute pyelonephritis in US hospitals in 1997: hospitalization and in-hospital mortality. *Ann Epidemiol*. 2003;13:144–50.
6. Talan, DA, Stamm, WE, Hooton, TM, et al. Comparison of ciprofloxacin (7 days) and trimethoprim-sulfamethoxazole (14 days) for acute uncomplicated pyelonephritis in women: a randomized trial. *JAMA* 2000; 283:1583.
7. McMurray BR, Wrenn KD, Wright SW. Usefulness of blood cultures in pyelonephritis. *Am J Emerg Med*. 1997;15:137–40.
8. Velasco M, Martinez JA, Moreno-Martinez A, Horcajada JP, Ruiz J, Barranco M, et al. Blood cultures for women with uncomplicated acute pyelonephritis: are they necessary? *Clin Infect Dis*. 2003;37:1127–30.
9. Safrin S, Siegel D, Black D. Pyelonephritis in adult women: inpatient versus outpatient therapy. *Am J Med*. 1988;85:793–8.
10. Bach D, van den Berg-Segers A, Hubner A, van Breukelen G, Cesana M, Pletan Y. Rufloxacin once daily versus ciprofloxacin twice daily in the treatment of patients with acute uncomplicated pyelonephritis. *J Urol*. 1995;154:19–24.
11. Warren, JW, Abrutyn, E, Hebel, JR, et al. Guidelines for antimicrobial treatment of uncomplicated acute bacterial cystitis and acute pyelonephritis in women. Infectious Diseases Society of America (IDSA). *Clin Infect Dis* 1999; 29:745.
12. Hooper, DC, Wolfson, JS. Fluoroquinolone antimicrobial agents. *N Engl J Med* 1991; 324:384.
13. Mombelli, G, Pezzoli, R, Pinoja-Lutz, G, et al. Oral vs intravenous ciprofloxacin in the initial empirical management of severe pyelonephritis or complicated urinary tract infections: a prospective randomized clinical trial. *Arch Intern Med* 1999; 159:53.

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