

Update: Community Acquired Urinary Tract Infection

GIM Noon Conference

Alan M. Stamm, M.D.

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Today's speaker has no conflict of interest to disclose.

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Disclosures

- No financial disclosures or conflicts of interest.



Objective

- Review the diagnosis and treatment of various types of urinary tract infection.
 - acquired in the community
 - unrelated to health care

Case #1

- A previously healthy 25-year-old woman telephones on Saturday complaining of dysuria last night and this morning.
- What could cause this symptom?
- What questions should be asked?
- Can this be handled over the telephone?

Dysuria

- What could cause this symptom?
 - vaginitis, cystitis, pyelonephritis, urethritis, interstitial cystitis, etc.
- What questions should be asked?
 - vaginal discharge or itching
 - frequency, nocturia
 - fever, flank pain
 - nausea, vomiting

Telephone Management

- Can this be handled over the telephone?
 - yes, potentially
 - no mandate for culture with simple cystitis
 - without co-morbidities
 - if no antibiotics in past 3 months

Case #1a

- The same lady telephones again, this time from the drug store, requesting reassurance that trimethoprim/sulfamethoxazole DS 1 PO BID x 3 days is going to be effective after her **Google** search & review.
- What can be said?

Cystitis / treatment

IDSA & ESMID. Clin Infect Dis 2011; 52: 561

- There is a new international clinical practice guideline.
- Recommended agents:
 - nitrofurantoin (e.g., *Macrobid* 100 mg BID) x 5 days (simple vs. 7 days complicated)
 - trimethoprim/sulfamethoxazole (e.g., DS BID) x 3 days (simple vs. 7 days complicated)
 - alternative: fluoroquinolone (e.g., ciprofloxacin 250 mg BID) x 3 days (simple vs. 5-7 days complicated)
 - not: moxifloxacin (*Avelox*), amoxicillin, cephalexin

nitrofurantoin (*Macrobid*)

- Administered orally; absorption enhanced by food; serum levels low-undetectable.
- Eliminated predominantly by glomerular filtration and tubular secretion.
- Active *in vitro* against urinary pathogens:
 - *E. coli*, *S. saprophyticus*, *K. pneumoniae*, *E. fecalis*
- Used only for cystitis.
- Adverse effects: nausea & vomiting >> rash.
- Cost about \$35-40.

trimethoprim/sulfamethoxazole

- About 80% of isolates causing cystitis are susceptible; treatment is successful in 95% of these individuals.
- Among the 20% with resistant isolates, treatment is still successful in 50%.
 - this is unique
- Overall, $(80 \times 0.95) + (20 \times 0.50) = 86\%$ rate of success.
 - vs. 95% for *Macrobid*

ciprofloxacin (*Cipro*)

- “Highly efficacious in 3-day regimen.”
- “Propensity for collateral damage.”
 - defined as ecological adverse effects of antimicrobial therapy
- “Should be reserved for important uses other than acute cystitis.”

Case #2

- A 27-year-old woman complains of dysuria and frequency for 24 hours. U/A reveals 25 WBC/hpf + bacilli. This is her 5th episode in 4 years; the last was 8 months ago.
- Should a urine C&S be ordered?
- Is an imaging procedure indicated?
- Describe appropriate empiric therapy.

Recurrent Cystitis

- Should a urine C&S be ordered?
 - urinalysis yes, C&S not necessary
- Is an imaging procedure indicated?
 - no, CT not useful with recurrent cystitis
 - neither is cystoscopy
- Describe appropriate empiric therapy:
 - *Macrobid* 100 mg BID x 5 days
 - *Bactrim* DS BID x 3 days

Case #3

- A 30-year-old woman has had at least 8 episodes of acute cystitis in the past year. She is well today, and her medical history is otherwise unremarkable.
She has hope and wants change!
- What additional information might be helpful?
- What can be implemented to alter the present course of events?

Pathogenesis

- Question regarding...
 - personal hygiene – use of douche
 - estrogen sufficiency – premature ovarian failure
 - sexual activity – temporal association with sexual intercourse or trauma
 - contraception – use of spermicide

Recurrent Cystitis / intervention

- Chemoprophylaxis:
 - single-dose event triggered prophylaxis
 - self-initiated 3-5 day treatment
 - continuous prophylaxis for 6-12 months:
 - trimethoprim/sulfamethoxazole SS daily
 - trimethoprim 100 mg daily
 - *Macrobid* 100 mg daily
 - norfloxacin (*Noroxin*) 200 mg daily

Case #4

- A 50-year-old woman telephones complaining of 2-3 days of dysuria, urgency, and frequency. She has diabetes mellitus and 5 children.
- Is this simple or complicated cystitis?
- How should she be managed?

Cystitis / assessment

- Classification as simple vs. complicated affects therapy; search for these factors:
 - diabetes, impaired immunity
 - pregnancy, stone disease, anatomic/functional abnormality
 - hospital-acquired, post catheterization or instrumentation
 - recent UTI
 - recent antibiotic therapy
 - symptoms of >7 days duration

Complicated Cystitis

- Do U/A and C&S because it is complicated.
 - greater likelihood of occult pyelonephritis
- Start ciprofloxacin:
 - because of efficacy with both cystitis and pyelonephritis
 - 250 mg BID
 - follow-up on symptoms and C&S after 2-3 days
 - finish 5-7 day course of effective antibiotic

Case #5

- A 25-year-old woman presents to ER with 1 day of fever, chills, nausea, flank pain, dysuria, and frequency; T 101.5° F; U/A +.
- What criteria are useful in deciding whether to treat her at home or in the hospital?
- Are additional tests indicated?
- Describe appropriate initial therapy.

Pyelonephritis / assessment

- Initiate therapy in the hospital or at home; questions to address:
 - is the diagnosis secure?
 - is the patient well hydrated?
 - is the patient free of underlying renal or urologic disease?
 - is the patient free of complicating medical, neurologic, or obstetric conditions?

Urine Testing: What to Order

- Cystitis:
 - simple - just a urinalysis
 - complicated - urinalysis, Gram stain, culture & susceptibility
- Pyelonephritis:
 - urinalysis, Gram stain, culture & susceptibility
 - do blood cultures if hospitalized (15-20% +)
- Prostatitis:
 - urinalysis, Gram stain, culture & susceptibility

Pyelonephritis / treatment

- Recommended agent if hospitalized:
 - a 3rd-generation cephalosporin IV (e.g., ceftriaxone (*Rocephin*) 1 gm q 12-24 hours)
 - alternative: fluoroquinolone IV (e.g., *Cipro* 400 mg q 12 hours)
 - not: a penicillin, 1st-generation cephalosporin, trimethoprim/sulfamethoxazole, or nitrofurantoin
- Duration:
 - 2 weeks (3-4 days IV, then PO)
 - selection of PO drug depends on susceptibility; try to avoid a fluoroquinolone

piperacillin/tazobactam (*Zosyn*)

- Two multi-center, open-label, non-comparative trials were completed.
 - patients with pyelonephritis
 - all isolates were susceptible
 - at 4-6 weeks post-therapy:
 - clinical cure in 160/195 (82%)
 - bacteriologic cure in 131/173 (76%)
- Conclusion: *Zosyn* does not work as well as *Rocephin* or *Cipro*.

cefpodoxime (*Vantin*)

- A 3rd generation cephalosporin:
 - for oral administration
 - 200 mg BID
- Another option to complete therapy in patients with more drug-resistant gram-negative bacillary isolates.
 - avoiding a PICC and home infusion therapy
- Cost about \$130.

Case #5a

- Culture report at 24 hours: 15,000 cfu/ml coagulase-negative staphylococci - no further work-up intended.
- What is the correct interpretation of this report?
- Should the antimicrobial prescription be changed?

Urine Culture

- Colony count is done at 24 hours.
- Pyelonephritis is usually associated with $\geq 10^5$ microorganisms per milliliter of urine.
 - 20% have 10^3 - 10^5
- *Staphylococcus saprophyticus*, a coagulase-negative staphylococcus, is the 2nd most common cause of cystitis and pyelonephritis in young women.
 - generally broadly susceptible

Case #6

- A 29-year-old woman is hospitalized with acute pyelonephritis; urine and blood are + for *E. coli*; after 48 hours of therapy, nausea and flank pain persist; T_c 101° F.
- What are possible explanations?
- Are additional tests indicated?
- Should therapy be altered?

Failure to Improve

- Error in diagnosis?
 - differential diagnosis
 - natural history of pyelonephritis
 - median time to resolution of symptoms is 48 hours, 95% within 96 hours
 - median time to resolution of fever is 36 hours, 95% within 72 hours
- Error in treatment?
 - failure to order or administer antibiotic
 - antimicrobial resistance
 - anatomic problem: obstruction, abscess

Evaluation

- Are additional tests indicated?
 - check original susceptibilities
 - do urinalysis & compare to original
 - imaging not indicated
 - unless symptoms/fever persist >4 days

Kanel KT, et al. Arch Intern Med 1988; 148: 2144

- Should therapy be altered?
 - depends on susceptibilities

Case #7

- A 76-year-old man complains of 2-3 days of dysuria, urgency, hesitancy, and nocturia; T 100° F, prostate moderately enlarged & tender; U/A +.
- Describe appropriate management.

Prostatitis / assessment

- Consider the certainty of the clinical diagnosis of acute prostatitis.
- Evaluate the need for hospitalization:
 - hydration status
 - renal or urologic problems
 - emptying of bladder (post-void residual)
 - co-morbidities
- Order urinalysis, culture & susceptibility.
 - not a “4-glass” test

Prostatitis / management

- Do not massage the prostate.
 - painful, not helpful, and may cause bacteremia
- Treat with an agent that penetrates the prostate:
 - ciprofloxacin 500 mg PO BID x 3 weeks
 - if hospitalized, give 400 mg IV q 12 hours
 - trimethoprim/sulfamethoxazole DS PO BID x 4 weeks
 - doxycycline 100 mg PO BID x 4 weeks
- Prescribe an NSAID to relieve pain and reduce inflammation.

Case #8

- A 65-year-old woman with diabetes presents for routine follow-up. She denies polyuria and nocturia. A urine specimen is submitted for microalbumin. A U/A is actually done: 25 WBC/hpf, bacilli +, protein +.

The lab automatically does a C&S: $>10^5$ *E. coli* per ml, susceptible to ciprofloxacin but resistant to ampicillin and trim/sulfa.

- What do you do for this patient?

Management

- Reorder urine for microalbumin at a time when pyuria is absent.
- Telephone and question about dysuria or frequency.
 - the differential diagnosis is asymptomatic bacteriuria vs. cystitis
- Does the titer of bacteria, species, or degree of pyuria help sort things out?

Philadelphia Geriatric Center

- Facility:
 - self-care apartments ½
 - nursing home ½
- Population:
 - ~1000 men and women
 - mean age 85 years
 - middle and upper socioeconomic class



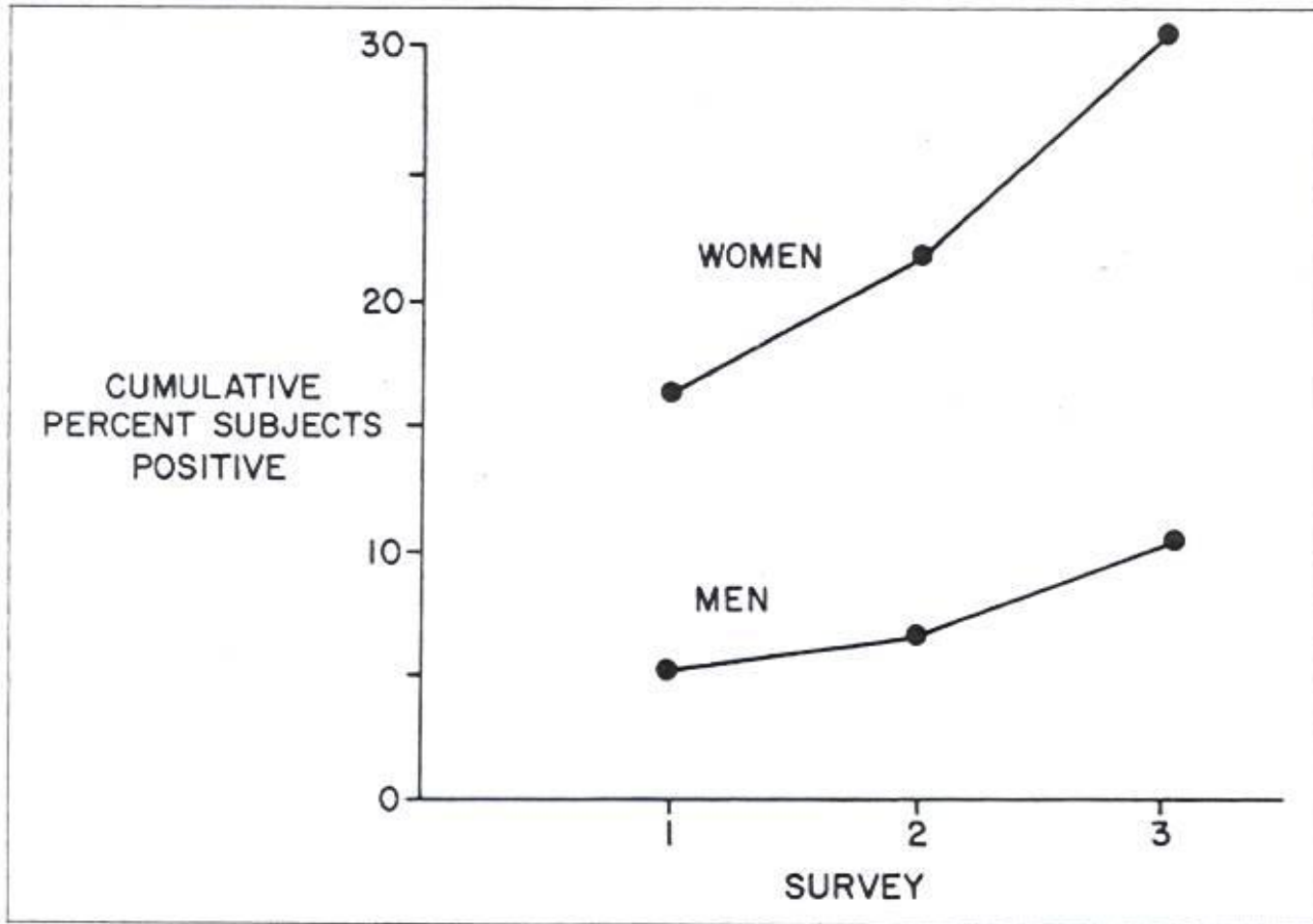
Study

Boscia JA, et al. Am J Med 1986; 80: 208

- **Criteria:**
 - no urinary collection devices
 - able to do mid-stream collection
 - no symptoms of UTI
- **Methods:**
 - surveyed every 6 months
 - functional assessment
 - urine tests

Findings

- Prevalence of asymptomatic bacteriuria (in 523 sampled up to 3 times at 6 month intervals):
 - women 18% vs. men 6%
 - nursing home 24% vs. apartment 12%
 - impaired ADLs 20% vs. intact 13%
 - impaired mental status 18% vs. intact 12%



Urine Culture / bacteriology

- Definition:
 - required $>10^5$ bacteria/ml
 - confirmed by replication within 1 week
- Species:
 - none had $>10^5$ of >1 microorganism
 - women $>90\%$ *Enterobacteriaceae*, $>85\%$ *E. coli*
 - men 50% *Enterobacteriaceae*, 50% *Enterococcus*
- Patterns in women:
 - persistence with same species 6%
 - persistence with different organisms 4%

Urinalysis / pyuria

- Titer:
 - defined as ≥ 10 WBC/mm³ (= ≥ 5 WBC/hpf)
 - range ≥ 10 to ≥ 1000 WBC/mm³
- Correlations:
 - among 46 with asymptomatic $>10^5$ bacteriuria, $>90\%$ had pyuria
 - among 257 with $<10^2$, $>30\%$ had pyuria
- Conclusions:
 - pyuria is very common and nonspecific
 - in the absence of pyuria, the likelihood of significant bacteriuria is $<5\%$

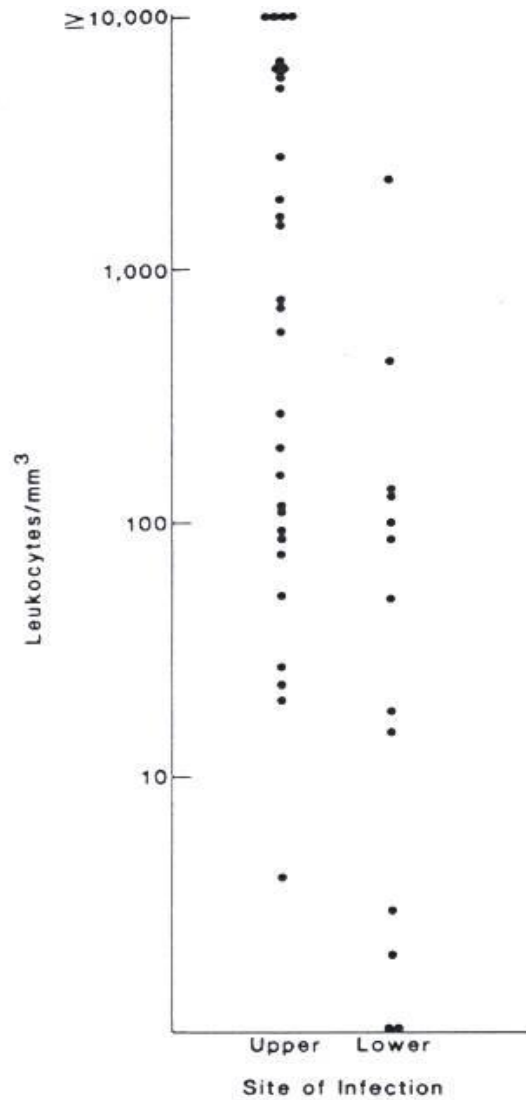


Figure 1. Distribution of number of leukocytes/mm³ in urine of elderly women with asymptomatic bacteriuria by site of infection (upper or lower urinary tract).

Lack of association between bacteriuria and symptoms in the elderly.

Boscia JA, et al. Am J Med 1986; 81: 979

- Included:
 - 72 subjects, each serving as their own “control”
 - 24 in whom bacteriuria resolved spontaneously, restudied at 6 months
 - 25 who acquired bacteriuria, at 6 months
 - 27 whose bacteriuria resolved with treatment, at 2 weeks
- Excluded:
 - 4 patients with recent onset dysuria

Symptoms

- Urinary:
 - frequency
 - urgency
 - suprapubic pain
 - flank pain
 - fever
 - incontinence
- General:
 - anorexia
 - difficulty sleeping
 - fatigue
 - weakness
 - malaise

Findings

- No differences in symptoms were found when bacteriuric individuals were compared with themselves when they were nonbacteriuric.

Prediction of Disease

- Positive value:
 - recent onset dysuria
- Negative value:
 - lack of pyuria
- No value:
 - other symptoms
 - cloudy or smelly urine
 - titer of bacteria
 - species of bacteria
 - titer of pyuria

Treatment

- Outcomes:
 - no influence on symptoms
 - adverse drug effects
 - isolation of increasingly resistant microorganisms
 - no differences in morbidity or mortality

- may decrease the 6-month risk of symptomatic UTI from 16% to 8%

Boscia JA, et al. JAMA 1987; 257: 1067

A prospective study of asymptomatic bacteriuria in young women.

Hooten TM, et al. N Engl J Med 2000; 343: 992

- Point prevalence of 5% at 18-40 years.
- Cumulative prevalence over 6 months 21-24%.
- Transient.
- *E. coli* the isolate in >75%.
- Pyuria present in 24% with $>10^5$ bacteriuria.
- Urinary tract infection (with the same strain) occurred within 1 week in 8%.
 - with both bacteriuria and pyuria in 15%

IDSA guidelines for the diagnosis and treatment of asymptomatic bacteriuria in adults.

Nicolle LE, et al. Clin Infect Dis 2005; 40: 643

- Pyuria accompanying AB is not an indication for antimicrobial treatment.
- Screening for and treatment of AB before TURP or other urologic procedures are recommended.
- Screening for or treatment of AB is not recommended for:
 - premenopausal, nonpregnant women
 - diabetic women
 - elderly, institutionalized persons
 - individuals with spinal cord injury
 - catheterized patients

Summary

- Diagnosis of community-acquired, non-catheter-associated UTI is based upon acute symptoms (i.e., dysuria) plus appropriate urine test results (e.g., pyuria, significant bacteriuria, plausible pathogen).
- Asymptomatic bacteriuria is common – much more so than clinical UTI.
- True UTIs are not incidental findings.

Andrew Wyeth

1917-2009



Comments or Questions?

