

Pharmacy 407
Case Studies
Urinary Tract Infections
2011

Learning Objectives

1. *To learn about the pathophysiology of acute cystitis.*
2. *To learn about the appropriate diagnosis of acute cystitis.*
3. *To learn about the appropriate pharmacotherapy of acute cystitis.*
4. *To learn about the appropriate pharmacotherapy of recurrent cystitis.*
5. *To learn about the pathophysiology of acute pyelonephritis.*
6. *To learn about the appropriate diagnosis of acute pyelonephritis.*
7. *To learn about the appropriate pharmacotherapy of acute pyelonephritis.*
8. *To learn about the pathophysiology of prostatitis.*
9. *To learn about the appropriate diagnosis of prostatitis.*
10. *To learn about the appropriate pharmacotherapy of prostatitis.*
11. *To learn about issues in the treatment of asymptomatic bacteruria.*
12. *To become familiar with the literature and guidelines regarding UTIs.*

Recommended Reading

1. Guidelines from the Infectious Diseases Society of America (IDSA) – International Clinical Guidelines for the Treatment of Uncomplicated Acute Bacterial Cystitis and Pyelonephritis in Women: A 2010 Update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases; Clinical Infectious Diseases 2011;52(5):e103-e120 **(These are new guidelines published in 2011, please use these guidelines for the treatment of Uncomplicated UTI and Pyelonephritis)**
2. Uncomplicated Urinary Tract Infections in Adults Including Uncomplicated Pyelonephritis. Lindsay E. Nicolle; Urologic Clinics of North America. Urol Clin N Am 35 (2008) 1-12. 9 (A very nice review of the pathophysiology and treatment of uncomplicated urinary tract infections. Please rely on the new treatment guidelines by IDSA (ref1) for treatment)
3. Society of Obstetrics and Gynecology – Clinical Practice Guidelines – Recurrent Urinary Tract Infections – Journal of Obstetrics and Gynecology, November 2010. Google SOGC Guidelines Recurrent Urinary Tract Infections
3. Pharmacotherapy- A Physiologic Approach : Chapter: Urinary Tract Infections and Prostatitis: Joseph T. DiPiro editor et al. (This reference provides a good overview of prostatitis, for pathophysiology of UTI please rely on the reference 2 by Lindsay Nicolle and for the treatment of Uncomplicated UTI and Pyelonephritis, please rely on reference 1 the new IDSA Guideline for Treatment of Uncomplicated Acute Bacterial Cystitis and Pyelonephritis.
4. Empirical Therapy for Uncomplicated Urinary Tract Infections in an Era of Increasing Antimicrobial Resistance: A Decision Cost Analysis. Thuan P Le and Loren G. Miller. Clinical Infectious Diseases 2001;33:615-21
5. Infectious Diseases Society of America Guidelines for Diagnosis and Treatment of Asymptomatic Bacteruria in Adults. Clinical Infectious Diseases 2005;40:643-54.
6. Bugs & Drugs 2006 Antimicrobial Pocket Reference (Please defer to the new IDSA guideline for uncomplicated UTI and Pyelonephritis)

Other Suggested References

1. Acute Uncomplicated Urinary Tract Infections in Women: Stephen D. Fihn, NEJM 349;3, July 17, 2003
2. Diagnosis and Treatment of Uncomplicated Urinary Tract Infection: Thomas Wooton, Walter E. Stamm; Infectious Diseases Clinics of North America, Vol. 11, No 3, September 1997.
3. C.P.S.

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Summary: 32 y.o. F (55kg) w/ 2 day Gx of urinary freq/urgency/dysuria -- no previous Hx of UTI. Dx is lower UTI (cystitis) based on midstream urine sample collection.

CASE #1

A 32 year old woman 5'3", 55 kg presents in her physicians office with a 2 day history of urinary frequency, urgency and dysuria. She is otherwise healthy and has no previous history of urinary tract infections. On physical examination, her temperature is 37.2°C, pulse 85 BPM, and RR 15/min. She has no signs of flank pain or C.V.A. tenderness. A clean-catch mid-stream urine sample was taken and a working diagnosis of an uncomplicated lower urinary tract infection (cystitis) is made. She has no known allergies.

1. Which are the most likely pathogens in an uncomplicated urinary tract infection?

Enterococcus, enterobacteriaceae --> E. coli (80%), Klebsiella, Proteus mirabilis (pseudomonas and occasionally candida spp) for chronic indwelling catheterization

2. Which antibiotics (dose, route and duration) would be most appropriate for empiric therapy in this patient? What advantages are there with your choice? Are there any other medications that may help?

Alternative: Ofloxacin & ciprofloxacin (A-I) but they have too many s/e's and we want to prevent side effects

DONT USE AMPICILLIN or AMOXICILLIN -- Low efficacy & resistance

Nitrofurantoin 100mg bid x5days -- avoid if early pyelonephritis suspected
 TMP/SMX 160/800 bid x3day --> avoid >20% resistance
 Fosfomycin 3g one dose-- -- low resistance & collateral damage; less efficacious
 pivmecillinam 400 bid x5days -- not avail.

3. If this patient was a male the same age and with the same history would it change any of your choices for treatment?

Not the treatment but may reconsider the diagnosis as it may be pyelonephritis or complicated UTI
 No such thing as uncomplicated UTI in males --> tx as complicated (duration changes to 10-14 days)

4. If the treatment is effective, when should her symptoms resolve?

Within 24-48 hours,... even within 6 hours

6. The results of the urinalysis come back showing 20 WBC/ HPF, 5 RBC/HPF and $>10^8$ bacteria/L. Which of these findings and the findings on physical exam and history are consistent with the diagnosis? How?

Some WBC & RBC as well as a ton of bacteria ($>10^5$) in urine

Pyeurea (WBC in urine) if >10 WBC/HPF Shouldn't have any erythrocytes

7. The results of the culture and sensitivity come back as follows:

E. coli:

Sensitive: Cephazolin, Cefotaxime, Gentamicin, Trimethoprim, Trimethoprim/Sulfamethoxazole, Nitrofurantoin, and Norfloxacin

Resistant: Ampicillin

How does this affect the choice of treatment? Is this unusual? Are culture and sensitivity results required in this case?

Doesn't affect therapy ...not unusual -- although E. coli can be resistant to many more ABx. Culture and sensitivity is required for TMP/SMX to see if $>20\%$ or not

8. What is a leukocyte esterase test and nitrate reduction test and what does a positive test indicate?

--> A leukocyte esterase test is a urine test to detect esterase in the urine and often indicates the presence of WBC in urine --> thus a UTI (as WBCs release esterase). It can also be used to screen for gonorrhea and for amniotic fluid infections

--> A nitrite test complements a leukocyte esterase test and if both are positive, a culture should be done
 A positive nitrite test indicates a gram (-) organism present as they convert endogenous nitrates to nitrites
 The test is performed by adding iron sulfate to an acidified sample (usually with sulfuric acid) and if it turns dark brown, then it is (+)

False negative with staph saprophyticus as they don't convert nitrates

80% of the time it's E. Coli.

Other significant pathogens include Staphylococcus saprophyticus, Klebsiella pneumoniae, and Proteus mirabilis, which each cause approximately 4% of all episodes of acute cystitis. Citrobacter and Enterococci are less likely causes of UTI in women

9. What follow-up is required for this patient?

No need for asymptomatic patients. Otherwise, a follow-up culture and sensitivity testing is recommended.

10. If this woman goes back to see her physician with cystitis again in 3 1/2 weeks what would the appropriate treatment be?

Either extend therapy or switch to fluoroquinolone.????

Offer prophylaxis with nitrofurantoin since she developed > or = 2 infections within 6 weeks

Treated as new infection if after 2 weeks

if relapse --> do culture and sensitivity and see if relapsed (same organism) b/c it is resistant - if sensitive tx longer

11. If this woman has 4 cases of cystitis in the next year what recommendations would be appropriate? What are the risk factors for recurrent infections?

Risk Factors: inc. freq of intercourse, use of spermicide, and new sexual partners, history of UTI
maternal Hx of UTI, --- anatomic & genetic factors present

Offer prophylaxis?

No dose or dosing interval has been investigated and also no comparison with current therapies available

12. Is there any evidence that cranberry juice/ cranberry products will prevent or treat UTIs.

Where would you look for such information? prevent bacteria from adhering to uroepithelial cells

Cochrane review of 10 studies with a total of 1049 subjects showed some evidence that cranberry juice and derivatives may decrease the number of symptomatic UTIs over a period of 12 months, particularly for women with recurrent UTIs. A meta-analysis of the results of 4 RCTs found that cranberry products significantly reduced the incidence of UTIs compared with placebo or control.

13. If this patient had an IgE mediated penicillin allergy in the past, how would it change the management of the case.

Eliminate cefixime,

14. If this patient had an IgE mediated penicillin allergy in the past and a documented serum sickness reaction to sulfonamides, which agents would you choose for treatment of the infection?

Not SMX/TMP or penicillin-related products

Nitrofurantoin, fosfomycin ok

Case #2

R.T. is a 29 year old woman who is 7 months pregnant. She presented to her physician for a routine prenatal examination and the result of the routine urine culture showed $>10^8$ bacteria/L and >10 WBC/HPF. She denied any symptoms of dysuria or flank pain. She has had an uneventful pregnancy and is otherwise healthy. She has no known allergies (NKA).

1. How should this patient with asymptomatic bacteruria be treated and why?

aSx or Sx bacteriuria in prego inc. preterm delivery and low birth weight risk and bacteremia for mother

Treat with cipro or cefixime, TMP/SMX, x3 days? 7 days for some

However because she's in the last 4 months of pregnancy this is not recommended.

2. What follow-up would be appropriate for this patient?

F/U monthly until completion of pregnancy

fever, chills, dizziness, N/V, flank pain, urinary freq & dysuria, CVA tenderness, --> started on TMP/SMX 160/800 IV TID
 Culture: Gm(-) rods CVA pain = costovertebral angle pain

Case # 3

A recent study reports a familial susceptibility to pyelonephritis that may be attributable to low expression of CXCR1, an interleukin (IL)-8 receptor

An 22 year old female, 5'5" and 60 Kg. presents in the emergency department with a fever, chills, nausea, vomiting, dizziness, flank pain, urinary frequency and dysuria. She is otherwise healthy and has no known allergies.

On examination her temperature is 40°C, RR 22/min, BP 110/80, and she has C.V.A. tenderness. She is admitted to hospital and started on TMP/SMX 160/800 mg I.V. t.i.d. Urine samples were sent for culture and sensitivity. A gram stain of the urine showed gram- rods.

90% of the time *E.coli* causes the pyelonephritis b/c of their virulence factor: P pilus and disacch adhesins

Results of the urinalysis show

Usually not hospitalized & tx with oral ABx but if they're hemodynamically unstable, have N/V, then must hospitalize

Protein	+1	
W.B.C.	18 /HPF	(HPF = High power field)
RBC	3-4/HPF	
White cell casts	1-2/HPF	
Bacteria	> 10 ⁸ /L	if >10 ⁴ CFU/mL, then must be infection That equals >10 ⁷ / L

- Which diagnosis would you expect with the findings presented and which findings are consistent with that diagnosis?

Pyelonephritis b/c of CVA pain, flank pain, high fever, N/V (severe cases)

However, all women presenting with pyelonephritis require imaging of genitourinary tract (ultrasound usually)

- What drug related problems do you find with this case?

Really, first line is a FQ with renal excretion, 2nd or 3rd gen cep, amoxi/clav or aminoglycoside with or without ampicillin. TMP/SMX should be BID -- should determine susceptibility of the bacteria first (alternate only)

Eg. gentamicin + ampicillin, ceftriaxone. Alternates: TMP/SMX and 3rd gen cephs

10% cutoff for resistant organisms as opposed to 20% in cystitis

- What are the usual pathogens causing uncomplicated pyelonephritis?

90% of the time, it's *E.coli*, but proteus, klebsiella & enterococcus may cause it

- Which therapeutic alternatives might be appropriate for this patient at this stage? Which choice would you make and why?

Since she's presenting with N/V and pretty much all Sx, I categorize her infection as severe. I would start fluoroquinolone therapy (Cipro IV 400mg BID x14 days or until leukocytosis has resolved)

- By the second day of her hospital stay, her temperature returns to normal and she has no further chills, nausea, vomiting, dysuria or urinary frequency.

Culture and sensitivity results have come back as follows:

E.coli > 10⁸/L

Sensitive: Cephalothin, cefotaxime, gentamicin, trimethoprim/sulfamethoxazole, nitrofurantoin, norfloxacin, ciprofloxacin

Resistant: Ampicillin

At this point, would you recommend any changes in her therapy?

switch to oral cipro 500mg BID or Cipro XL 1000mg QD

If resistance an issue (>10%), then use 14 day cefixime 400mg qd

- How long should therapy continue in this case?

Levofloxacin for 5 days
750mg qd

14 days --> 7 days has been shown to be effective for cipro, but just to be sure

- What kind of follow-up would be required in this case?

F/U only if Sx persist or recur following therapy

- If a relapse was discovered with follow-up testing which treatment would be appropriate?

C&S first --> switch to

side effects with nitrofurantoin, including aplastic anemia, polyneuritis, acute cholestatic and hepatocellular reactions, and pulmonary toxicity.

Case #4

Mrs. S.K. is an 87 year old 5'2", 50 kg lady who lives in her own apartment. She has had problems with recurring urinary tract infections and her physician has ordered nitrofurantoin 50 mg b.i.d. continuously. **shouldn't be continuously but 6-12 months to start**

On questioning, you find that she is in exceptional health for her age and her only other medications include:

Enteric coated ASA 650 mg q.i.d. for arthritic symptoms
Maalox i-ii tbsp prn
Metamucil i package daily.

She has had previous allergies to ampicillin and sulfas.

- 1. What problems do you find with her drug therapy?**
- 2. What therapeutic alternatives might there be for this patient? Which of the alternatives would you chose for this lady.**

Case # 5

Mr. J.D. is a 65 year old gentleman who has had a history of 3 urinary tract infections in the past year which had been treated with Cephalexin each time. He now comes into your pharmacy with a prescription for Cephalexin 250 mg tid x 10 days and tells you that the doctor has now diagnosed his problem to be chronic prostatitis. From his profile, you note that he has been in fairly good health except for the treatment of mild hypertension which has been well controlled with hydrochlorthiazide and propranolol. He has no known allergies.

- 1. What drug related problems do you find in this case?**
- 2. What are therapeutic alternatives for this patient?**
- 3. What changes in drug therapy would you recommend?**
- 4. What follow-up would be appropriate for the pharmacist?**

Case 6

Mrs. G. W. is a 87 year old woman living in a nursing home. She has previously had a stroke but is now quite highly functional. The nurses noted that her urine had quite an odour and asked that urine culture be done. She had no symptoms of dysuria, urgency or frequency. The culture came back as *E.coli* $10^5/L$.

Mrs. G.W. is taking candesartan 4mg/day and aspirin 81 mg/day. She has had rash when taking sulfonamides in the past.

1. What is the most appropriate treatment for her this lady?
2. How long should she be treated?
3. Should she be placed on any long-term prophylaxis?