

# URINARY TRACT INFECTIONS

## CASES AND DISCUSSION

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# LEARNING OBJECTIVES

1. Define an uncomplicated urinary tract infection and a complicated urinary tract infection.
  2. Describe the clinical presentation of a patient with cystitis and the preferred treatment regimens, including antibiotic choices and duration of therapy.
  3. Describe the clinical presentation of a patient with pyelonephritis and the preferred treatment regimens, including antibiotic choices and duration of therapy.
  4. Which groups of patients with asymptomatic bacteriuria warrant treatment?
  5. Describe the clinical presentation of a patient with acute bacterial prostatitis and the preferred treatment regimens, including antibiotic choices and duration of therapy
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# CASE 1

A 22 year old woman is evaluated for one day history of dysuria and urinary urgency and frequency in your office. She had an episode of cystitis 2 years ago. The patient has a sulfa allergy.

On PE : Afebrile, BP 110/60, HR 60 and RR 14. Mild suprapubic tenderness but no flank tenderness. The remainder of the examination is normal.

Urine dipstick analysis shows 3 +leukocyte esterase. A pregnancy test is negative.




# CASE 1

Based on the information present, describe what your diagnosis for the patient is.



TREATMENT WITH WHICH OF THE FOLLOWING ANTIBIOTIC REGIMENS IS APPROPRIATE?

- A) Amoxicillin
  - B) Fosfomycin
  - C) Levofloxacin
  - D) Nitrofurantoin
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# URINARY TRACT INFECTIONS

Uncomplicated UTI: infection in a premenopausal, non-pregnant woman with no urological abnormalities

Complicated UTI: infection and a urinary tract with functional or structural abnormalities (men, pregnancy, foreign body, CKD, immunocompromised, ?recent abx use).



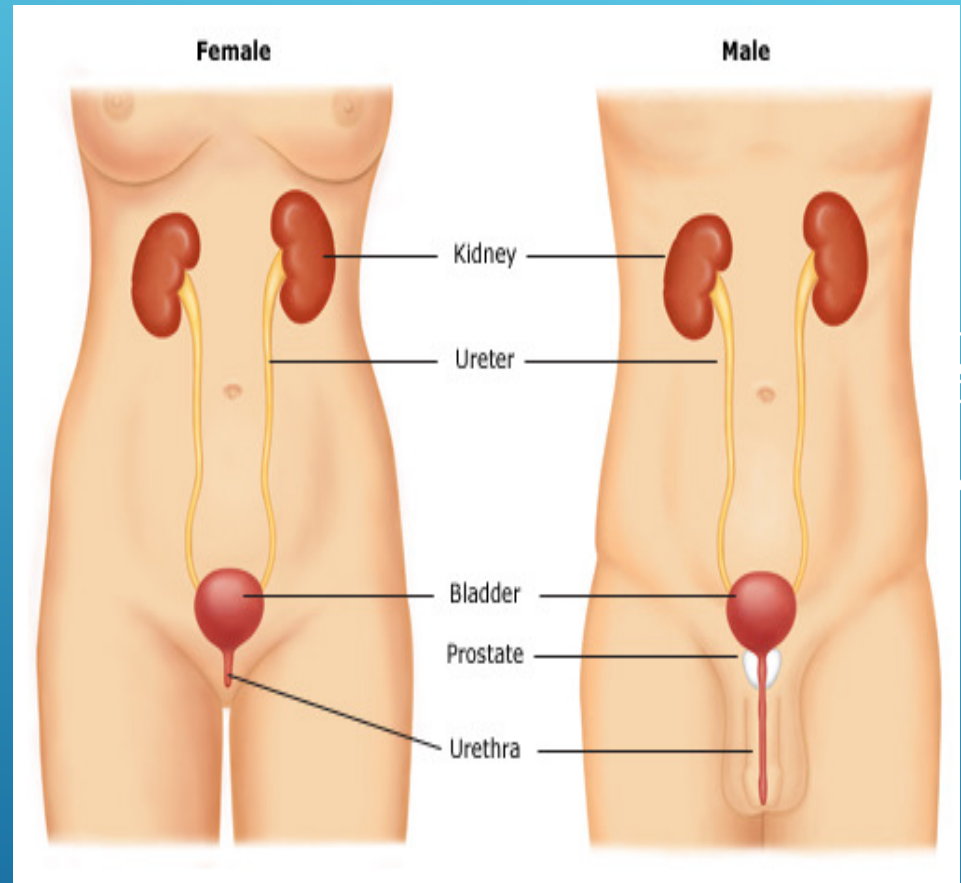
# PATHOGENESIS OF UTI

UTIs are a result of bacterial virulence, host biologic and behavioral factors. They can occur via:

Ascending infection

Hematogenous spread

Lymphatic spread  
(less common)



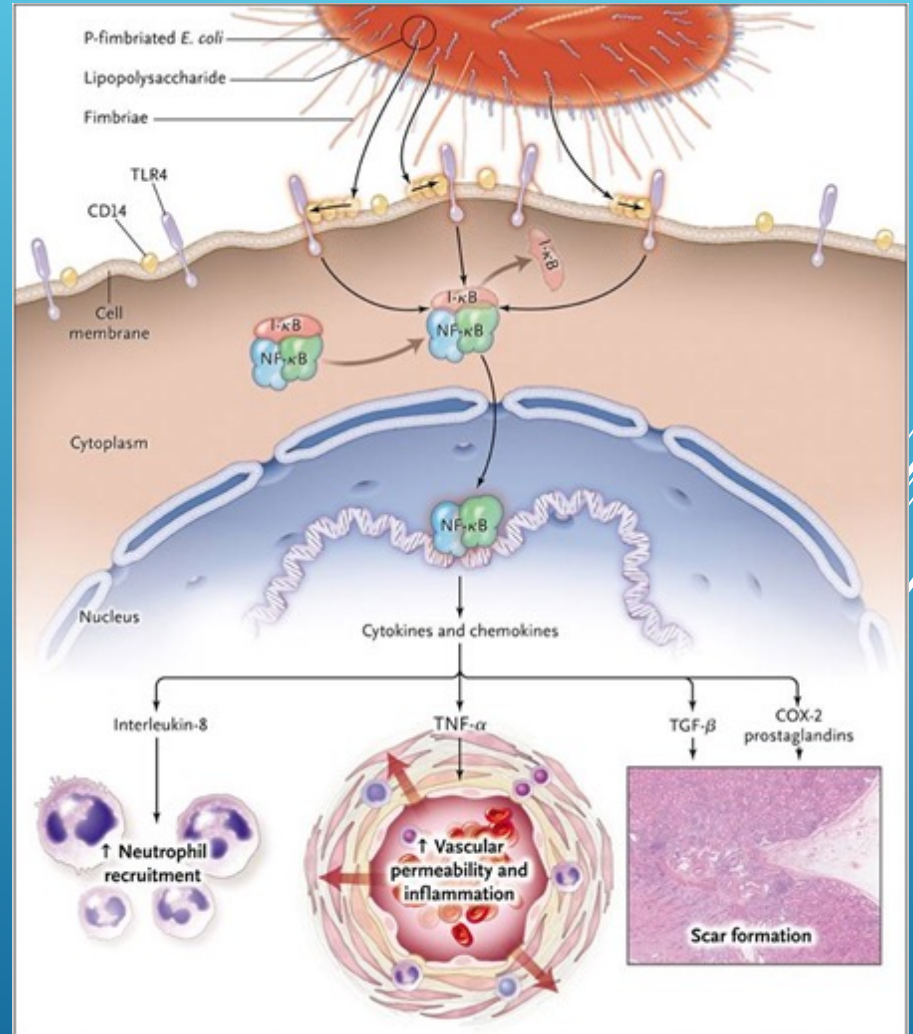
# PATHOGENESIS OF UTI

Uropathogenic *E. coli* (UPEC) cause a high proportion of infections

Isolates causing cystitis and pyelonephritis are genetically distinct

Many strains of UPEC use fimbriae to help bind to the urinary tract

P fimbriae strains frequently adhere, persist, invade kidney and cause bacteremia





# DIAGNOSIS OF UTI

Collection of specimens

Urinalysis microscopic examination

- WBC upper limit 5-10 leukocytes hpf.
- presence of bacteria

Urine dipstick test : rapid screening test

- Leukocyte esterase test (rapid pyuria screen)
  - ▶ Se (detect >10 WBC/mL) 75-96%, Sp 94-98%
- Nitrate->Nitrite test positive in only 25%
  - ▶ Se ~20%, Sp 95%

# DIAGNOSIS OF UTI

Indications for urine culture

Pyelonephritis

Complicated UTI

Recurrent UTI

Patients with multiple allergies

Suspect MDRO



# MICROBIOLOGY OF UTI

*E. coli* 75-90%

*S. saprophyticus* 5-15%

Klebsiella, Proteus, Enterococcus, Pseudomonas  
small percentages

Hospital acquired : Enterobacter, Klebsiella,  
Acinetobacter, Serratia, Citrobacter,  
Providencia, Pseudomonas, Enterococcus

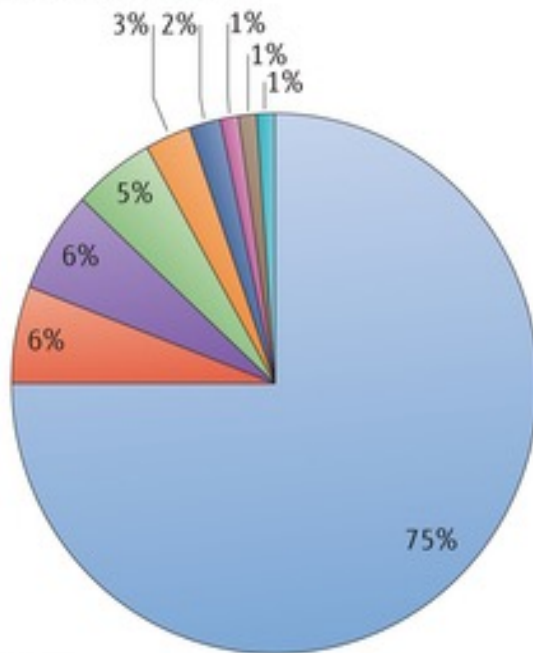
Staphylococcus aureus as a cause from  
hematogenous dissemination

Anaerobes rarely cause UTI

Candida rarely a cause of UTI

# MICROBIOLOGY OF UTI

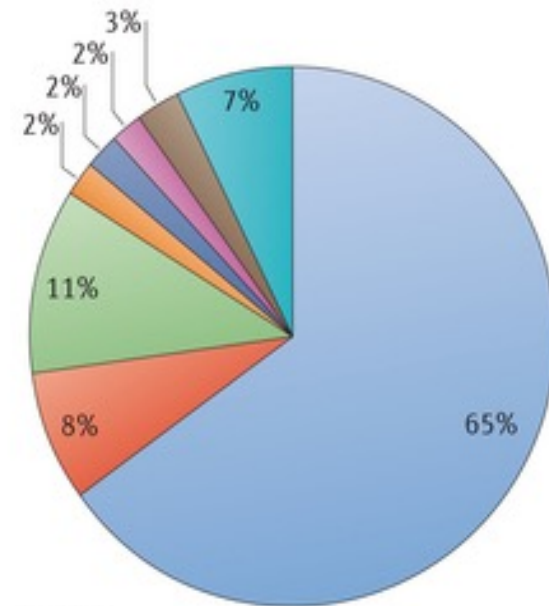
## Uncomplicated UTI



### Risk factors

- Female gender
- Older age
- Younger age

## Complicated UTI



### Risk factors

- Indwelling catheters
- Immunosuppression
- Urinary tract abnormalities
- Antibiotic exposure

Nature Reviews | Microbiology

# CYSTITIS

Bacteria produce irritation of urethral and vesical mucosa, causes frequent and painful urination, cloudy urine


Suprapubic pain/heaviness may be present

Bloody or blood tinged urine possible

Fever is generally absent with cystitis



# WHICH OF THESE IS NOT RECOMMENDED BY THE IDSA FOR TREATMENT OF UNCOMPLICATED CYSTITIS?

- ▶ A) TMP/SXT (Bactrim) x3 days
  - ▶ B) Ciprofloxacin x3 days
  - ▶ C) Fosfomycin x1 dose
  - ▶ D) Nitrofurantoin x5 days
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# CASE 2

A 32 year old woman is evaluated for 2 day history of dysuria, urgency and frequency as well as 1 day history of fever . She has no nausea or vomiting.

PE : Temp 102.3 F, BP 120/70, HR 90/ min, RR 12 /min. R flank tenderness at palpation

A urinalysis shows more than 20 leukocytes /hpf and 4 + bacteria. A pregnancy test is negative.

# CASE 2 – WHICH OF THE FOLLOWING IS MOST APPROPRIATE?

- A) Admit to the hospital and start IV ampicillin
  - B) Check urine culture, prescribe PO ciprofloxacin x5 days
  - C) No urine culture, prescribe nitrofurantoin 100mg PO BID x5 days
  - D) No urine culture, prescribe TMP/SMX DS PO BID x5 days
- 



# PYELONEPHRITIS

Upper tract: pyelonephritis

Fever, sweating

Nausea, vomiting, flank pain, dysuria

Dehydration, hypotension

Vaginal discharge (h/o STD)

Severe cases may lead to papillary necrosis and rapidly progressive renal failure

# PYELONEPHRITIS

Obtain urine culture and susceptibility testing

Oral ciprofloxacin 500 BID x 5-7 days (w or wo initial IV). Resistance < 10%

Oral TMP/SMX (160/800) if uropathogen known to be susceptible x 14 days. If susc not known initial IV (ceftriaxone or broader if needed)

Oral B- lactam less effective. If used initial IV (ceftriaxone) 10-14 days

Imaging?

Only if no improvement >72 hours or clinical suspicion for complication

# CASE 3

A 55 year old woman is evaluated for 4 day history of dysuria, urgency and frequency as well as 1 day history of fever.

PE : Temp 102.1 F, BP 100/65, HR 110/ min, RR 16 /min. R flank tenderness at palpation.

A urinalysis shows more than 20 leukocytes /hpf and 4 + bacteria. CBC shows WBC 14.2K and Cr is 1.51 (baseline 1.07).

She is admitted for IV antibiotics and further care


# CASE 3

The next morning the lab pages you to inform you her blood cultures are positive for gram negative rods. She continues to have fevers of 101F, but overall she is no worse. Her renal function is improving.

On hospital day 3, her fever has resolved, and she is feeling better and would like to go home. The blood cultures grew E coli susceptible to all common antibiotics.

What is your next step?

# CASE 3 – NEXT STEP

- A) Stop the patient's antibiotics and discharge her home to follow up with her PCP
  - B) Order a PICC line and home infusion services for 14 days ceftriaxone
  - C) Change her antibiotics to ciprofloxacin and discharge her home to complete 7 total days of therapy
  - D) Consult ID for one time dose of Dalbavancin prior to discharge
- 

# CASE 3

*Clinical Infectious Diseases*

MAJOR ARTICLE



## Seven Versus 14 Days of Antibiotic Therapy for Uncomplicated Gram-negative Bacteremia: A Noninferiority Randomized Controlled Trial

Dafna Yahav,<sup>1,2</sup> Erica Franceschini,<sup>3</sup> Fidi Koppel,<sup>4</sup> Adi Turjeman,<sup>2,5</sup> Tanya Babich,<sup>2,5</sup> Roni Bitterman,<sup>4</sup> Ami Neuberger,<sup>4,6</sup> Nesrin Ghanem-Zoubi,<sup>4</sup> Antonella Santoro,<sup>3</sup> Noa Eliakim-Raz,<sup>1,2</sup> Barak Pertzov,<sup>5</sup> Tali Steinmetz,<sup>5</sup> Anat Stern,<sup>4</sup> Yaakov Dickstein,<sup>4</sup> Elias Maroun,<sup>4</sup> Hiba Zayyad,<sup>4</sup> Jihad Bishara,<sup>1,2</sup> Danny Alon,<sup>7</sup> Yonatan Edel,<sup>2,8</sup> Elad Goldberg,<sup>9</sup> Claudia Venturelli,<sup>3</sup> Cristina Mussini,<sup>3</sup> Leonard Leibovici,<sup>2,5</sup> Mical Paul,<sup>4,6</sup>; for the Bacteremia Duration Study Group<sup>a</sup>

**Methods.** This was a randomized, multicenter, open-label, noninferiority trial. Inpatients with gram-negative bacteremia, who were afebrile and hemodynamically stable for at least 48 hours, were randomized to receive 7 days (intervention) or 14 days (control) of covering antibiotic therapy. Patients with uncontrolled focus of infection were excluded. The primary outcome at 90 days was a composite of all-cause mortality; relapse, suppurative, or distant complications; and readmission or extended hospitalization (>14 days). The noninferiority margin was set at 10%.

**Results.** We included 604 patients (306 intervention, 298 control) between January 2013 and August 2017 in 3 centers in Israel and Italy. The source of the infection was urinary in 411 of 604 patients (68%); causative pathogens were mainly Enterobacteriaceae (543/604 [90%]). A 7-day difference in the median duration of covering antibiotics was achieved. The primary outcome occurred in 140 of 306 patients (45.8%) in the 7-day group vs 144 of 298 (48.3%) in the 14-day group (risk difference, -2.6% [95% confidence interval, -10.5% to 5.3%]). No significant differences were observed in all other outcomes and adverse events, except for a shorter time to return to baseline functional status in the short-course therapy arm.

**Conclusions.** In patients hospitalized with gram-negative bacteremia achieving clinical stability before day 7, an antibiotic course of 7 days was noninferior to 14 days. Reducing antibiotic treatment for uncomplicated gram-negative bacteremia to 7 days is an important antibiotic stewardship intervention. **Clinical Trials Registration.** NCT01737320.

# ASYMPTOMATIC BACTERURIA

Bacteruria in patients without symptoms of a UTI

Screening/treatment recommended for:

- Pregnant women (at least once)

- Patients who will undergo invasive urologic procedure (TURP, cystoscopy)

Screening NOT recommended for:

- Non pregnant women

- Diabetics

- Older persons in community or institutions

- Spinal cord injury patients

- Catheterized patients



PATIENTS BELOW ARE ASYMPTOMATIC.  
URINE SEDIMENT: 50 WBC, UCX: >100K CFU  
KLEBSIELLA PNEUMONIAE

Which of these patient's should receive antibiotics?

- A) 48F with new diagnosis DM, HbA1c 12, Glu 396
- B) 36M quadriplegic man, chronic foley, cloudy urine at rehab facility
- C) 62M pre-op eval for TURP
- D) A and C
- E) All of the above



# ASYMPTOMATIC BACTERURIA – WHO TO TREAT?

Pregnant women

Patients who are going to undergo  
an invasive urologic procedure  
(NOT FOLEY INSERTION)

Recent renal transplant recipients

That's it. The list. Don't do it if you  
don't see it listed here.




# CASE 4

A 67 year old male with HTH, DM, BPH presents to your office with complaint of increased urinary frequency, dysuria, low grade fevers ongoing for 2 weeks. He tried drinking cranberry juice but it did not help. His urine culture grows E coli (which he has grown two other times in the past 6 months) Based on this information, you recommend the following treatment:

- A) Ciprofloxacin 500mg PO BID x4 weeks
- B) Ciprofloxacin 500m PO BID x5-7 days
- C) Doxycycline 100mg PO BID x4 weeks
- D) Admission to the hospital for IV antibiotic therapy

# RECURRENT UTI

- 2 or > episodes 6M or 3 or > in a year.  
Non pregnant adult women
  - ▶ Relapse: If current infection is caused by same pathogen as the initial UTI and occurs within 2 weeks
  - ▶ Re infection: If current infection is caused by a different strain than initial UTI of Urine culture was sterile
- 

# RECURRENT UTI: RISK FACTORS

AGE	FEMALE	MALE
All ages	Previous <b>UTI</b>	Lack of circumcision (children and young adults)
	Urologic instrumentation or surgery	Urologic instrumentation or surgery
	Urethral catheterization	Urethral catheterization
	Urinary tract obstruction, including calculi	Urinary tract obstruction, including calculi
	Neurogenic bladder	Neurogenic bladder
	Renal transplantation	Renal transplantation
	Adults	<b>UTIs</b> in female relatives
Sexual intercourse		Vaginal <i>Escherichia coli</i> colonization in partner
New sex partner		
Lack of urination after intercourse		
Spermicidal contraceptive jellies		
Diaphragm use		
Pregnancy		
Lower socioeconomic group		
Diabetes		
Possibly sickle cell trait in pregnancy		
Older age	Functional or mental impairment	Functional or mental impairment
	Estrogen deficiency (loss of vaginal lactobacilli)	Prostatic enlargement Condom catheter drainage

Mandell: Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, 8<sup>th</sup> ed.; Chapter 74: Urinary Tract Infections p886-913.

# PREVENTIVE MEASURES

## Recurrent cystitis

Provide patient education regarding natural course of recurrent UTI  
Assess potential modifiable risk factors and family history  
Discuss patient preference regarding antimicrobial management  
Discuss non-antimicrobial measures

### Acute management

Obtain urine culture if no previous culture

Start empiric oral therapy

Trimethoprim (in UK) 200 mg twice daily  
(or TMP-SMX DS in USA) for 3 days

Nitrofurantoin 100 mg twice daily for  
5 days

Fosfomycin 3 g, single dose (not  
available in UK)

Alternative regimens

Ciprofloxacin 250 mg twice daily for 3 days  
β lactam (cefepodoxime, cefuroxime;  
dose varies by regimen) for 5 days

The choice between these agents should  
be individualized and based on patient  
history (microbiology, tolerance, previous  
response)

Alternative agents should be reserved for  
cases when a preferred agent cannot be  
used – for example, in patients with in vitro  
resistance, allergy, or lack of response

### Prophylaxis

Antimicrobial prophylaxis

Trimethoprim (in UK) 100 mg at bedtime  
TMP-SMX SS (in USA) at bedtime, three  
times a week, or postcoitally

Nitrofurantoin 50-100 mg at bedtime or  
postcoitally

Cephalexin 250 mg at bedtime or  
postcoitally

Cefaclor 250 mg at bedtime

The choice of agent and dosing regimen  
(daily, three times a week, postcoitally)  
should be individualized and based on  
patient history (previous microbiology;  
timing of UTI to coitus; ease of daily  
versus intermittent dosing)

### Expectant management

Consider patient initiated therapy

Trimethoprim (in UK) 200 mg twice daily  
(or TMP-SMX DS in USA) for 3 days

Nitrofurantoin 100 mg twice daily for  
5 days

Other previously successful regimen

# DIAGNOSIS OF CA-UTI

In patients with indwelling urethral, indwelling supra pubic or intermittent catheterization

Presence of symptoms or signs cw UTI with no other identified source of infection along with  $10^3$  CFU/ml of  $\geq 1$  bacterial species in a single urine specimen.

3-10% develop bacteruria each day, related to catheter duration

# DIAGNOSIS OF CA-UTI

Signs and symptoms cw UTI include: new onset of worsening fever, rigors, altered mental status, malaise, or lethargy with no other identified cause, flank pain; CVA tenderness; acute hematuria; pelvic discomfort

When catheter removed: dysuria, urgent or frequent urination, supra pubic pain or tenderness

# DIAGNOSIS OF CA-UTI

A urine culture should be obtained prior to initiating antimicrobial treatment

If an indwelling catheter has been in place for  $> 2$  weeks at the onset of CA-UTI and is still indicated, the catheter should be replaced and a urine sample sent from freshly placed catheter

If catheter can be discontinued, a culture of voided midstream urine specimen should be obtained



# CANDIDA UTI

Candidemia rarely results from asymptomatic candiduria

Patients who have symptoms of UTI should be treated . Oral fluconazole .

Candiduria + indwelling catheter ,remove catheter. If not possible -> repeat UA

Treatment of asymptomatic candiduria:

- Very low birth weight infants
- Patients undergoing urologic procedures
- Neutropenic patients

# RECOMMENDED READING

Clinical Practice Guidelines CID 2011:52 e 103-120

Urinary Catheter Guidelines CID 2010:50 625-663

Infect Dis Clin N Am 28 (2014) 1-159

Uncomplicated Urinary Tract Infection N Engl J  
Med 366;11

Approach to a Patient with Urosepsis J Glob Infect  
Dis 2009 Jan-Jun; 1 (1): 57-63

Mandell: Mandell, Douglas, and Bennett's  
Principles and Practice of Infectious Diseases, 8<sup>th</sup>  
ed.; Chapter 74: *Urinary Tract Infections* p886-913.