UTI: A practical approach

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Clinical Scenario # 1

- A 22-yo woman evaluated for one day history of dysuria and urinary urgency and frequency. 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 N.
- Urine dipstick analysis shows 3 +leukocyte esterase. A pregnancy test is negative.

Treatment with which of the following options is most appropriate?

A) AmoxicillinB) Fosfomycinc) Levofloxacind) Nitrofurantoin

Clinical scenario # 2

- A 32 yo woman is evaluated for 2 day history of dysuria and urinary urgency and frequency and a 1 day history of fever . She has no nausea or vomiting.
- PE : Temp 38.5 C (101.3 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.

In addition to obtaining a urine culture, which of the following is the most appropriate empiric treatment?

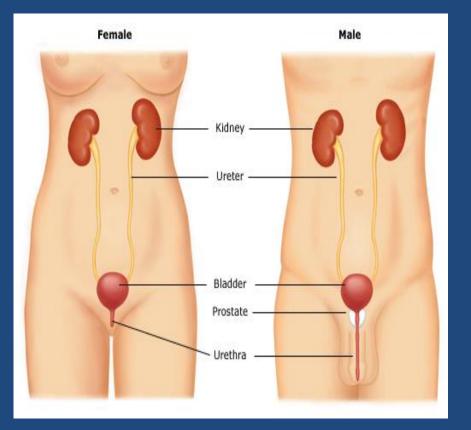
A) AmpicillinB) CiprofloxacinC) NitrofurantoinD) TMP/SMX

Urinary Tract Infections Outline

- Definition
- Diagnosis
- Microbiology
- UTI (syndromes)
- Treatment

Urinary tract infection

- Uncomplicated UTI: infection in a premenopausal , non pregnant women with no urological abnormalities
- Complicated UTI: infection and a urinary tract with functional or structural abnormalities.



UTI : Clinical symptoms and presentation in adult

- Lower tract : cystitis
- Dysuria urinary urgency and frequency lateral fullness discomfort.
 - hemorrhagic cystitis bloody urine (10%)
- Upper tract: pyelonephritis
 -Fever, sweating
 -Nausea, vomiting, flank pain, dysuria
 Dehydration, hypotension
- Vaginal discharge (ho STD)

Diagnosis of UTI

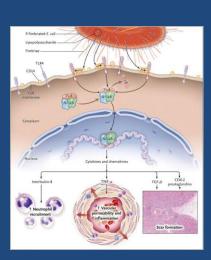
- Collection of specimens
- Urinalysis microscopic examination
 - WBC upper limit 5-10 leukocytes hpf.
 - presence of bacteria
- Urine dipstick test : rapid screening test
 -Leukocyte esterase test (rapid pyuria screen)
 Se (detect >10 WBC/mL) 75-96%, Sp 94-98%
 -Nitrate->Nitrite test positive in only 25%
 Se ~20%, Sp 95%

Diagnosis of UTI

- Indications for urine culture
 - -Pyelonephritis
 - complicated UTI
 - Recurrent UTI
 - Patients with multiple allergies
 - -Suspect MDRO

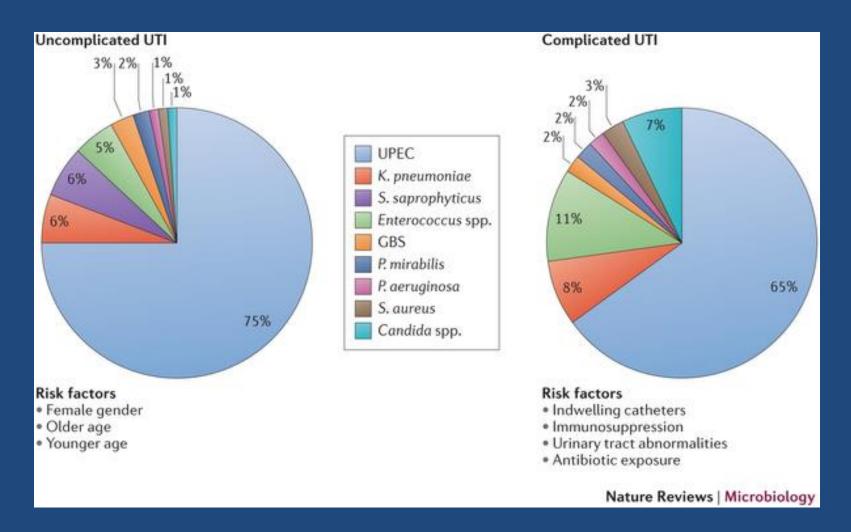
Microbiology of UTI

- E. coli 75-90%
- S. saprophyticus 5-15%
- Klebsiella, Proteus, Enterococcus, Pseudomonas small percentages



- Hospital acquired : Enterobacter, Klebsiella, Acinetobacter, Serratia, Citrobacter, Providencia, Pseudomonas, Enterococcus
- Anaerobes rarely cause UTI
- Candida increasingly recognized as a cause of UTI

Microbiology of UTI



Nature Reviews Microbiology 13, 269-284 (2015)

Urinary Tract Infections

- Acute uncomplicated cystitis
- Acute uncomplicated pyelonephritis
- Recurrent UTI
- Complicated UTI- sepsis
- CA UTI
- Candida UTI

Treatment of UTIs

- Acute uncomplicated cystitis
- Acute uncomplicated pyelonephritis

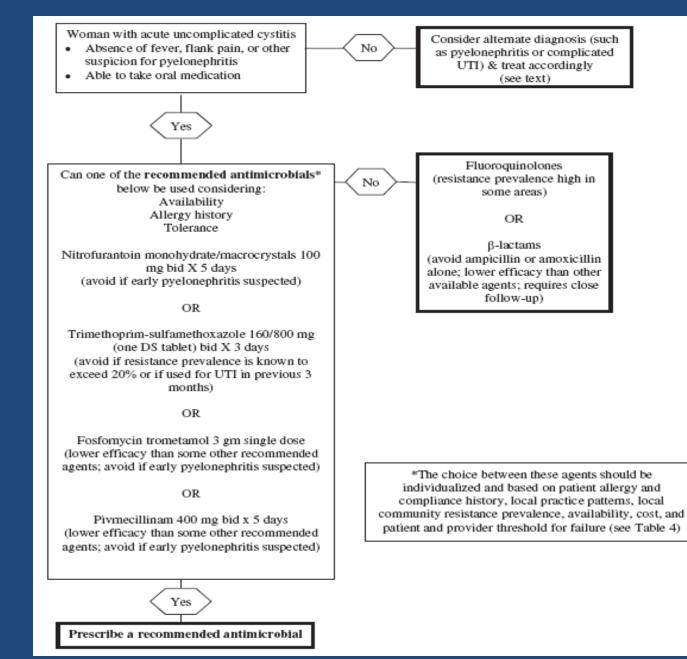
Clinical Practice Guidelines CID 2011;52 (1 March)

Treatment of UTIs

For AUC and AUP consider :

- Antimicrobial resistance
- Collateral damage
- -Cephalosporins linked to subsequent infections VRE, ESBL Klebsiella, Beta lacatamse R acinetobacter, C Dif
- -Fluoroquinolones linked to infection with MRSA and FQ R in GN

Clinical Practice Guidelines CID 2011;52 (1 March)



Clinical Practice Guidelines CID 2011:52 e103-e120

Acute uncomplicated pyelonephritis

- Urine culture and susceptibility testing
- Oral ciprofloxacin 500 BID x 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 AG)
- Oral B- lactam less effective. If used initial IV (ceftriaxone or AG) 10-14 days

CDC Warning on FQ Antibiotic use: Rolling Back Use for Patient Safety

- 1. FDA recommendations state that risks of serious side effects with fluoroquinolones generally outweigh benefits for patients with the following:
 - a. Acute bacterial sinusitis
 - b. Acute exacerbation of chronic bronchitis
 - c. Uncomplicated UTI
- 2. The FDA has determined that fluoroquinolones should be reserved for the previous three conditions only when there are no alternative treatment options.
- 3. Fluoroquinolones may be considered in the following scenarios:
 - a. Patient with type 1 hypersensitivity reaction to both penicillin and cephalosporins
 - b. Definitive therapy for multidrug resistant organism in which the isolate is resistant to all beta-lactams and susceptible to fluoroquinolone.
 - c. For bacteremia stepdown therapy in which organism is susceptible
 - d. For serious bacterial infections (i.e. anthrax & plague) where the benefits of fluoroquinolones outweigh the risk.

Fluoroquinolone Boxed Warning							
July 2008	 increased risk of tendinitis and tendon rupture 						
February 2011	 increased risk of exacerbating muscle weakness related to Myasthenia gravis 						
August 2013	 increased potential risk for irreversible peripheral neuropathy 						
July 2016	 increased CNS effects ((i.e. anxiety, depression, hallucinations, suicidal thoughts, confusion) 						
July 2018 (new labeling	 new mental health side effects updated to include ddisturbances in attention, disorientation, agitation, nervousness, memory impairment and delirium 						
change)	 serious blood sugar disturbances, particularly risk of coma with hyopglycemia 						

Recurrent UTIs

- 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

- Spermicidal products
- Sexually active
- Genetic factors
- Variations in innate immune system low CXCR1 and CxCR2 expression)

BMJ 2013;346:f3140

Preventive measures

- Antimicrobial prophylaxis
- Patient centered approach

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 fo-5 days Fosfomycin 3 g, single dose (not available in UK)

Alternative regimens

Clprofloxacin 250 mg twice daily for 3 days β lactam (cefpodoxime, 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

BMJ 2013;346:f3140

Non antimicrobial strategies

- Lactobacillus : L crispatus intravaginal suppositories, oral capsules with L rhamnosus GR-1 and L reuteri RC- 14
- Estrogens
- Cranberries
- Urination before and after sexual activity
- Diet (alcalinizing agents and siderocalin)

Infect Dis Clin N Am 28 (2014) 135-147 CID 2013 : 57 719-24 Shields-Cutter RR et al. Human urinary composition controls antibacterial activity of siderocalin J Biol Chem 2015;290(26):15949-15960

Drug induced UTI's

- Recent reports of drug induced UTI's related to sodium-glucose coransporter 2 (SGLT2) inhibitors "flozins"
- Oral hypoglycemics that work by increasing the amount of glucose spilled in the urine
- Include canagliflozin (Invokana), empagliflozin (jardiance) and dapagliflozin (Farxiga)

www.fda.gov/Drugs/DrugSafety/ucm47 5463.htm

Complicated UTIs

Initial evaluation:

- Detailed history- Previous UTI, prior ATB use
- Physical exam Sepsis ?
- UA and Urine culture
- Imaging
- <u>If obstruction</u>
- Prompt urologic evaluation

Complicated UTIs

- Diabetes Mellitus
- Acute pyelonephritis
- Emphysematous pyelonephritis
- Renal abscess
- Renal papillary necrosis
- UTI in renal transplant recipients
- Nephrolithiasis
- Prostatitis

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 ≥ 1 bacterial species in a single urine specimen.

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

CID 2010:50 (1 March) 625-63

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

CID 2010:50 (1 March) 625-63

Banner Clinical Practice

- Discuss with patient indication and risk of placing an indwelling urinary catheter and document in chart.
- Select an indication for the catheter when ordering.
 - Urinary retention or obstruction
 - U.O. monitoring in critically ill, incontinent, uncooperative
 - Peri-operatively for selected surgical procedures
 - Fluid challenge in patients with ARF
 - Urinary incontinence posing risk to patient
 - Prolonged immobilization
 - Palliative care in terminally ill
- Continuing the catheter requires daily renewal order.
 - Nursing will contact you on daily basis for indication and order
 - Exceptions include certain urologic/gyn/perineal procedures

CA UTIs

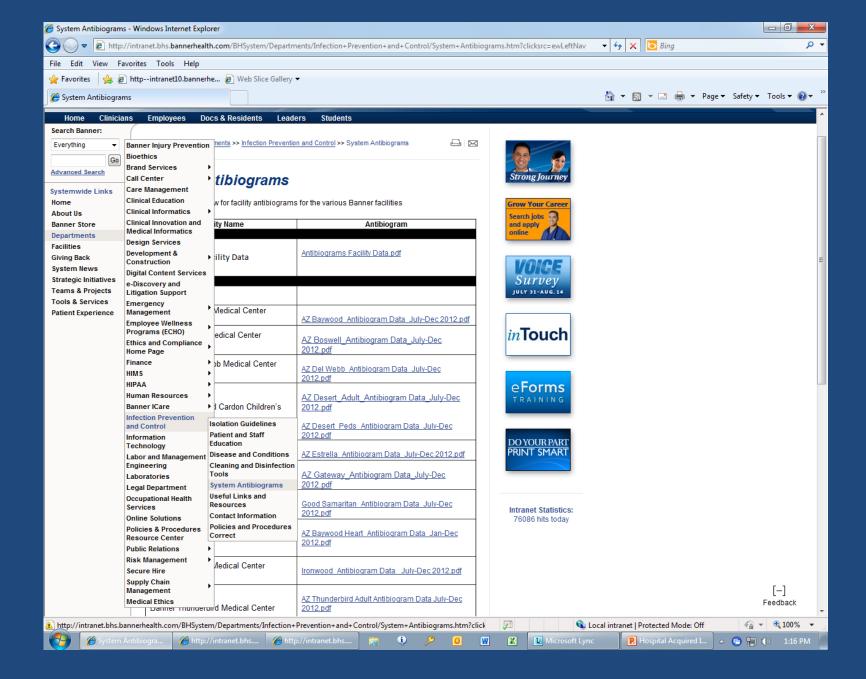
- Cefepime 2 gm IV q 12h, Pip/tazo 3.375 gr q 6h or IMP 500 mg q 6h
- Discontinue or exchange catheter
- Duration 5-14 days
- Shorter duration in uncomplicated UTI 3d
- Do not use moxifloxacin

Zosyn extended infusion

- Zosyn 4.5 gm IV q 6h will be automatically replaced 3.375 GM IV extended infusion (4hs) q 8h. MIC <16
- ER 30 min infusion will continue

CID 2013; 56(2): 272-282 J Pharm Pract.2011 Dec ;24(6):571-6 J Expert Opin Drug Metab Toxicol.2010 Aug; 6(8): 1017-31

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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

Treatment Guideline for Candidiasis CID 2009 503-537 Fungal UTI Infect Dis Clin N Am 28 (2014) 61-74

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
- In the Clinic. Urinary Tract Infection. Ann Intern Med 2017; 167: ITC 49-63