UTI: A practical approach

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UTI Pathophysiology

- Uropathogens colonize urethra, vagina or perineal area -> Enter lower urinary tract ->bladder ->kidney
- How does urine stay sterile?
 - pH (acidity), epithelial secretions
 - Normal free flowing urine from kidney through meatus
 - Male prostatic secretions

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) Amoxicillin
B) Fosfomycin
C) Levofloxacin
D) 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) Ampicillin
B) Ciprofloxacin
C) Nitrofurantoin
D) 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 (h/o 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
- Asymptomatic bacteruria

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

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 Diff
- -Fluoroquinolones linked to infection with MRSA and FQ R in GN (Pseudomonas)

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
- Imaging?

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

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:**f**3140

Non antimicrobial strategies

- Lactobacillus : L crispatus intravaginal suppositories, oral capsules with L rhamnosus GR-1 and L reuteri RC- 14
- Estrogens (post-menopausal)
- 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 If obstruction
- 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.
- 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

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

CID 2010:50 (1 March) 625-63

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



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

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

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