Urinary Tract Infection

epidemiological problem

most common form of bacterial infections affecting humans

- 50% of women (at least one episode)
- men at both life extremities
- patients with structural abnormalities of the urinary tract
- kidney transplant recipients

with potential serious long-term consequences

- 10 - 15% of secondary hypertension
- cause of ESRD in 10 - 15% of patients

Definitions

Microbiology

pathogenic organisms present in the urine samples from urethra, bladder, kidneys

Clinics

acute infection subdivided into two categories

lower UTI: urethiritis, cystitis

upper UTI: pyelonephritis

chronic - pyelonephritis - interstitial nephritis resulting from bacterial infection of the kidney - at this stage it is exclusively difficult to identify the causative pathogen

Clinical symptoms

- **dysuria, frequency, urgency, suprapubic pain with cloudy, malodorous or bloody urine**

  likely to have cystitis, urethritis

- **rapidly developing shaking chills, fever above 103^0 F (38^0 C), nausea, vomiting, diarrhoea**
- **tachycardia, muscle tenderness, tenderness of costovertebral areas and abdominal at deep palpation**

  likely to have acute pyelonephritis

BUT:

- **10-20%of pts with symptoms of cystitis, upper urinary tract is also involved**
- **pts with bacteriuria and urinary tract involvement may be asymptomatic**

UTI – route of invasion

98% - ascending

Reservoir of pathogens – GI
Colonisation of urethra and periurethral tissue, vaginal vestibule
Introduction of pathogen into the bladder:
intercourse
instrumentation on urinary tract
Pathogen virulence
Ineffective protection
Predisposing factors

2% - hematogenous

Certain strains of bacteria has potential to cause kidney infection even in case of low level of invading microorganisms
Predisposing factors

UTI – Predisposing Factors

Physiological: pregnancy, advanced age

Pathological

- Urinary tract obstruction: prostatism
  neurogenic bladder
  bladder diverticuli
- Vesicoureteral reflux
- Foreign bodies in urinary tract
  - indwelling Foley catheter
  - any urologic intervention
  - calculi
- Metabolic: diabetes mellitus, gout, potasium depletion
- Vascular constriction
- Other: any chronic kidney disease
  analgesics exposure

UTI – etiologic agents

Outpatient UTI:

- 70 - 90% E. coli
- St. saprofiticus (sexually active women)
- E. fecalis (elderly men, prostatism)
- Proteus sp (boys 1-12 yrs)
- Pseudomonas sp

Inpatient UTI:

- 50% E. coli
- Serratia sp
- Pseudomonas sp
- Proteus
- Klebsiella
- St. aureus
- fungi– Candida Cryptococcus Aspergillus

Pathogen virulence

- **ability to adhere to uroepithelium**
  - **type 1 (common) fimbrie**
  - **type 2 - P (mannose -resistant) fimbrie**
  - **other non-fimbrial adhesins**
- **ability to initiate inflammatory response**
  - **endotoxin**
  - **P fimbrie**
  - **acute symptoms intensity, chronic pyelonephritis**
- **aerobactrin presence** (bacteria iron uptake)
- **haemolysin activity** (haemolysis, iron release)
- **urease activity**

Protective mechanisms

- **urethra lenght**
- **ureter peristaltics**
- **competency of vesicoureteral valve**
- **low pH, extreme osmolalities, organic acids, urea in urine**
- **bactericidal activity of prostatic secretion**
- **Mechanisms preventing pathogen adherence to urinary tract mucose:**
  - ***elimination by voiding***
  - ***normal flora of vaginal vestibule and distal urethra***
  - ***GAG on the surface of bladder mucose***
  - ***Tamm-Horsfall protein***
  - ***antibodies present in urine***

- **uncomplicated UTI– infection in individual with no local or systemic predisposing factor**
- **complicated UTI– infection in individual with local or systemic predisposition**
- **relapse – in urine culture taken < 21 days after symptoms resolution other then original pathogen is present**
  ***or* in urine culture taken > 21 days after original pathogen elimination same or other pathogen is present**
- **recurrent UTI - at least 3 episodes per year**

UTI - clinical presentation

possible interrelation between infection and clinical symptoms

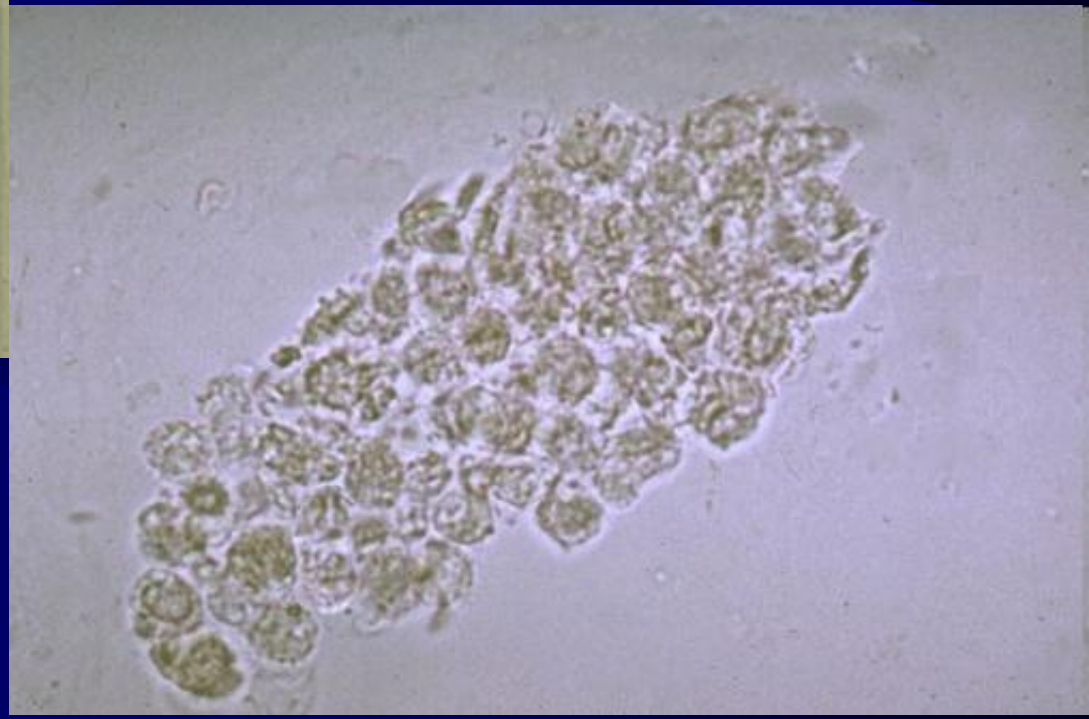
- **Infection without inflammation = asymptomatic bacteriuria**
- **Infection with local symptoms - *lower UTI***
- **Infection with local and systemic symptoms - *nearly always upper UTI***

Laboratory evaluation

urinalysis

- pyuria defined as 5-10 leukocytes / HPF

  shows poor correlation with significant bacteriuria
- pyuria (>10 leukocytes per ml of midstream urine)
- esterase positive test (dipstic test for leukocytes presence)
- erytrocyturia (>2 per HPF) - occasionally, hemorrhagic cystitis
- low-grade proteinuria - may be present in the acute infection
- white cell casts - strong evidence of pyelonephritis
- positive nitrate test (screening test for bacteria presence)



Laboratory evaluation 2

Urine culture

- **mid-stream, clean-catch specimen**
- **after collection the specimen should be processed expeditiously**
- **room temperature storage increases bacterial colony counts**
- **+4 ^{0} C for 24 hours - bacteria count remains stable**

interpretation of culture depends on clinical presentation

- **in patients with dysuria syndrome bacterial titre 10^3 is regarded significant**
- **in patients with pyelonephritis symptoms bacterial colony count 10^4 - 10^5 is regarded significant**
- **asymptomatic bacteriuria – bacteria titer $\geq 10^5$ in individual with no clinical or laboratory symptoms of UTI**

Pyuria and negative urine culture

Infection with pathogens not growing on standard media

- **mycobacterium**
- ***Chlamydia***
- ***Mycoplasma***
- ***anaerobic bacteria***
- **fungi**
- **viruses**
- **parasites**

Non-infectious kidney pathologies

- **non-infectious interstitial nephritis**
- **acute, subacute glomerulonephritis**
- **secondary glomerulonephritis**
- **resolution phase of aute non-inflamatory renal failure**

non-renal

- **extreme exercise**
- **fever**
- **dehydratation**
- **inflammation of neighbouring organs (*colitis, adnexitis, vulvovaginitis)***

When to start diagnostic procedure

- Laboratory diagnostics
- Urinary tract visualisation
  - first episode of UTI
    - in children < 5 years
    - in men
  - in women with relapsing UTI

Treatment recomendations

General principles:

superficial mucose infection:

- effective antibiotic concentration in the urine
- blood concentration unimportant

deep-tissue infection (kidney, prostate)

- effective drug concentration at the site of infection mandatory
- effective serum concentrations advantegaous

Approach to the women with dysuria or frequency

Short-term therapy

asymptomatic

no further intervention

symptomatic

urinalysis, urine culture

both negative

follow up

pyuria

no bacteriuria

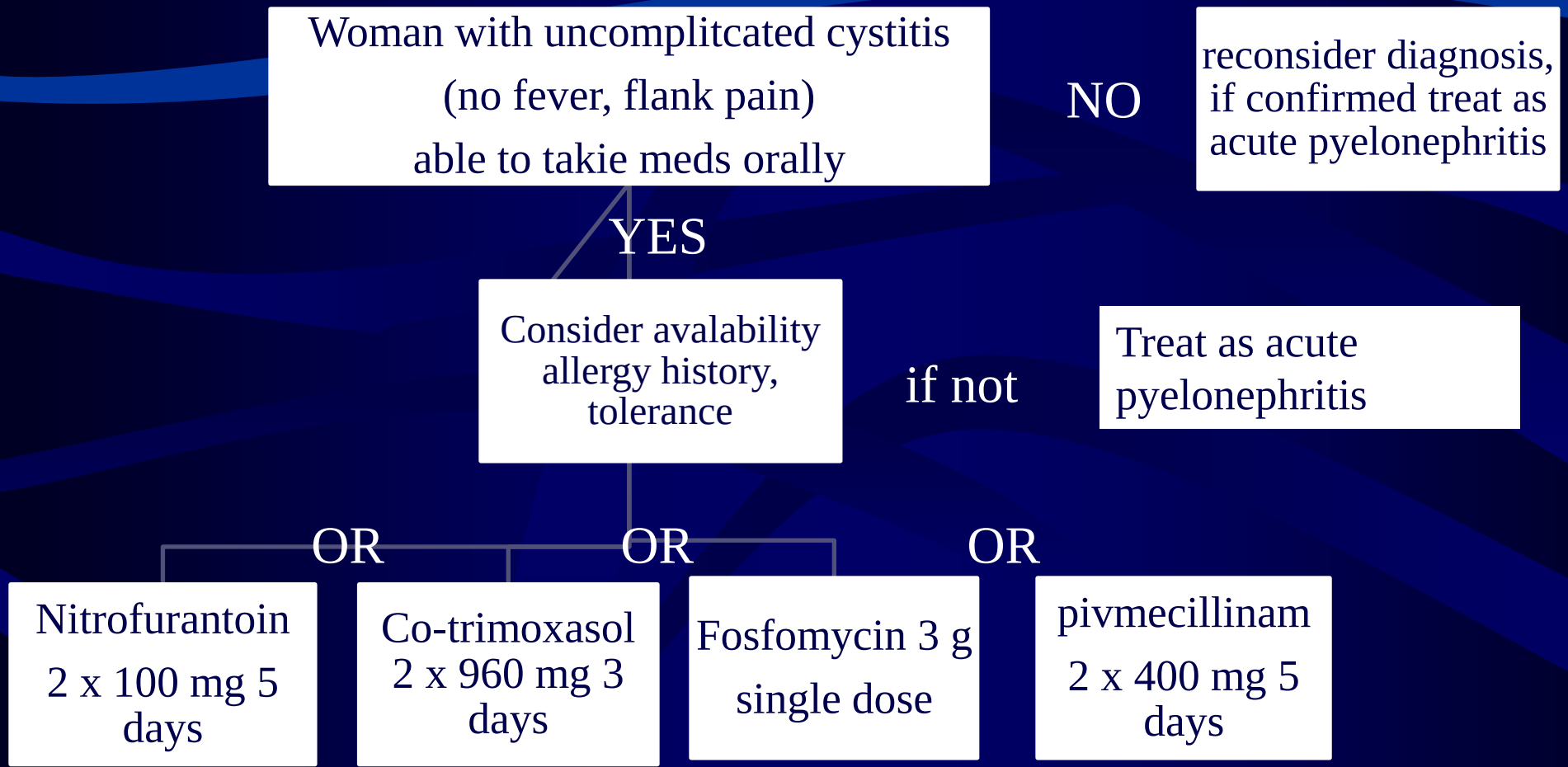
treatment for chlamydia

with/out pyuria

bacteriuria

extended treatment

Chosing an optimal antimicrobial agent for empirical treatment of acute uncomplicated cystitis



Gupta K et al. Clin Infect Dis. 2011;52:e103-e120

UTI treatment

- **Uncomplicated in young women – outpatient**
  - **lower UTI 3-5 days**
  - **acute pyelonephritis, first treatment 14-21 days**
  - **serious cases, GI symptoms, excesive fluid loss - hospitalise**

Complicated UTI - always obtain urine culture

- **treated by nephrologist**
- **eliminate predisposing factors**
- **control coexisting systemic disease**

UTI treatment

Out -patient treatment

co-trimoxazole, trimetoprime
Fluorochinolones: cipro, norfloxacin
nitrofurantoine , furazidin - only lower UTI
fosfomycin
cephalosporines I, II gen
amoxycyllin - only first episode and lower UTI

Pyelonephritis with GI symptoms - in-patient treatment

cephalosporins II, III
amoxicilllin +clavulenic acid
ampicyllin+sulbactam
fluorochinolones
aminoglicosydes - monitor kidney function
karbapenem, astreonam

Symptomatic treatment

fluids, electrolytes, antiemetics ect.

Prophylaxis

- **Non pharmacological**
  - **– fluid intake 2 – 3 l daily**
  - **– frequent mictuition (after intercourse)**
  - **- personal hygiene**
  - **- constipation prophylaxis**
  - **- bubble bath avoidance**

- **Chemoprophylactics**
  - **continuous (single nightly dose)**
  - **after intercourse, at symptoms appearance**

Asymptomatic bacteriuria

who needs treatment

- **pregnancy**

  asymptomatic bacteriuria in I trimester means

  - **50% risk of symptomatic UTI**
  - **25% risk of acute pyelonephritis**
  - **increased risk of eclampsia, anaemia, hypertension, decreased GFR**
  - **increased risk of low birth weight and other complications**

- **before any instrumentation on urinary tract**
- **kidney allograft recipients**
- **diabetics (?), erderly (?)**

UTI in elderly

- do not treat asymptomatic bacteriuria
- non-specific symptoms: anorexia, faintness , fatigue general condition deterioration
- increased risk of side-effects of antibiotics – lower GFR!