

He who studies medicine without books sails an uncharted sea, but he who studies medicine without patients does not go to sea at all"
William Osler

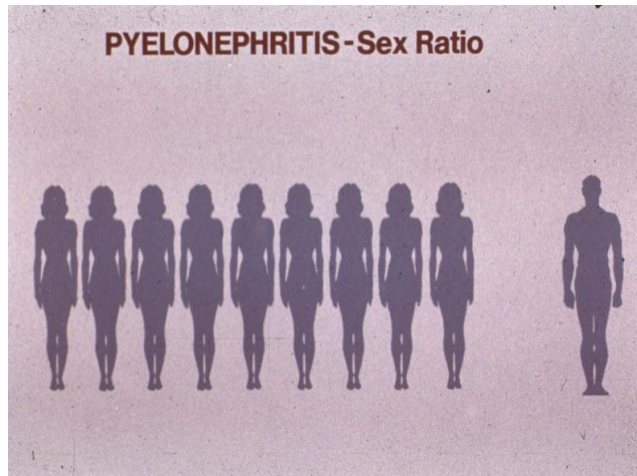
Medicine

430

Urinary Tract Infections

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URINARY TRACT INFECTIONS



Pyelonephritis is much more common on females than in men

Epidemiology of UTI

Most UTIs are lower tract infections; upper tract infections are less common

Worldwide, 150 million cases / year

- 90 % cystitis (bladder infection)
- 10 % pyelonephritis

From all cases:

- 75 % of all cases are sporadic
- 25 % are recurrent
- 2 % get complicated

Prevalence of Urinary Tract Infections (Uti)

- almost half of all **women** will have at least one UTI in their lives.
- the risk of UTI in women increases after menopause
- after a UTI: 20 - 40 % will have a recurrence
- Recurring infections are usually reinfections.
- asymptomatic bacteriuria in women ↑with age & occurs in
 - 2.7% of 15 - 24 year olds
 - 9.3% of over 65 year olds
 - 20 - 50% of over 80 year olds
- UTI are **rare** in young and middle-aged **men**
- But when they do occur it is often with catheterisation or urological procedures.
- Urinary **catheter** increases the risk almost ten-fold in hospitalised patients and those in other care homes.
- Pyelonephritis is common in patients who **have been catheterised for over a month.**

- **Bacteriuria in elderly men** occurs in
 - 10% of those living at home,
 - 20% of those living in nursing homes
 - 30% of those who are in hospitals

Gender and Sexual Contact

Infant and children Male >> female

Adolescent-menopause Female >> male

Older age: Female = male (more than 60 years)

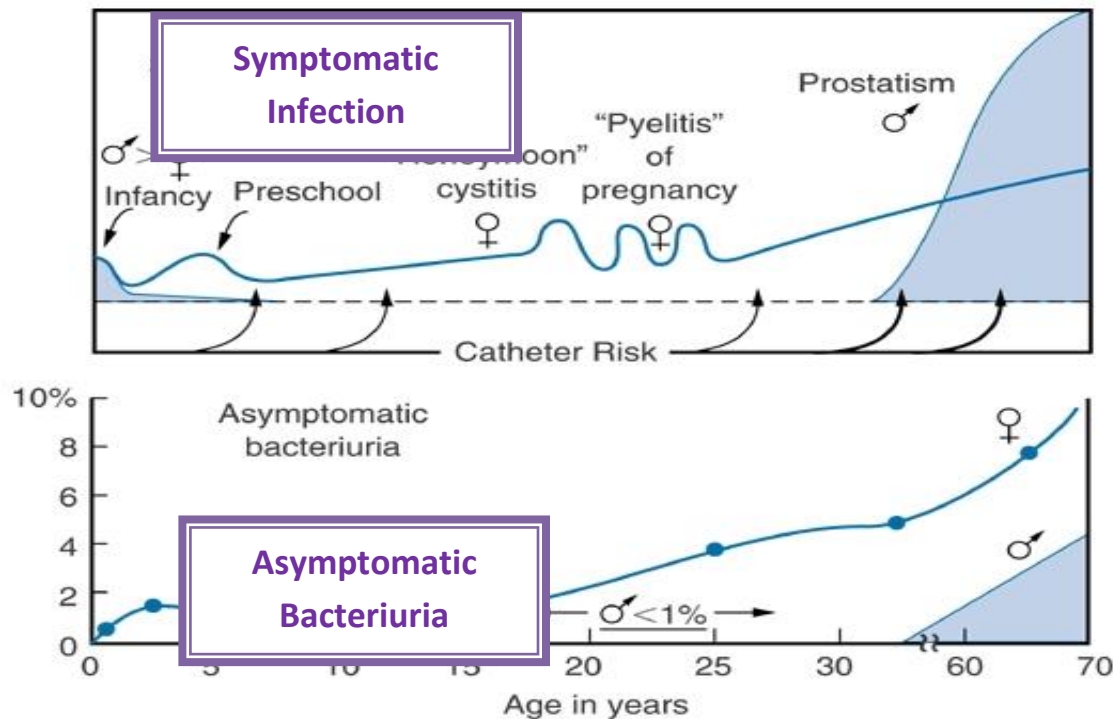
Reason:

Women:

- **Short urethra**
- Sexual contact: colonization of pathogen in bladder
- Spermicidal : Change of normal flora

Men (<50):

- Prostate infection, prostate enlarges causing obstruction which increases the risk of infection
- anatomical defects ,
- Lack of circumcision
- homosexuals



In preschool years, honeymoon years as well as in pregnancy age it is more common in females, so generally in almost all ages except old age it is more common in females

Classification of UTIs

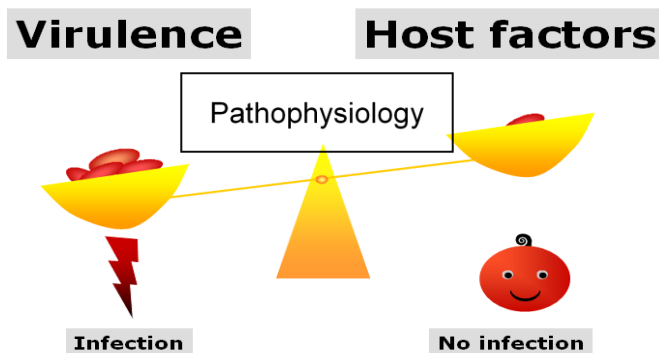
Classification by	
Location of UTI	
Lower	Cystitis, urethritis prostatitis,
Upper	Pyelonephritis, abscess (Intrarenal & Perinephric)
Symptoms	Symptomatic Asymptomatic
Recurrence	Sporadic ≤ 1 UTI / 6 m Recurrent ≥ 1 UTI / 6m
Complicating factors	Uncomplicated Complicated

- Above the bladder is upper UTI

- Recurrent: more than 2 in 6 months, or 3 in 1 year

Uti- Types By Complicating Factor

- **Uncomplicated UTi:** infection in a structurally and neurologically **normal** urinary tract
(occurring in a healthy young nonpregnant woman)
- **Complicated UTI:** infection in tract with functional or structural(**anatomical**) **abnormalities**
(is the one occurring in anyone else).



A UTI happens due to Interplay between the host protective factor and microorganism factors

Host protective factors in UTI

- Flushing mechanism of micturition
- Acid pH of urine (4.6- 6) anti-bacterial
- Acid vaginal pH (3.5-4.5)) suppresses colonization

The acidity discourages growth of any microorganism

- Urinary Tamm-Horsfall protein (secreted by ascending loop of Henle) & blocks *E. coli*
- Chemotactic factors - interleukin-8

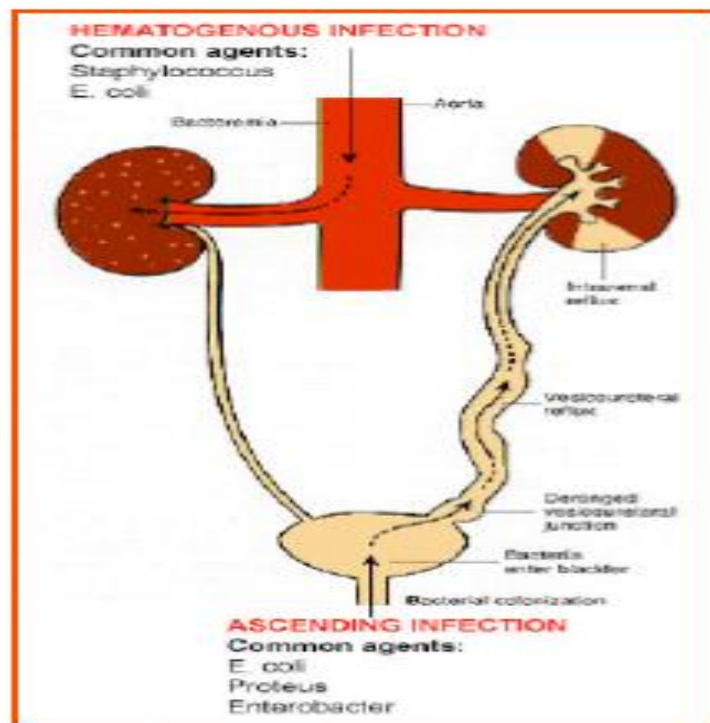
Immune Responses In UTI

- Submucosal IgA-producing plasma cells in bacterial cystitis
- IgM & IgG antibodies produced against bacterial antigens
- Protective role of antibodies unclear, may limit damage within the kidney & prevent persistent colonization & thus recurrence of infection

Bacterial Virulence Factors in UTI

- *Escherichia coli* strains expressing **O-antigens** cause high proportion of infections
- **Capsular antigens** of *E. coli* associated with clinical severity (antiphagocytic)
- **P-fimbriae** enhance attachment of *E. coli* to uroepithelial cells
- **Motile** bacteria ascend the ureter against urine flow
- **Bacterial urease** (*Proteus*) splits urea → NH₄ ion alkalinizes urine with loss of acid pH → stone formation → obstruction & survival of bacteria within stones resisting eradication
- **Gram-negative endotoxin** decreases ureteral peristalsis
- **Hemolysin** damages renal tubular epithelium & promotes invasive infection
- **Aerobactin** of *E. coli* promote iron accumulation for bacterial replication

Pathways of renal infection



Ascending route most common Colonization of urethra and peri-urethral tissue is the initial event . Once in the bladder, multiply, then pass up the ureters (esp. if vesico-ureteral reflux) to the renal pelvis & parenchyma

Pathogenesis of UTI

- **Ascending route** most common
- Colonization of urethra and peri-urethral tissue is the initial event
- More in women than men due to short female urethra ,so urethral organisms enter bladder during micturition & in close proximity to perianal areas
- Once in the bladder , multiply, then pass up the ureters (esp. if vesico-ureteral reflux) to the renal pelvis & parenchyma
- **Hospital infection** associated with lower urinary tract instrumentation (catheterization, cystoscopy)

Vesico-ureteral reflux: the abnormal movement of urine from bladder into the ureters and in some cases can go up to the kidneys, can be primary (congenital) where one or both ureters are shorter than normal, or secondary which happens when a blockage in the urinary tract causes an increase in pressure and pushes urine back up into the ureters, this can ruin the valve where it stops closing completely. This causes the urine to go back to the kidneys

Pathogenesis of UTI- **blood borne**

- Hematogenous seeding **less frequent** than ascending infection (**very rare**)
- Kidney a common site of abscess formation in *Staphylococcus aureus* bacteremia, less often in candidemia, rarely with gram-negative bacteremia
- Hematogenous seeding of kidney also occurs with *Salmonella* (typhoid) and *Mycobacterium tuberculosis*
- Source of uropathogens: **enteric bacteria** (imp)

Risk Factors

- ↓resistance of mucous membranes (e.g. in menopause) there is disturbance in vaginal pH and epithelium allowing the bacteria to grow
- sexual intercourse
- disturbances in ureteral functioning (example in last trimester of pregnancy)
- in children the re-entering of urine back into the ureters (vesicoureteral reflux),
- Uterine prolapse (after multiple pregnancies and deliveries where the ligaments get relaxed so the uterine may prolapsed causing obstruction of urine passage causing UTI)
- Diabetes
- benign prostatic hypertrophy
- any illness, eg diabetes, affecting the emptying -Neurogenic Bladder
- spinal injury →disturbances in bladder emptying or urinary catheter)
- Stones
- catheterisation & other urological procedures
- Renal Transplantation

Terminology of UTI

- **“Urethral syndrome”**: clinical manifestations of lower UTI without significant bacteriuria

The patient complains of dysuria frequency and burning sensation, on culture no bacteria is found (negative culture) thus no antibiotic is given. Reassure patient and don't give antibiotic

- **Cystitis**: localized infection of the bladder (suprapubic pain)
- **Prostatitis**: localized infection of the prostate = lower UTI
- **Pyelonephritis**: infection of the kidney with acute inflammation of the pelvis, medullary and cortical tubules, & intersitium = upper UTI
- **Urosepsis**: bacteremia (in blood) due to pyelonephritis
- **Perinephric abscess**: associated with obstruction of an infected kidney with abscess formation in the peri-nephric space due to extension of infection across the renal capsule
- **Renal abscess**: in parenchyma

TYPES OF UTI	TYPICAL SIGNS AND SYMPTOMS
Cystitis	<ul style="list-style-type: none">• Frequent voiding,(frequency & urgency)• suprapubic pain• Burning micturition (dysuria),• Hematuria• cloudy urine(subjective not important),
Pyelonephritis	<ul style="list-style-type: none">• Cystitis Symptoms ±• Fever• Chills• flank pains• N/Vomiting• renal angle Tenderness
Urosepsis	<ul style="list-style-type: none">• Fever• Chills• Shock (hypotension)

Pyelonephritis

- Fever, chills
- Nausea/Vomiting, diarrhea, tachycardia,
- Costo-vertebral (renal) angleTenderness or deep abdominal tenderness
- Leukocytosis
- Urine microscopy: Pyuria + WBC casts, bacteria & hematuria
 - Possibly signs of Gram negative sepsis

Aggressive treatment to not get complications

Complications:

- sepsis, abscess,
- papillary necrosis
- ureteral obstruction
- ↓renal function if scarring,
- in pregnancy – ↑incidence of preterm labor

Long run can cause kidney failure

Factors complicating acute pyelonephritis in adults

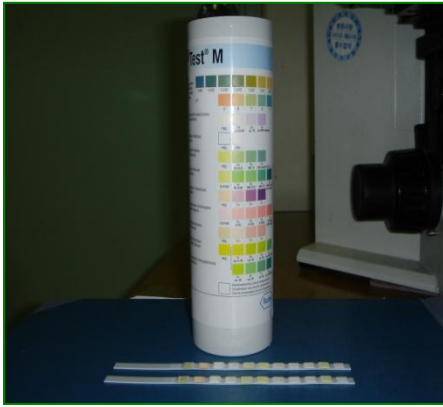
Obstruction
Diverticula
Fistulae
Ileal conduits and other urinary diversions
Neurogenic bladder
Vesicoureteral reflux
Indwelling catheter
Ureteral stent
Nephrostomy tube
Pregnancy
Diabetes
Renal failure
Renal transplantation
Immunosuppression
Multidrug-resistant uropathogens
Hospital-acquired infection

Diagnosis:

- history is the most important part (the symptoms)
- then physical examination
- ask about risk factors

Diagnosis (confirmation)- Urinalysis

- **Leukocyte-esterase** positive. = pyuria
 - **Nitrite** positive from urease producing bacteria
eg proteus (but not always)
 - **Microscopy**
- WBC (> 5 in pt with symptoms)
- Bacteria



Urinalysis: Dipstick Methods

pH, Sp.Gravity, protein, glucose, blood, ketone,
Leukocyte esterase +ve
Pyuria

Nitrite +ve

Gram(-) bacteriuria
except pseudomonas

Microscopic Examination

Pyuria: WBC > 5 / HPF in spun urine
(Normal is 5)

WBCs/puss cells/leukocytes are all the same

Bacteriuria > 10^5 cfu/ml



Collecting a Sample Is Important

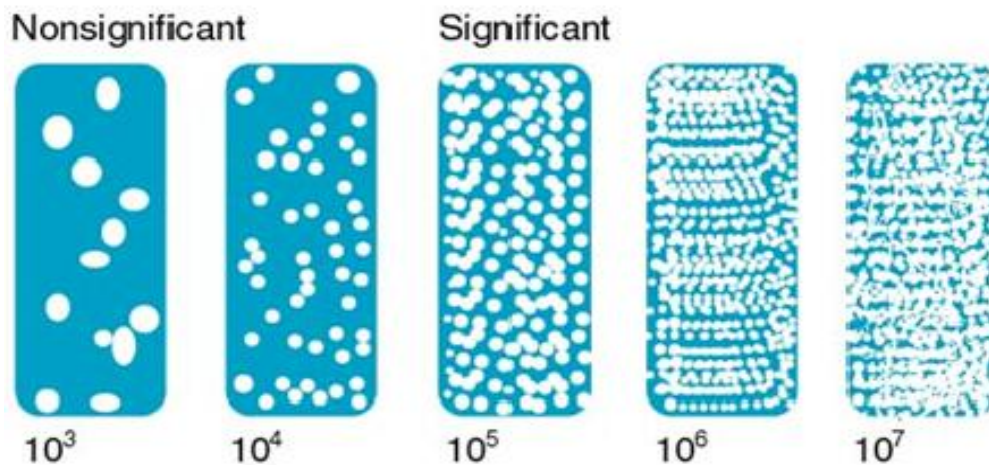
- **mid stream urine (MSU)** sample usually reliably represents the urine in the bladder.
- samples from urinary bags or bedpans should not be used as they invariably will be contaminated
- the most reliable sample is obtained from the bladder via a **suprapubic puncture**
- **urine in bladder >4 hours** (any shorter time will increase the risk of false negative findings) Any time less than 4 hours allows false negative because not enough time passed for the colonies to grow
if urine is very concentrated, or has a lot of glucose in urine, or using drugs like:tetracyclines, or having a lot of vaginal debris
pseudomonas and enterococcus gives -ve

Diagnosis- interpretation of Urine Cultures

- **Urine culture**
 - **10^5** colonies per mL considered **standard** for diagnosis - but misses up to 50%
 - Now, 10^3 to 10^4 accepted as significant if patient symptomatic

- if **several bacterial strains** are grown on culture; **contamination** of the sample is the likely cause , (you disregard it and take a new one)
- Sensitivities for better tailoring of therapy

Interpretation after 24-hour incubation at 37 C



Clinical status or methods of sampling

Significant concentration (microbes / ml)

MSU; symptomatic patient or urine in bladder <4 h

$>10^3$

MSU; urine in bladder >4 h

$>10^{4-5}$

Male patient, catheter specimen sample

$>10^3$

Female patient, catheter specimen sample

$>10^4$

Asymptomatic bacteriuria

$>10^5$

Suprapubic puncture sample

any growth

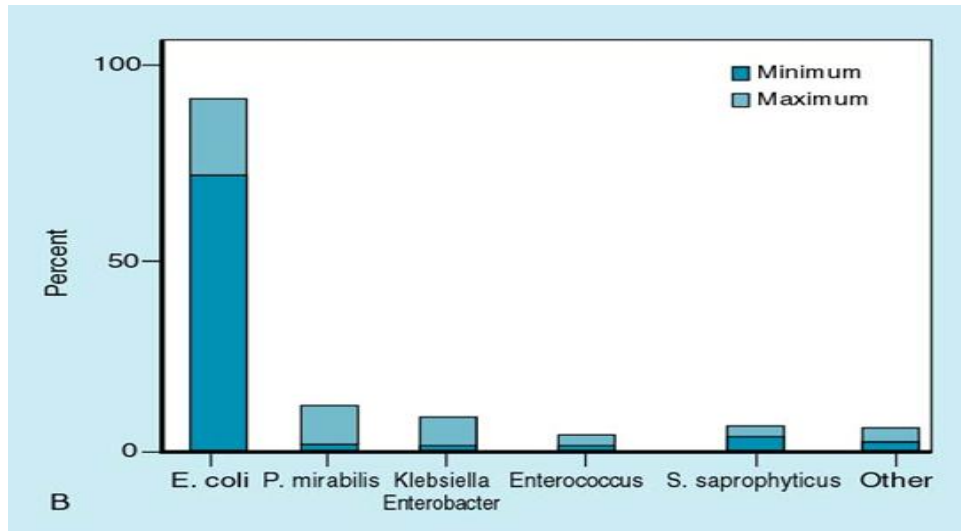
Easier in men

Catheter specimen sample is hopeless (contamination)

Asymptomatic bacteriuria means there is bacteria but no manifestations

Causative Agents Of UTIs

- *Escherichia coli*
 - most common
 - 80% of community - acquired
 - 50% of hospital-acquired
- Others:
 - *enterococci*
 - *Staphylococcus saprophyticus* and
 - *klebsiella*
 - *pseudomonas* and *proteus* are more rare



Localization of UTI

No definite standard method

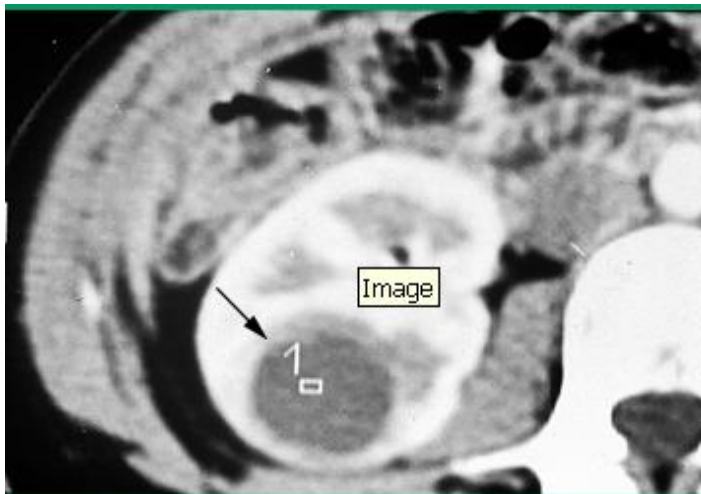
- Ultrasonography (easy non invasive and used when suspecting pyelonephric abscess or obstruction for example)
- IVP (Intra venous Urography)(haven't been used in the past 10-20 years for UTIs)
- Abdominal CT / MRI
- Tc-99m DMSA renal scan

Renal Abscess ON Ultrasonography



Ultrasonic examination of the kidney showing an abscess cavity (arrow). The internal echoes within the lesion can also be seen with a malignancy but not with a simple cyst.

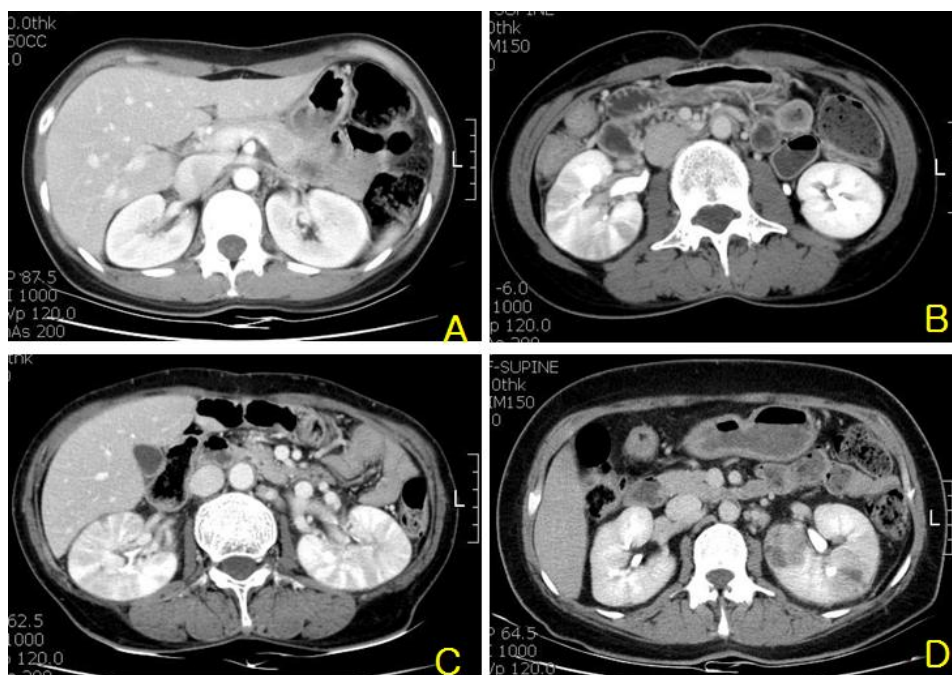
Renal abscess on CT scan



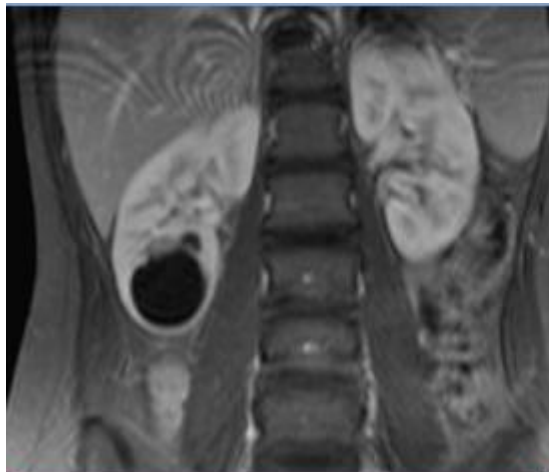
CT scan showing a large renal abscess with internal echoes in the right kidney (arrow).

Computed tomographic scan shows a large perinephric phlegmon with loculation adjacent to the right kidney

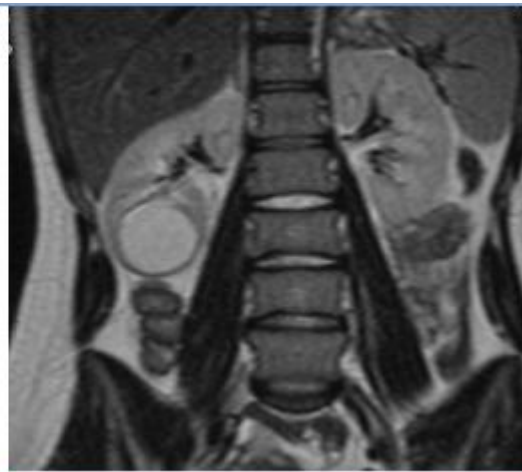
Perinephric Abscess



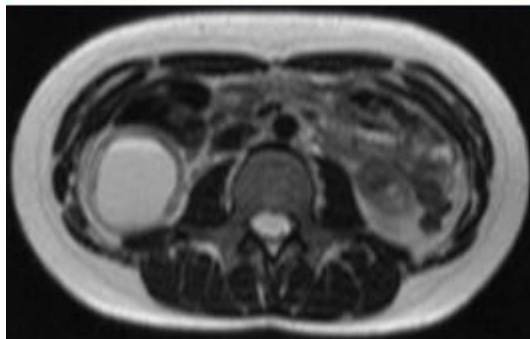
CT images at different levels → hypodense areas of ?pyelonehritis



T1 MRI- hypointense area



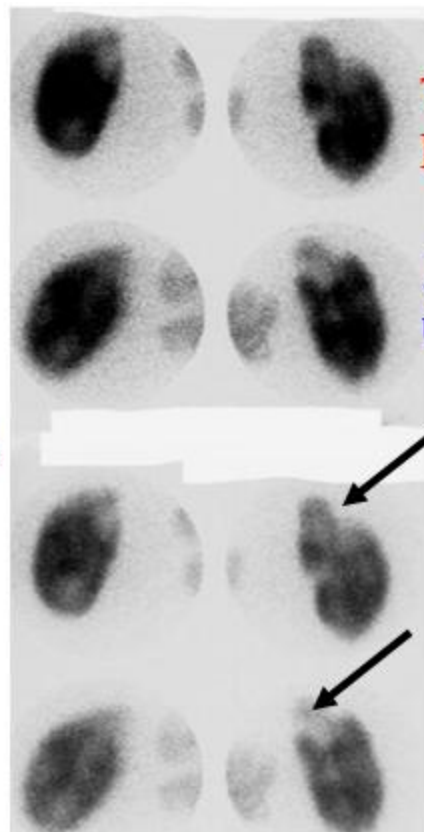
T2 MRI- hyperintense area



Axial MRI- hyperintense area

MRI – Fluid (abscess) in lower pole

DDx
Scar
Renal infarction



Tc-99m DMSA
Renal Scan

↓ **Renal cortical**
uptake

Indentation at upper pole

- You don't treat asymptomatic bacteriuria EXCEPT IN PREGNANT WOMEN!! Their chance in getting complications is much higher.
- Sterile pyuria: under the microscope a lot of pus cells but without organism, is caused most commonly by untreated UTI or inadequately treated UTI.

Therapy in UTIs - 1

Acute uncomplicated cystitis: in women

- patient with typical symptoms, not belonging to any of the risk groups, is treated **without** laboratory investigations
- if the symptoms are atypical, a **strip test** urinalysis may be carried out to support diagnosis
- if the strip test is negative, the urine should be **cultured** and other reasons for the symptoms should be considered

Treatments of UTI - options

■ **Lower UTI (Cystitis) : in women**

3-7 days course of antibiotics (short** is preferable)**

- Trimethoprim/SMX = 1st choice
 - Cephalosporines (Cefpodoxime)/ Nitrofurantoin
 - Fluoroquinolone (ciprofloxacin, Norfloxacin etc)
- (3 days usually unless you are worried you can give up to 7 days)

■ **Lower UTI (Cystitis) : in men**

Longer course for 7 days

- TMP/SMX
- Fluoroquinolones
- B-lactams(Augmentin) or Nitrofurantoin: not recommended

If no improvement→ consider Prostatitis

Any UTI in men and postmenopausal women is a complicated UTI

Simple are in young females, premenopausal.

Simple UTI 3 days, but in men and upper UTI at least 1 week

Selected oral antimicrobial regimens for use in acute uncomplicated cystitis

Drug, dose	Dose and interval	Duration
Levofloxacin	250 mg q 24 hours	3 days
Ciprofloxacin	100 to 250 mg q 12 hours	3 days
Ciprofloxacin XR	500 mg q 24 hours	3 days
Trimethoprim-sulfamethoxazole	160/800 mg q 12 hours	3 days
Trimethoprim	100 mg q 12 hours	3 days
Cefpodoxime proxetil	100 mg q 12 hours	3-7 days
Nitrofurantoin macrocystals	50 mg q 6 hours	5 days
Nitrofurantoin monohydrate macrocystals (Macrobid®)	100 mg q 12 hours	5 days
Amoxicillin/clavulanate	500 mg q 12 hours	7 days

Treatment of pyelonephritis-

Uncomplicated pyelonephritis:

- **Mild to moderate pts** be treated orally as outpatient with either a
- **quinolone** (ciprofloxacin or levofloxacin)
- **sulpha-trimethoprim** for

Duration : 7-14 days course of antibiotics

- B- lactams, Nitrofurantoin: not favoured

Inpatient management is appropriate in the following :

1. Severe illness with high fevers, pain, and marked debility
2. Pt unable to maintain oral hydration or take oral medications
3. Pregnancy
4. Concerns about patient compliance

(Mild to moderate treat as outpatient, else admit and treat as in patient)

Don't give quinolones to pregnant women or anyone less than 14 years old.

Oral Drugs

Oral regimens for treatment of pyelonephritis

Antibiotic	Dose, interval
Regimens for empiric treatment	
Levofloxacin	500 to 750 mg every 24 hours*
Ciprofloxacin	500 mg every 12 hours
Ciprofloxacin XR	1000 mg every 24 hours
Regimens for treatment of pyelonephritis when the isolate is known to be susceptible	
Trimethoprim-sulfamethoxazole	1 double strength tablet every 12 hours
Trimethoprim	100 mg every 12 hours or 200 mg every 24 hours
Cefpodoxime	100 to 200 mg every 12 hours
Cefixime	200 mg every 12 hours or 400 mg every 24 hours
Amoxicillin*	250-500 mg every 8 hours or 500-875 mg every 12 hours

Treatment of pyelonephritis-Complicated

**ie :progression to renal corticomedullary abscess,
perinephric abscess, emphysematous pyelonephritis,
or papillary necrosis**

Consider underlying anatomic or functional abnormalities

An unwell patient should be **admitted** to hospital

- *Parenteral treatment* is commenced with either
- **Cephalosporines i.v. (ceftriaxone)** or
- **fluoroquinolone orally/ I.V**
- & change to oral, when response is obvious

Note: Antibiotics alone may not be successful unless underlying conditions are corrected

I.V Drugs

Parenteral regimens for empiric treatment of pyelonephritis

Antibiotic	Dose, interval
Uncomplicated pyelonephritis	
Ceftriaxone	1 g every 24 hours
Ciprofloxacin	400 mg every 12 hours
Levofloxacin	750 mg every 24 hours
Aztreonam	1 g every 8 to 12 hours
Complicated pyelonephritis	
Piperacillin-tazobactam	3.375 g every 6 hours
Ticarcillin-clavulanate	3.1 g every 6 hours
Cefepime	1 g every 12 hours
Meropenem	1 g every 8 hours
Imipenem	500 mg every 6 hours

Prevention of UTI

■ Recurrent UTI

Women with > 3 episodes of UTI per year

Good hydration

- **Avoidance of spermicidal or diaphragm**
- frequent and complete voiding
- **Immediate voiding after sexual contact**
- **Antibiotics after sexual contact**
- **Low dose antibiotics prophylaxis**

Prophylaxis of Recurrent UTI with Antimicrobial Agents

- prophylaxis should be considered when **more than 3 infections per year or 2 in 6 months**
- prophylaxis to continue for 6 months
- if infections recur after prophylactic treatment, the prophylaxis is re-commenced for 6 – 12 months **(D)**