URINARY TRACT INFECTION

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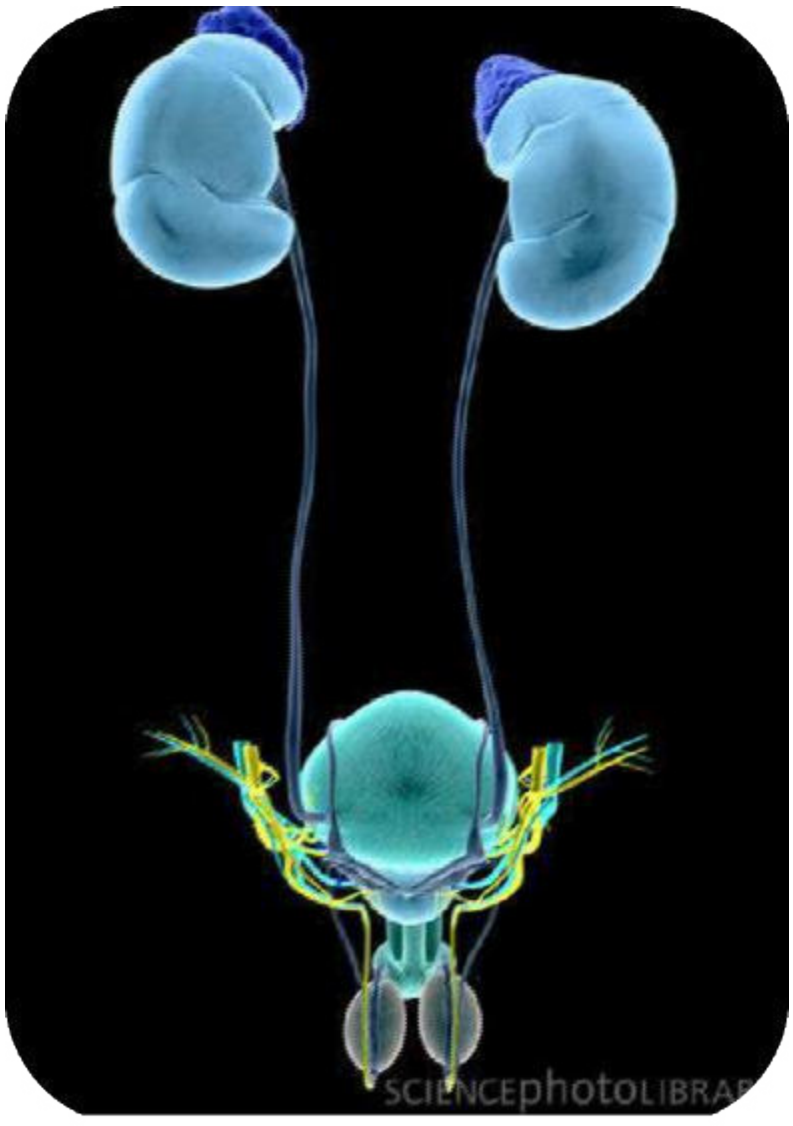
Introduction

- Symptomatic presence of micro organisms within the urinary tract

  i.e., kidney, ureters, bladder and urethra.

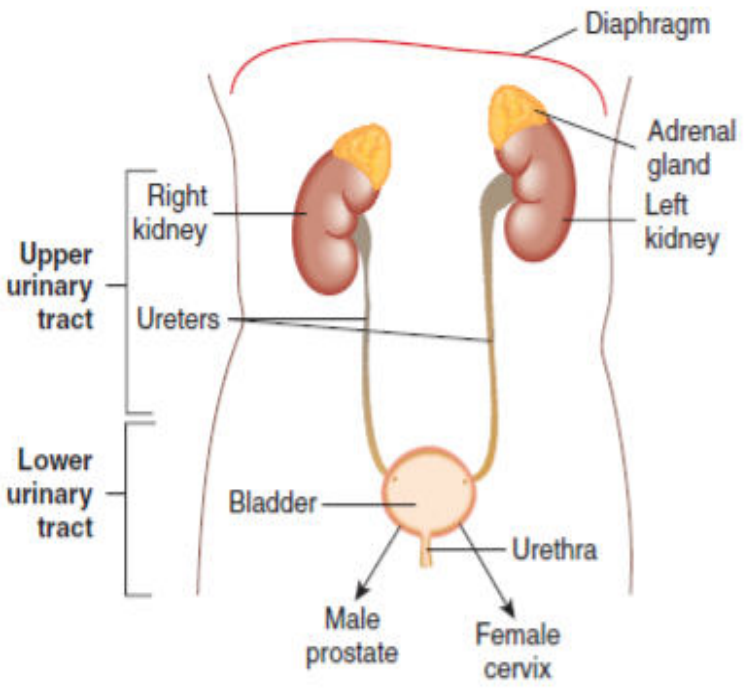


- Associated with inflammation of urinary tract.

Anatomy

❖The upper urinary tract, composed of the kidneys, renal pelvis, and ureters.

❖ the lower urinary tract that consists of the urinary bladder and the urethra.



- Upper urinary tract infections affect the ureters (ureteritis) or the renal parenchyma (pyelonephritis).

- Lower urinary tract infections may affect the urethra (urethritis), the bladder (cystitis), or the prostate in males (prostatitis).

UTI - Terminology

- **Significant bacteriuria**: presence of at least **10^5 bacteria/ml** of urine.

- **Asymptomatic bacteriuria** : bacteriuria with **No** symptoms.
- **Uncomplicated:** UTI **without** underlying renal or neurologic disease.

- **Complicated:** UTI **with** underlying structural, medical or neurologic disease.

- **Recurrent : > 3 symptomatic UTIs** within 12 months following clinical therapy.

- **Reinfection:** recurrent UTI caused by a **different pathogen** at any time

- **Relapse:** recurrent UTI caused by **same species** causing original UTI within 2 wks after therapy.
- **Urethritis**: infection of anterior **urethral tract**
- **Cystitis:** infection to **urinary bladder**
- **Acute pyelonephritis**: infection of one/both **kidneys**; sometimes lower tract also.
- **Chronic pyelonephritis**: particular type of **pathology of kidney**; may/may not be due to infection.

Pyuria

- the presence of ≥10 WBC/cumm in a urine specimen,
- 1-5 white cells per high-power field of uncentrifuged urine,
- or a urinary dipstick test that is positive for leukocyte esterase.

Sterile pyuria

- the persistent finding of white cells in the urine in the absence of bacteria.

Classification

- Acute pyelonephritis
- Chronic pyelonephriitis
- Interstitial pyelonephritis
- Renal abscess
- Perirenal abscess

- Cystitis
- Prostatitis
- Urethritis

- Both upper & lower UTI are further divided into complicated and uncomplicated.

Epidemiology

- Seen in all age groups
- Infants up to 6 months – 2/1000
- More common in boys than girls

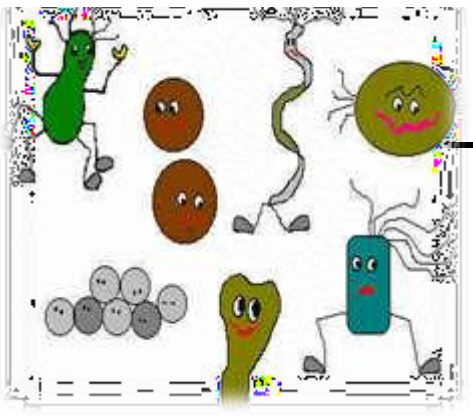
- Women – at greater risk than men; prevalence 40-50% in women and 0.04% in men.
- 10% women have recurrent UTI in their life
- 7 million new cases of lower UTI / year
- 1 million hospitalizations / year

- Incidence of UTI increases in old age; 10% of men and 20% of women are infected.

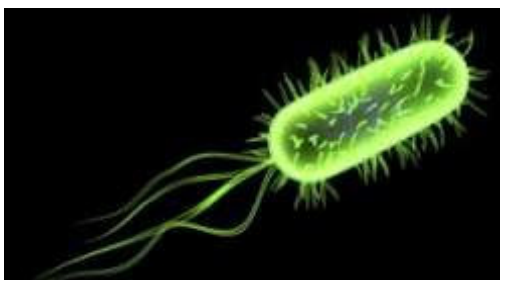
Criteria for Classification of Urinary Tract Infections by Clinical Syndrome

Category	Clinical	Laboratory
Acute, uncomplicated UTI in women	Dysuria, urgency, frequency, suprapubic pain No urinary symptoms in last 4 weeks before current episode No fever or flank pain	≥10 WBC/mm³ ≥10³ CFU/mL uropathogens* in CCMS urine
Acute, uncomplicated pyelonephritis	Fever, chills Flank pain on examination Other diagnoses excluded No history or clinical evidence of urologic abnormalities	≥10 WBC/mm³ ≥10⁴ CFU/mL uropathogens in CCMS urine
Complicated UTI and UTI in men	Any combination of symptoms listed above One or more factors associated with complicated UTI†	≥10 WBC/mm³ ≥10⁵ CFU/mL uropathogens in CCMS urine
Asymptomatic bacteriuria: female patients	No urinary symptoms	± >10 WBC/mm³ ≥10⁵ CFU/mL in two CCMS cultures >24 hours apart
Asymptomatic bacteriuria: male patients	No urinary symptoms	± >10 WBC/mm³ ≥10³ CFU/mL (suggestive) ≥10⁵ CFU/mL (definitive) in one CCMS

*Uropathogens: Organisms that commonly cause UTIs.
†Factors associated with complicated UTI include any UTI in a male patient, indwelling or intermittent urinary catheter, more than 100 mL of postvoid residual urine, obstructive uropathy, urologic abnormalities, azotemia (excess urea in the blood, even without structural abnormalities), and renal transplantation.
CCMS, Clean-catch midstream urine; *CFU,* colony-forming unit; *UTI,* urinary tract infection; *WBC,* white blood cells.



Etiology



Acute uncomplicated UTI: Infection in a structurally and neurologically normal urinary tract.

- 80% by *Escherichia coli*
- 20% by :

Gram negative enteric bacteria – *Klebsiella*

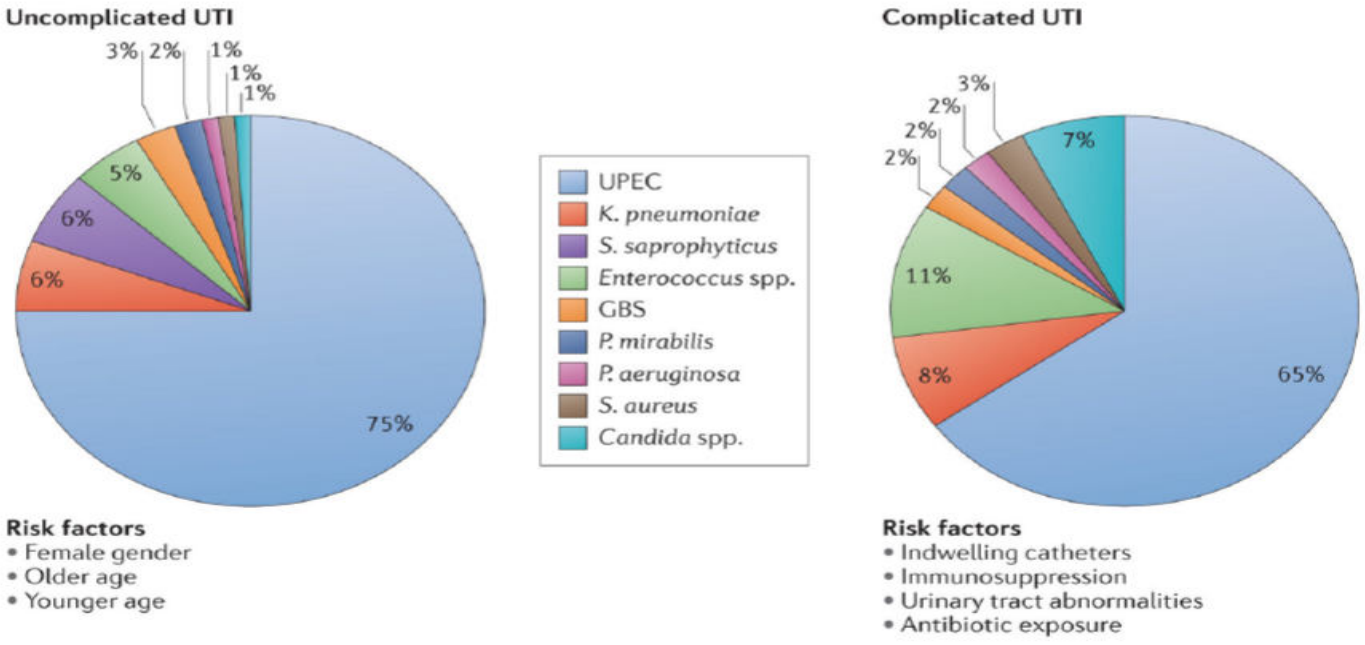
Gram positive cocci – *Streptococcus faecalis*

Staphylococcus saprophyticus

- S.saprophyticus – restricted to infections in young **sexually active women**.

Complicated UTI : Infection in a urinary tract with functional or structural abnormalities

- *Proteus*
- *Pseudomonas*
- *Klebsiella*
- *Enterobacter*



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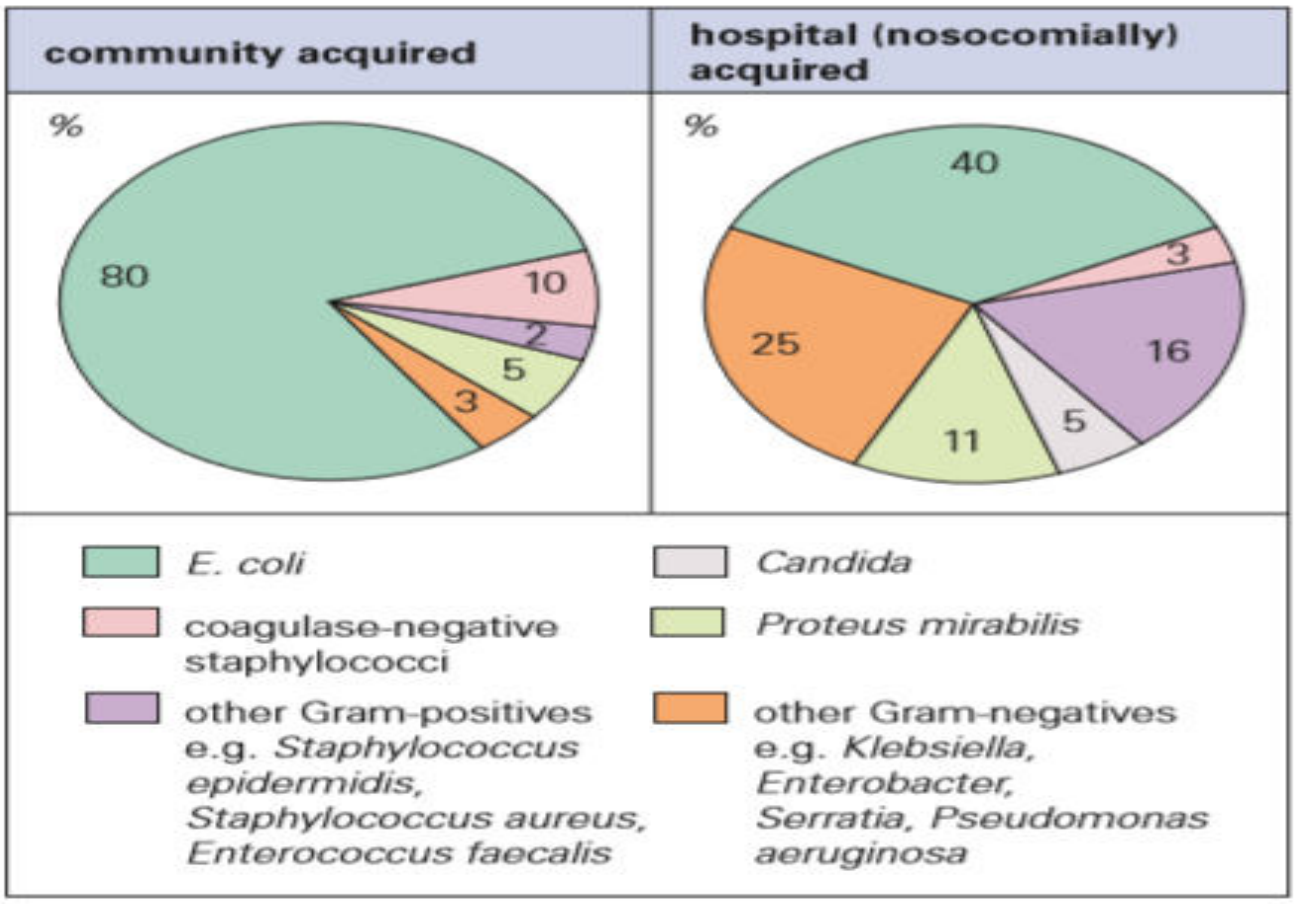

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Resident microflora of urinary tract

- Coagulase-negative staphylococci (excluding *Staphylococcus saprophyticus*)
- Viridans and nonhemolytic streptococci Lactobacilli (adult females)
- Diphtheroids (*Corynebacterium spp*.)
- Nonpathogenic (saprobic) *Neisseria spp*. (adult women)
- Anaerobic cocci
- *Propionibacterium spp*. (adult patients)
- Commensal *Mycobacterium* spp.
- Commensal *Mycoplasma* spp.
- Yeasts (pregnant, adult females)

Hospital Acquired UTI (HAUTI)

- 80 % because of indwelling catheters.
- Organisms responsible are :

E.coli
Klebsiella
Proteus
Staphylococci
Pseudomonas
Enterococci
Candida

Catheter Associated UTI (CAUTI)

- 10-30% of catheterized patients developed bacteriuria.

- After hospitalization, patient become colonized with bacteria endemic to the institution, often gram negative aerobic and facultative bacilli carrying resistance markers.

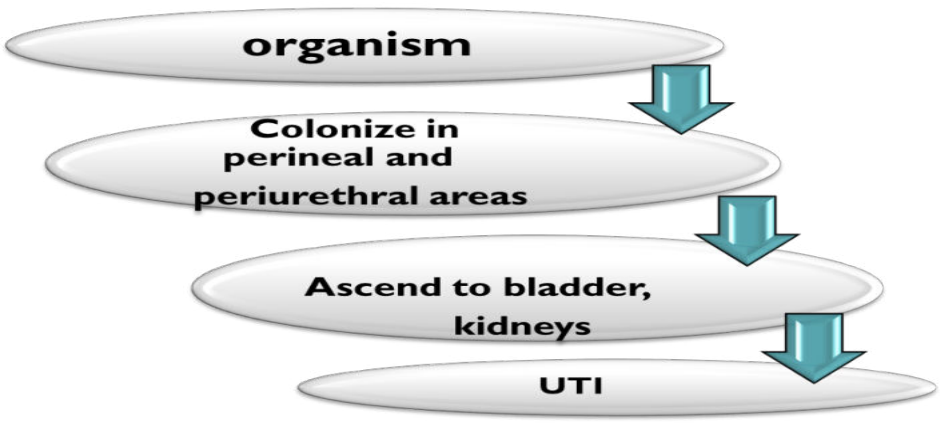
Pathogenesis

- 4 routes of bacterial entry to urinary tract.

1. Ascending infection
2. Descending infection (Blood borne spread)
3. Lymphatogenous spread
4. Direct extension from other organs

ASCENDING INFECTION

- Most common route.
- Organisms ascend through urethra into bladder.



DESCENDING INFECTION

Caused by hematogenous route

Common organisms:

staphylococcus aureus,

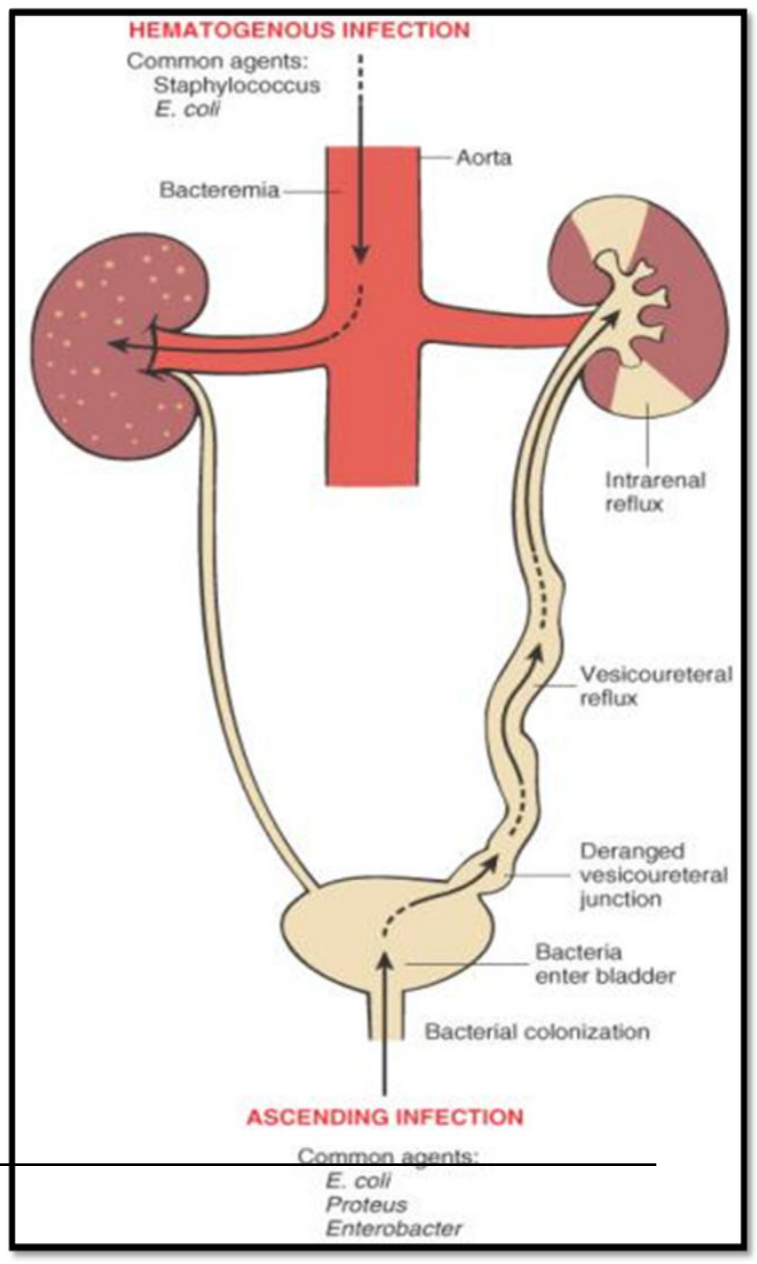
mycobacterium tuberculosis,

salmonella sp,

leptospira,

yeast (candida albicans),

rickettsia



- **LYMPHATOGENOUS SPREAD**

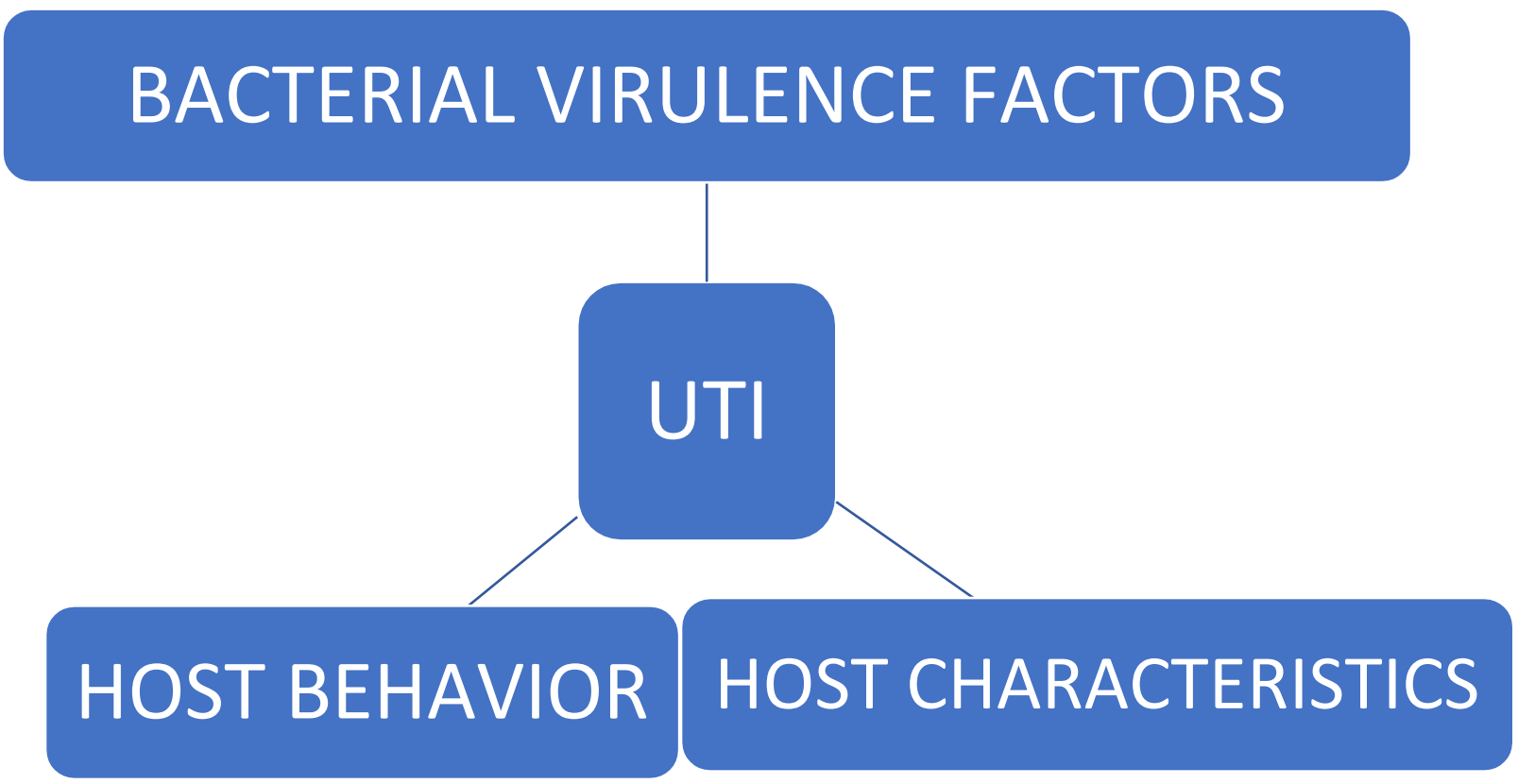
Men- Through rectal and colonic lymphatic vessels to prostate and bladder.

Women- Through periuterine lymphatics to urinary tract.

- **DIRECT EXTENSION FROM OTHER ORGANS**

Pelvic inflammatory diseases

Genito-urinary tract fistulas



UTI – RISK FACTORS

1. *Aging:* diabetes mellitus
   urine retention
   impaired immune system

2. *Females*: shorter urethra
   sexual intercourse contraceptives
   incomplete bladder emptying with age

3. *Males*: prostatic hypertrophy
   bacterial prostatis age

Risk factors for complicated UTI

- Functional/structural abnormalities of urinary tract
- Recent urinary tract instrumentation
- Recent antimicrobial use
- Diabetes mellitus
- Immunosuppression
- Pregnancy
- Hospital acquired infection

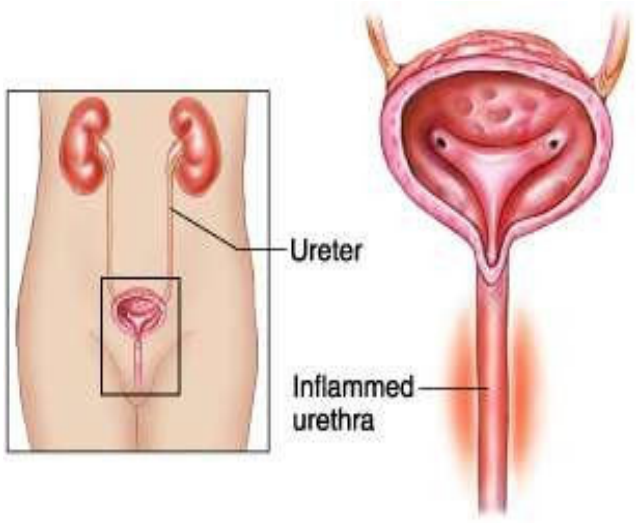
UTI-CLINICAL PRESENTATION

- Clinical manifestations depending on site of infection

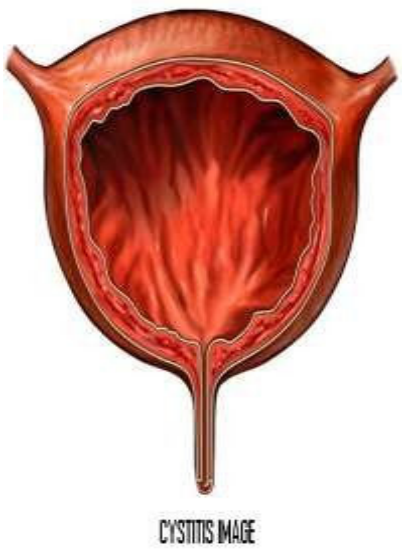
- Clinical manifestations depending on age of patient

Clinical manifestations depending on site of infection

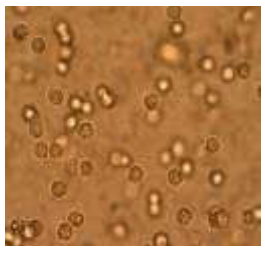
- ***Urethritis:***
  - Discomfort in voiding
  - Dysuria
  - Urgency
  - frequency



- ***Cystitis:***
  - dysuria, urgency and frequent urination
  - Pelvic discomfort
  - Abdominal pain
  - Pyuria



- ***Hemorrhagic cystitis:***
  - Visible blood in urine.
  - Irritating voiding symptoms



- ***Pyelonephritis:***
  - Invasive nature
  - Suprapubic tenderness
  - Fever and chills
  - White blood cell casts in urine
  - Back pain
  - Nausea and vomiting

➢**Complications** include sepsis, septic shock and death.

Clinical manifestations depending on age

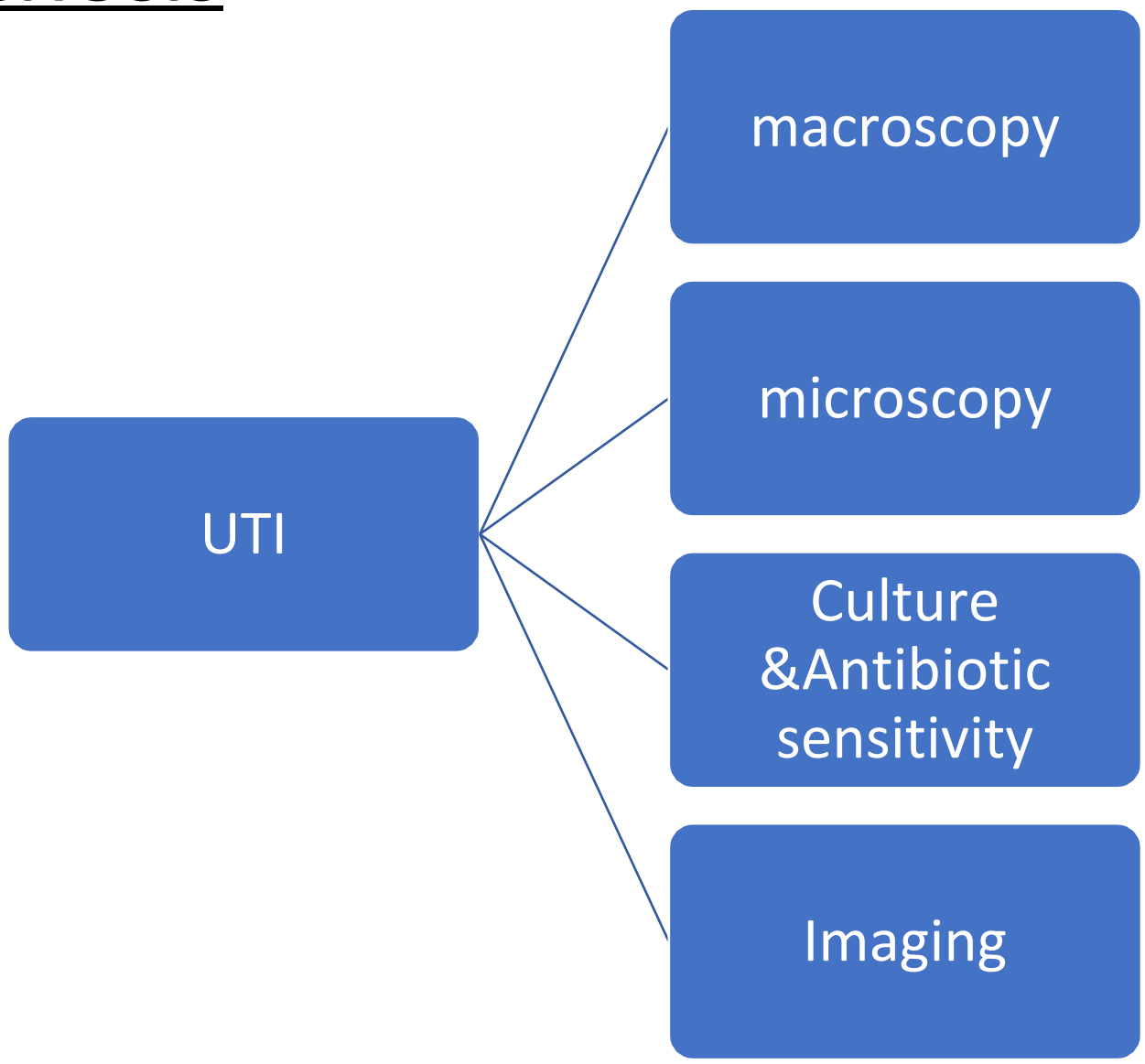
- ***infants :***
  - Failure to thrive
  - Fever
  - Apathy
  - Diarrhoea

- ***Children:***
  - Dysuria, urgency, frequency
  - Haematuria
  - Acute abdominal pain
  - Vomiting

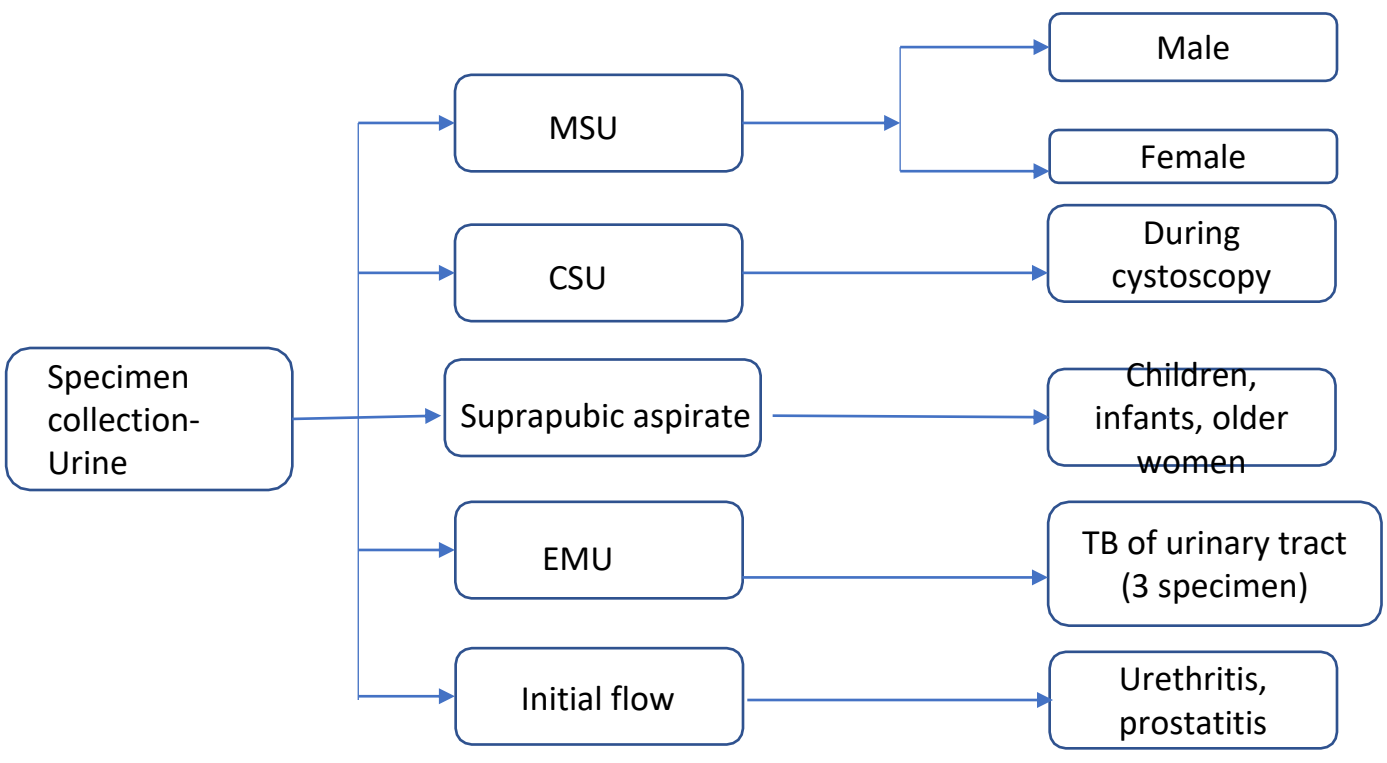
- ***Adults:***
  - **Lower UTI-** frequency, urgency, dysuria, haematuria
  - **Upper UTI-** fever, rigor and loin pain and symptoms of lower UTI.

- ***Elderly patients:***
  - Mostly asymptomatic
  - Not diagnostic as the symptoms are common with age.

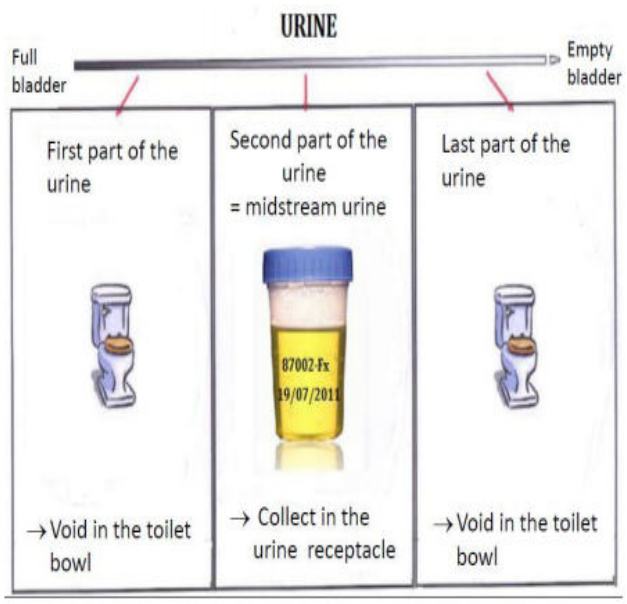
DIAGNOSIS

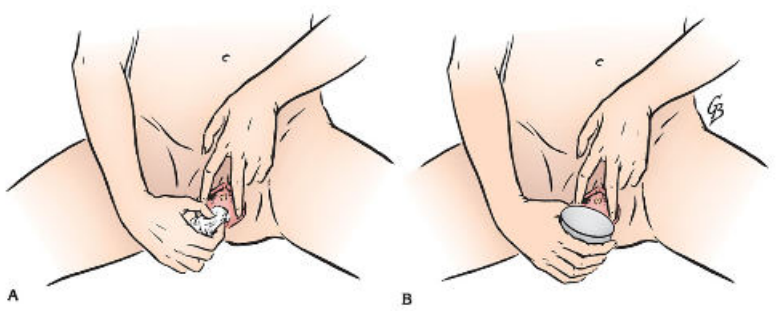


Specimen Collection



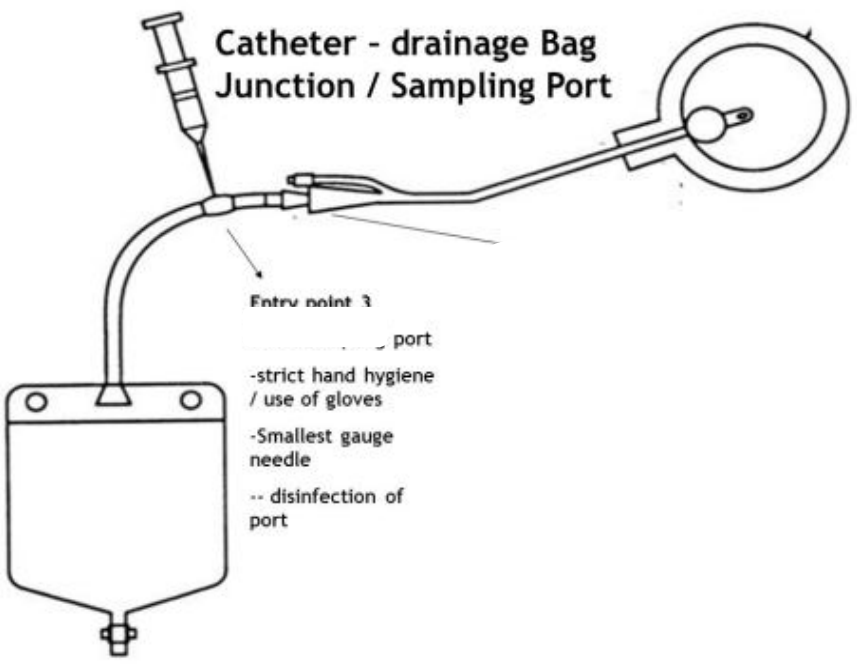
Clean-Catch Midstream Urine

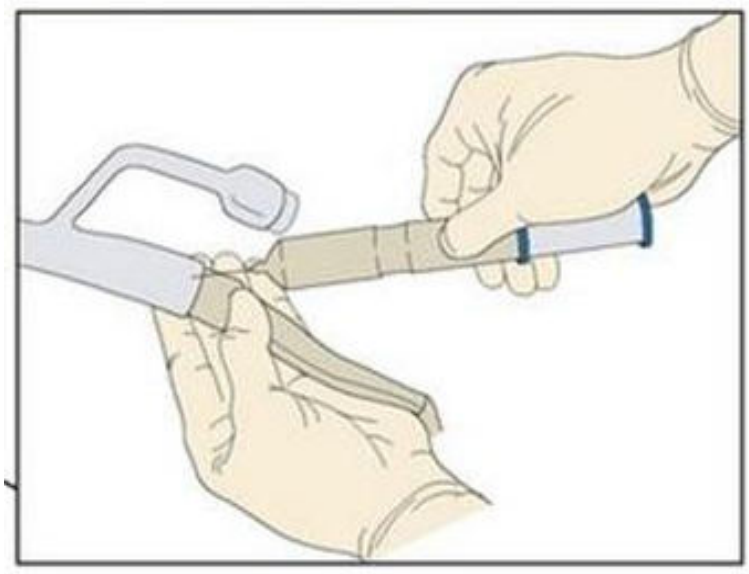




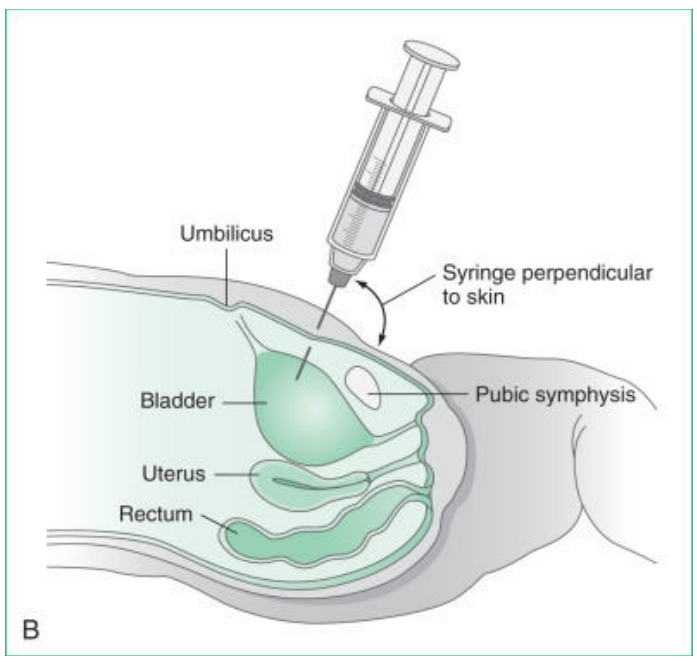
Midstream clean-catch urine collection. **A.** The labia are separated with the fingers and cleansed with a 4 × 4-inch gauze pad saturated with soap. **B.** The midstream portion of the urine is collected in a sterile container.

Catheter specimen of Urine





Suprapubic Bladder Aspiration



- Gold standard for obtaining urine specimens for culture in children under 2 years.
- Suprapubic aspirate is a simple, safe, rapid and effective procedure.
- The use of ultrasound increases the success of the procedure.
- Any growth of pathogenic bacteria in an SPA specimen is significant.

In Infants

For infants - the 'Quick-wee' method can be considered to increase the voiding and success rate of a 'clean-catch' urine
This method uses gentle cutaneous suprapubic stimulation with gauze soaked in cold 0.9% saline to trigger faster voiding.

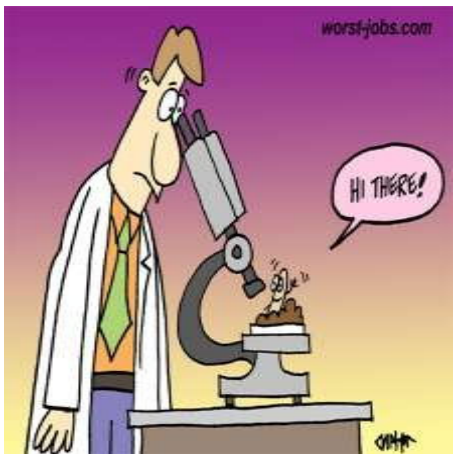
- Suprapubic aspiration
- Non-invasive-
  - By tapping just above the pubis with 2 fingers at 1h after feed,
  - 1tap/sec for 1 min, then 1min interval .

UTI- URINALYSIS

1. **Appearance** of the sample- colour of specimen
whether clear or turbid

2. **Microscopic examination** of urine as wet preparation to detect –

WBCs
RBCs
Yeast
Casts/Crystals
Bacteria
Trophozoites-trichomonas vaginalis
Egg
Epithelial cells



3. **Gram Stain**: Should be done when bacteria or pus cells are seen in wet mount.

Laboratory findings

Normal Findings

- pH - 4.6 – 8.0
- Appearance- clear
- Color – pale to amber yellow
- Odor – aromatic
- Blood – none
- Leukocyte esterase – none
- WBC- absent
- Bacteria- absent

Abnormal findings

- pH – Alkaline(increases)
- Appearance – cloudy
- Color - deep amber
- Odor – foul smelling
- Blood – maybe present
- Leukocyte esterase - present
- WBC- present
- Bacteria- present

BIOCHEMICAL TESTS

a) **Protein**- Proteinuria is found in most bacterial urinary tract infections.

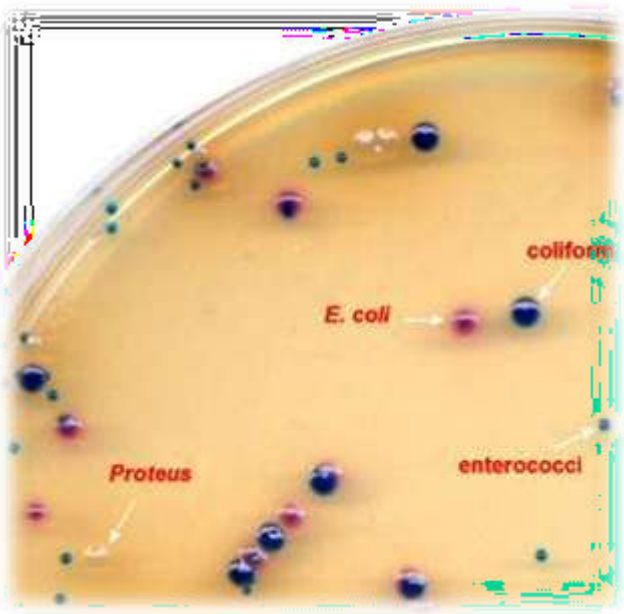
b) **Nitrite**- detected by **Greiss Test** or nitrite reagent strip test. This test is positive with infection by *E.coli, Klebsiella, Proteus* and negative with infection caused by *Enterococcus faecalis, Staphylococcus, Candida, Pseudomonas* sp.

c) **Leukocyte esterase enzyme** test which detects the presence of **pus cells** (pyuria).

False negative results occur when urine contains boric acid as preservative.

Urine culture :

- Not a rapid diagnostic tool
- >10^5 bacteria /ml
- Differential leukocyte count- increased neutrophils



GENERAL INTERPRETATIVE GUIDELINES FOR URINE CULTURES

RESULT	SPECIMEN TYPE/ ASSOCIATED CLINICAL CONDITION	WORKUP
$>10^4$ CFU/ml of a single potential pathogen or for each of two potential pathogens	CCMS/pyelonephritis, acute cystitis, asymptomatic bacteriuria, or catheterized urine	Complete
$>10^5$ CFU/ml of a single potential pathogen	CCMS/symptomatic males or catheterised urine or acute urethral syndrome	Complete
≥three organism types with no predominating organism	CCMS/ catheterised urine	None
Either two or three organism types with predominant growth of one organism type and $<10^4$ CFU/ML of the other organism types.	CCMS	Complete workup of predominant organism
$\geq 10^2$CFU/ML of any number of organismtype	Suprapubic aspirate, Any other surgically obtained urine	Complete

EXAMINE AND REPORT THE CULTURES

If colonies are < 10^3 CFU/ml – No significant Growth

- If >10^3 and < 10^5 CFU/ml --- No Significance

  ↓

  Significant
- Patients on antimicrobials,
- Female patients with urethritis,
- Symptomatic males,
- Presence of pus cells and absence of epithelial cells,
- Sample collected by suprapubic aspiration and
- from freshly inserted urinary catheter,
- Single type of growth from non-contaminated sample .

Clinical correlation is very important.

|

Organism identification

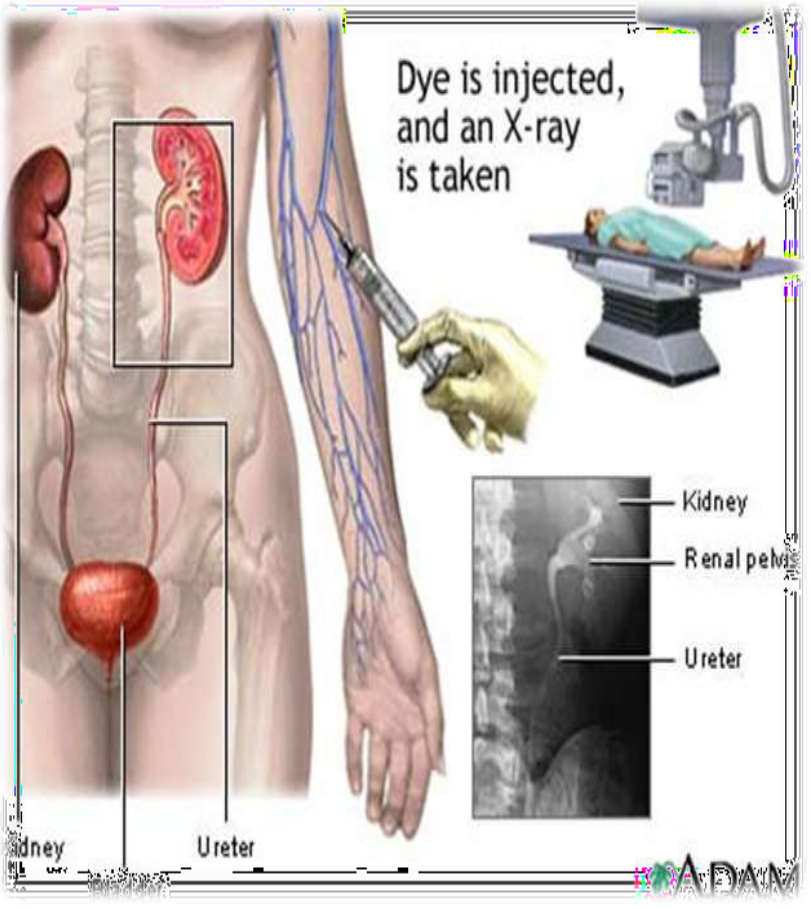
>10^5 CFU/ml --- Significant Bacteriuria

↓

Organism identification

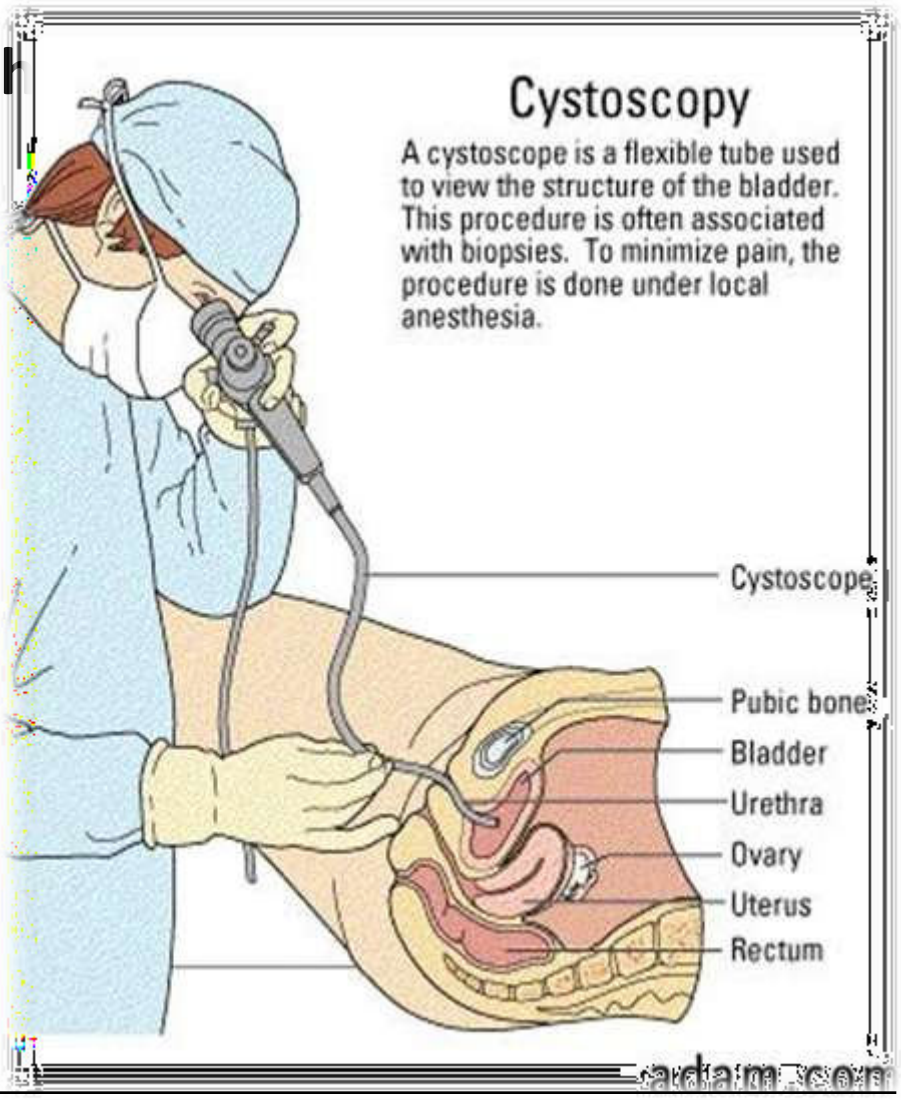
Diagnostic tests for adults with recurrent UTI

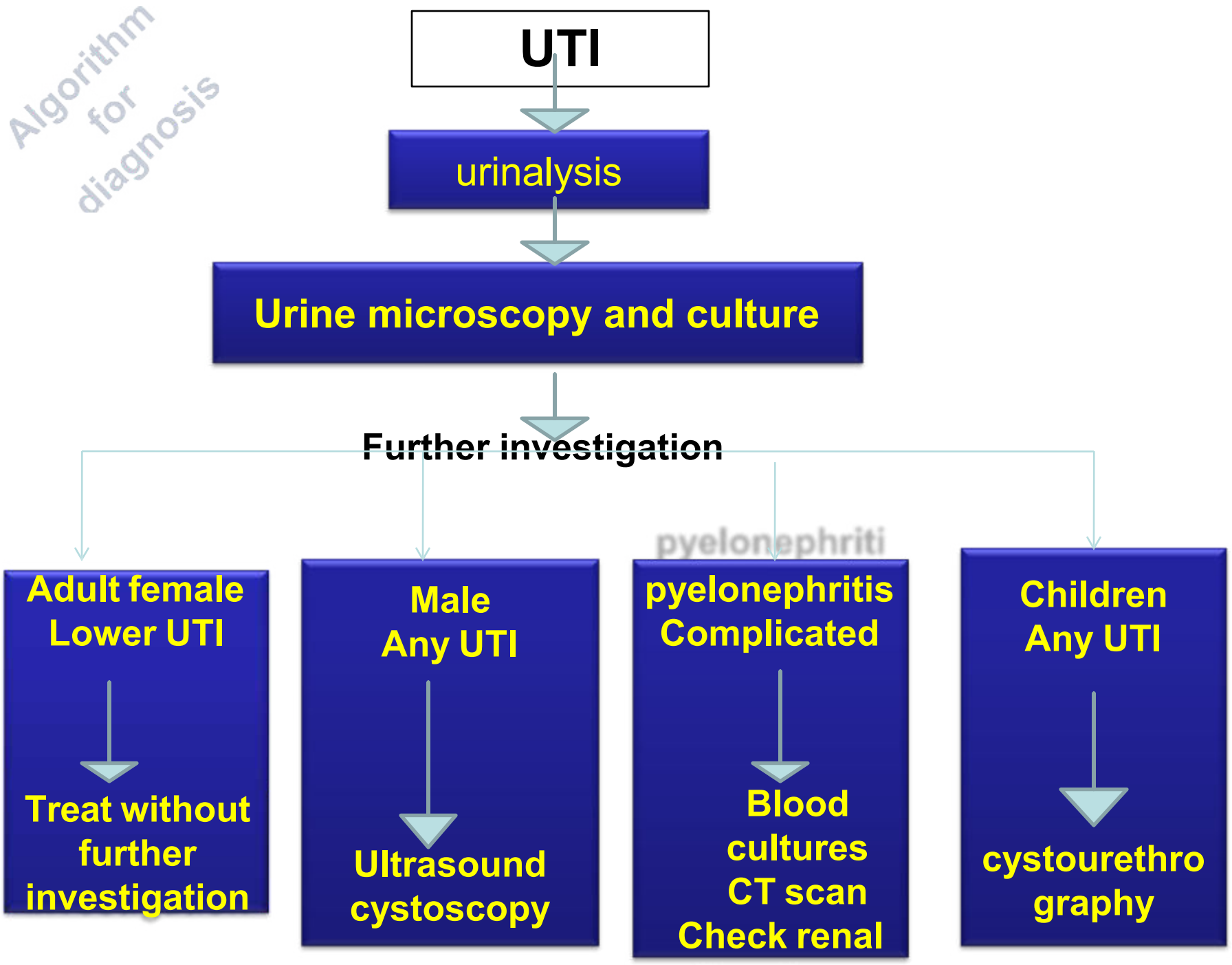
- **INDICATIONS:**
- H/O Calculus
- H/O surgery
- Polycystic kidneys
- Potential ureteral obstruction
- Neuropathic bladder
- Unusual infecting organism
- Poor response to treatment
- Diabetes mellitus



- **IVP/CT SCAN**
- **Voiding cystourethrograph**
- **Cystoscopy**

Manual pelvic and Digital Rectal examination





UTI - management

- **Symptomatic UTI-** antibiotic therapy
- **Asymptomatic UTI-** no treatment required except in special situations.
- **Non- specific therapy:**
  - more water intake.
  - Maintaining acidity of urine by fluids like canberry juice.

Anti-microbial therapy

- **Goals of therapy:**
  - ✓ Elimination of infection
  - ✓ Relief of acute symptoms
  - ✓ Prevention of recurrence and long term complications

- Decision to hospitalize ??

- Treatment considerations ??

- **Ideal antibiotic for UTI :**
  - Adequate coverage over E.coli
  - Concentration in urine
  - Duration of therapy
  - Low resistance
  - Cost
  - Low adverse effect profile

Principles of anti microbial therapy

- Levels of antibiotic in urine but not in blood
- Blood levels of antibiotic – important in pyleonephritis
- Penicillins and cephalosporins – drugs of choice for UTI with renal failure.

Treatment duration

- Single dose therapy
- 3 day course
- 7 day course
- 10 – 14 day course

Single dose therapy

Trimethoprim- sulfamethaxole
Amoxicillin- clavulnate 500mg
Ciprofloxacin 500mg
Norfloxacin 400mg

- For uncomplicated UTI
- Not for patients with
  1. past history of complicated UTI
  2. history of antibiotic resistance
  3. history of relapse with single dose
- advantages: compliance, cost, less side effects, less resistance
- Disadvantages: increased recurrence or relapse

3 day therapy

- Efficacy same as 7 day therapy with less adverse effects
- Drugs used include
  1. quinolines
  2. TMP-SMZ
  3. betalactam antibiotics

- Extended release ciprofloxacin 500mg for uncomplicated UTI 1000mg for complicated UTI

7 day therapy

- Used less for uncomplicated UTI
- Useful in
  1. recurrent cases
  2. pregnancy
  3. UTI with other risk factors

14 day therapy

- For complicated UTI
- High risk of mortality and morbidity

Antibiotics	Dose	Therapy Duration	Comments
Acute Uncomplicated Cystitis			
Recommended Agents			
Nitrofurantoin[a] monohydrate/ macrocrystal	100 mg PO BID	5 days	
Trimethoprim/sulfamethoxazole[c]	160/800 mg PO BID	3 days	
Trimethoprim	100 mg PO BID	3 days	
Fosfomycin	3 g PO once	Once	
Alternative Agents			
Amoxicillin/clavulanate	500/125 mg PO q8hr	5–7 days	
Cefpodoxime proxetil	100 mg PO BID	5–7 days	
Cefdinir	300 mg PO BID	5–7 days	
Cephalexin	500 mg PO BID	5–7 days	Widely used, but limited data
Ciprofloxacin[b]	250 mg PO BID	3 days	
Levofloxacin[b]	250–500 mg PO daily	3 days	

Acute Uncomplicated Pyelonephritis			
Recommended Antibiotics for Outpatient Management			
Ciprofloxacin[b]	500 mg PO BID	7 days	If local FQ resistance is > 10%, give ceftriaxone 1 g IV once or a dose of an aminoglycoside[g] pending culture results
Ciprofloxacin[b]	1 g ER PO daily	7 days	
Levofloxacin[b]	750 mg PO daily	5 days	
Alternatives or Definitive Therapy after susceptibility is confirmed			
Trimethoprim/sulfamethoxazole[c]	160/800 mg PO BID	14 days	Give ceftriaxone 1 g IV once or aminoglycoside[g] pending culture results
Cefpodoxime proxetil	200 mg PO BID	10–14 days	
Amoxicillin/clavulanate	500 mg PO TID	10–14 days	
Inpatient management or in those unable to take oral medications			
Ciprofloxacin	400 mg IV q12hr	7 days	May add aminoglycoside[g] pending culture results. Complete the course with PO antibiotics after afebrile for 48 hr
Levofloxacin	500 mg IV q24hr	7 days	
Ceftriaxone	1 g IV q24hr	14 days	
Cefepime	1–2 g IV q12hr		
Piperacillin/tazobactam	3.375 g IV q6hr		

Acute Complicated Cystitis or CA-UTI without upper tract symptoms			
Recommended Empiric Therapy			
Ciprofloxacin	500 mg PO BID	5–7 days	Empiric therapy on the basis of local antibiotic resistance patterns; then streamline on the basis of cultures and treat for 5–7 days
Ciprofloxacin	1 g ER PO daily	5–7 days	
Levofloxacin	750 mg PO daily	5–7 days	
Ampicillin/sulbactam	1.5–3 g IV q6hr		
Ceftriaxone	1 g IV q24hr		
Gentamicin/tobramycin	3–5 mg/kg IV once		
Pathogen-specific treatment	If susceptible, Nitrofurantoin, trimethoprim/sulfamethoxazole, fosfomycin, or PO β-lactams for 7 days		
ESBL *E. coli* Nitrofurantoin or fosfomycin		7 days	

Pathogen specific treatment

Pathogen	Treatment options
Escherichia coli	Ceftriaxone 50mg/kg i.v /I.M Qday
Pseudomonas aeroginosa	Gentamycin 6-7.5mg /kg i.v Q8hr / Qday
Klebsiella sps Enterobacter sps Proteus sps	Ceftadizine 100-150mg/kg/day i.v Q8hr
Enterococcus sps	Ampicillin 100-200mg/kg/day Q6hr

Acute pyelonephritis

- Parenteral antibiotics

  Cefuroxime – 750mg i.v. Q8h Gentamycin - 80-120g i.v. Q12h Ciprofloxacin – 200mg i.v. Q12h

- 10-14 days treatment

- Ceftazimide, imipenam, ciprofloxacin – for hospital acquired pyelonephritis

Asymptomatic bacteriuria

- **C**hildren – treatment same as symptomatic bacteriuria
- Adults –

  treatment required in cases of

  a. pregnancy
  b. patient with obstructive structural abnormalities

Bacteriuria in pregnancy

- To prevent risk of pyelonephritis
- 7 day course with following antibiotics
  - Cephalaxin
  - Nitrofurantoin
  - Amoxicillin
- Therapy continued at regular intervals of pregnancy.

Relapsing UTI

- 7-10 day course
- If fails – 2week course / 6week course

- Structural abnormalities corrected by surgery
- 6week course –
    a. children
    b. adults with continuous symptoms
    c. high risk of renal damage

Prophylaxis for urinary tract infection

Given when:

- Women of child bearing age have recurrent cystitis.
- Catheterization or instrumentation inflicting trauma to the lining of the urinary tract is performed; bacteremia frequently occurs and injured lining is especially susceptible.
- Indwelling catheters are placed.
- Uncorrectable abnormalities of the urinary tract are present.
- Inoperable prostate enlargement or other chronic obstruction causes urinary stasis.

The most frequently used drugs for prophylaxis of lower UTI are:

- Cotrimoxazole 480 mg*
- Nitrofurantoin 100 mg*
- Norfloxacin 400 mg*
- Cephalexin 250 mg*

* All drugs are given once daily at bed time.

Surgical treatment

- Surgical removal of renal calculi, bladder calculi
- Treatment of anatomic obstruction

Conclusion

- Urinary tract infections are the 2nd most common bacterial infections.
- Women are the most infected subjects in the population.
- Development of resistance to antibiotics by the bacteria result in problems during the treatment and lead to relapse or recurrence.
- Recent advances such as development of immunologicals like intranasal vaccines may result in life time cure of the infection