URINARY TRACT INFECTION

Points to be covered in this topic

1. INTRODUCTION
2. CLASSIFICATION OF DRUGS
3. TREATMENT OF UTI

❑ INTRODUCTION

- A urinary tract infection, or UTI, is an infection in any part of your urinary system, which includes your **kidneys, bladder, ureters, and urethra.**
- It may be **acute or chronic.**
- **Urinary antiseptics** are drugs which exert antibacterial activity only in the urinary tract (and no systemic activity).
- They include **Nitrofurantoin and Methenamine mandelate.**
- Most UTIs are caused by **gram-negative bacteria,**
- **Significant bacteriuria :** presence of at least 10^5 bacteria/ml of urine
- **Asymptomatic bacteriuria :** bacteriuria with no symptoms.
- **Urethritis:** infection of anterior urethral tract.
- **Cystitis:** infection to urinary bladder

❖ Sign and symptoms

i. **Urgency, frequency, burning, pain on urination, nocturia.**

ii. **Pain and spasms in the region of bladder.**

iii. **Pyuria (WBC in urine).**

iv. **Haematuria, bacterial colony count increases.**

- **UTI may present itself in acute or chronic form**

  i. **Acute infection**

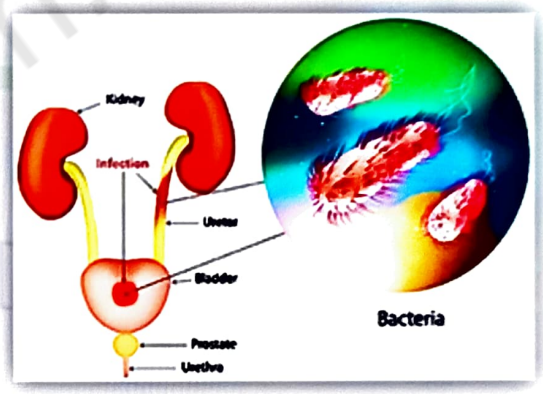
  ii. **Chronic infection**

i. Acute infection

- Infection localized to the **urethra and bladder (cysto-urethritis, lower UTI)** causes **increased frequency** and **urgency of micturition, dysuria and pain in the perineum.**
- **Fever, chills and leukocytosis** are generally **absent.**
- Urine is usually loaded with **pus cells.**
- Urine culture is positive and shows **bacteriuria'.**

ii. Chronic infection

- Patients with chronic infection may have few urinary symptoms un less renal failure has supervened, when **polyuria** may be present. .
- **Chronic pyelonephritis** is cause of **hyper tension** and **chronic renal failure.**
- The urine show a **few pus cells.**



UTI Terminology

i. **Acute pyelonephritis:** infection of one/both **kidneys**; sometimes **lower tract also- pyuria, fever, pain, micturition**

ii. **Chronic pyelonephritis:** particular type of pathology of **kidney** may not be due to infection.

iii. Uncomplicated : UTI without underlying **renal** or **neurologic disease.**

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

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

vi. Reinfection :

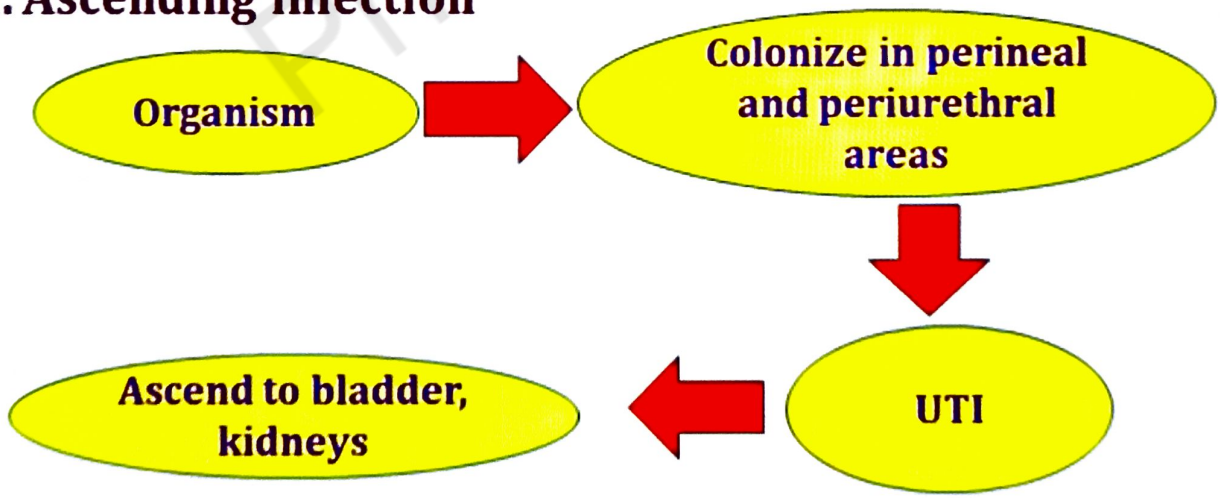
- **Recurrent UTI** caused by same species causing **original UTI** within **2 wks after therapy**

Pathophysiology

➢ **There are four routes of bacterial entry to urinary tract.**

i. **Ascending infection**
ii. **Blood borne spread (Hematogenous spread)**
iii. **Lymphatogenous spread**
iv. **Direct extension from other organs**

i. Ascending infection



ii. Hematogenous spread

- Blood borne spread to **kidneys.**
- Occurs in bacteremia mostly **S . Aureus**

iii. Lymphatogenous spread

- **Men-** Through **rectal and colonic lymphatic vessels to prostrate and bladder**
- **Women-** Through **peri uterine lymphatic's to urinary tract.**

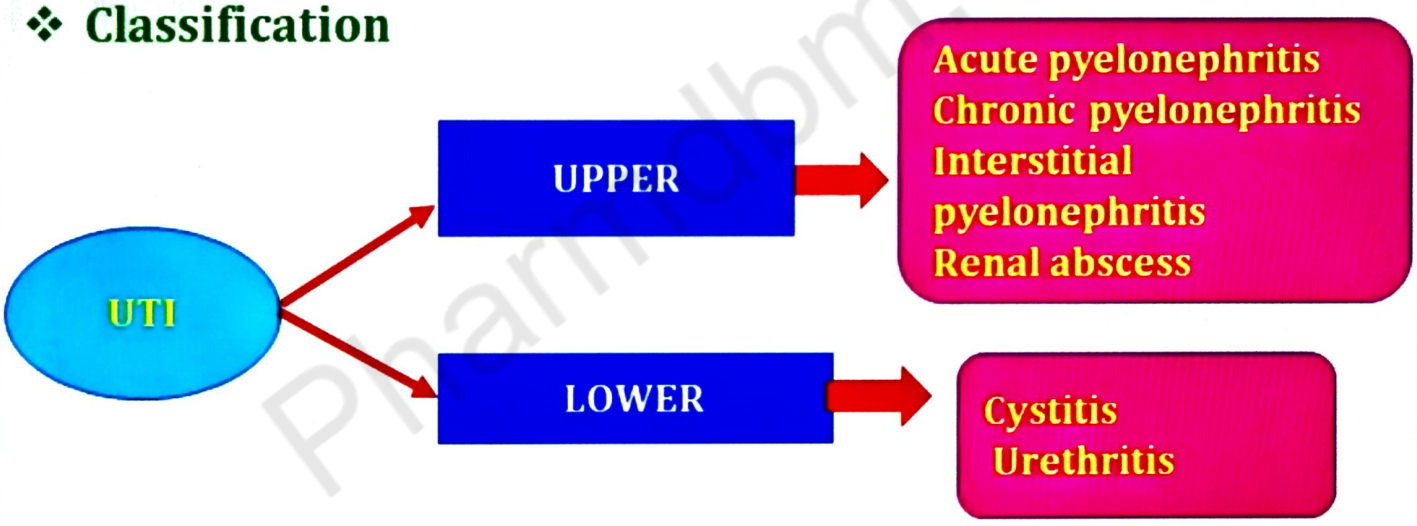
iv. Direct extension from other organs

- **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**

❖ Classification



❖ Goals for the treatment of UTI are:

(a) Symptomatic relief by monitoring the **pH of urine or** giving **Phenazopyridine.**

(b) Therapy of the infecting organisms.

(c) Prevention and treatment of recurrence

(d) Identification and treatment of **congenital** and acquired abnormalities of the **urinary tract** and any other predisposing factors such as **diabetes mellitus.**

❑ CLASSIFICATION OF DRUGS

Bacteriostatic agents	**Nitrofurantoin** **Sulfonamides** **Methenamine Mandelate** **Nalidixic acid** **Tetracyclines**
Bactericidal agent	**Cotrimoxazole** **Ampicillin** **Extended spectrum penicillins** **Aminoglycosides** **Fluoroquinolones** **Cephalosporins**

1.Bacteriostatic agents

Urinary antiseptics are the drugs which act as antibacterial agents only in the **urinary tract** **(nitrofurantoin, methenamine mandelate and nalidixic acid).**

i. Nitrofurantoin

- It is **bacteriostatic,** but at higher concentrations.
- It may be **bactericidal.**
- It is effective against many **gram-positive** and **gram-negative bacteria.**

❖ Mechanism of action

- Nitrofurantoin is **activated inside bacteria by reduction** via the **flavoprotein nitrofurantoin reductase** to **unstable metabolites,** which **disrupt ribosomal RNA, DNA** and other **intracellular components.**

❖ Pharmacokinetics

i. It is rapidly and completely absorbed from the **gut.**

ii. Plasma **t½ is 0.3–1 hr.**

❖ Adverse Effect

i. Nitrofurantoin may cause **nausea ,vomiting , diarrhoea , allergic reactions and rarely chronic-active hepatitis.**

ii. Nitrofurantoin turns the **urine dark brown** by its metabolites.

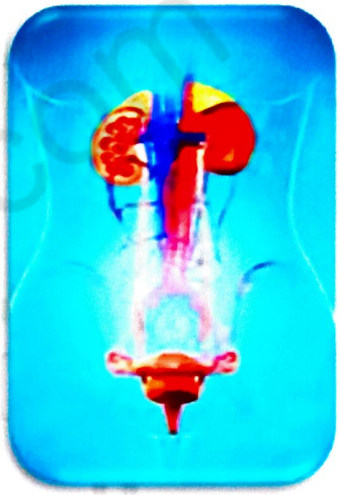
iii. **Pneumonitis and interstitial pulmonary fibrosis** may occur after long term which may be due to generation of oxygen radicals in the lung.

iv. **Neurological disorders** due to the formation of toxic metabolites in the body.

v. Haemolytic anaemia can occur in g6pd deficient individuals.

Dose: 50–100 mg 6 hrly, furadantin 50, 100 mg tab 25 mg/5 ml sus

❖ Uses



i. Nitrofurantoin is an useful in **acute UTI.**

ii. Long-term suppression of **chronic UTI (single dose 100 mg at bedtime) and for prophylaxis of UTI**

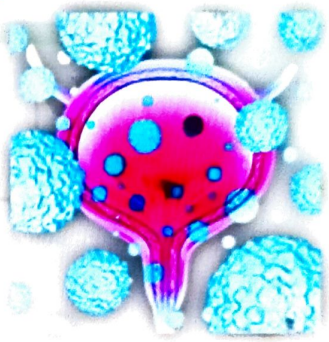
ii. SULFONAMIDES:

- Sulfonamides are effective against urinary pathogens including **E. coli.**
- They produce effective **urine and tissue levels.**
- Bacterial resistance is the major problem with these drugs
- short acting sulfonamide such as **sulfisoxazole** (which is bactericidal in the urine because of high concentration) should be administered in a dose of 2 g. initially, followed by **1 g. 6 hourly daily for 7-10 days.**
- Urinary pH should be **alkaline during such therapy** and fluid intake must be liberal.
- This initial treatment may be followed by **1 g. daily** for several months (chronic suppressive therapy).

iii. Methenamine Mandelate

- Methenamine (hexamine) mandelate, a **salt of mandelic acid and methenamine.**
- It is releases **formaldehyde in acidic urine below pH 5.5.** Formaldehyde is bactericidal and resistance does not develop to it.
- **Acidic pH of the urine** should be maintained by using **ascorbic acid, mandelic acid** or **hippuric acid.**
- Acidic pH is **bacteriostatic**—an added advantage of maintaining **low pH**
- **Urea splitting microorganisms** like **proteus** may counter the effects of **methenamine by raising the urinary pH .**
- Methenamine is used to **prevent or control returning urinary tract infections caused by bacteria.**
- **Dose: 1 g 3–4 times a day. MANDELAMINE 0.5 g, 1 g tab.**

❖ Adverse Effect

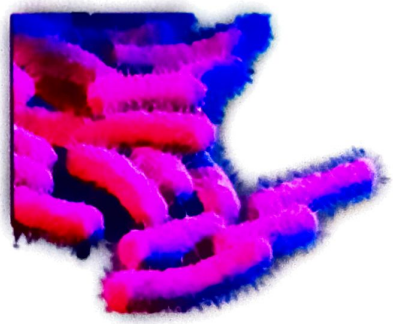


i. **Haematuria**
ii. **Chemical cystitis**
iii. **Painful micturition.**

- Methenamine mandelate should be **avoided in renal failure as mandelic acid** adds to acidosis

❖ Uses

- Methenamine mandelate is used orally in **chronic UTI** that is resistant to other drugs.



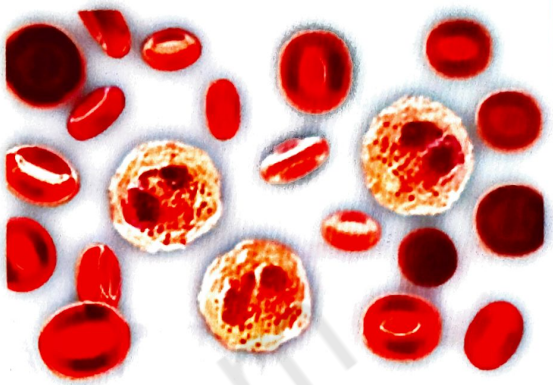
iv. Nalidixic acid

- (Neg-gram)
- It is a **4-quinolone derivative.**
- Nalidixic acid is effective against certain **gram negative bacteria,** especially **E. Coli** and **shigella.**

❖ Pharmacokinetics

- Nalidixic acid is readily **absorbed from the gastrointestinal tract.**
- Eliminated in the urine within 8 hours.
- It is present in the urine in both active (20 per cent) and inactive, conjugated (glucuronide)forms.

❖ Adverse reactions



i. **Allergic reactions**

ii. **Nausea, vomiting and diarrhoea.**

iii. **Pruritus, rash, urticaria, fever,**

iv. **Eosinophilia**

v. **Photosensitivity.**

vi. **CNS** include **headache, malaise, drowsiness and myalgia.** **Convulsions** may appear with over dosage, in children.

vii. It may cause **hemolytic anemia** which has been reported in a **two week old baby fed on breast milk,** due to the **presence of the drug in the breast milk.**

v. Tetracyclines

- They are used only on the basis of sensitivity report and in **Ch.Trachomatis cystitis.**

❖ Mechanism of action

- Tetracyclines interfere with **protein synthesis by blocking the attachment of aminoacyl transfer RNA to the acceptor site on the messenger RNA-ribosome complex.**
- Tetracyclines chelate cations like **calcium and magnesium.**

❖ Tetracycline resistance

- **Staphylococci, Group A Streptococci, H. influenzae, Pneumococci, and E. coli**

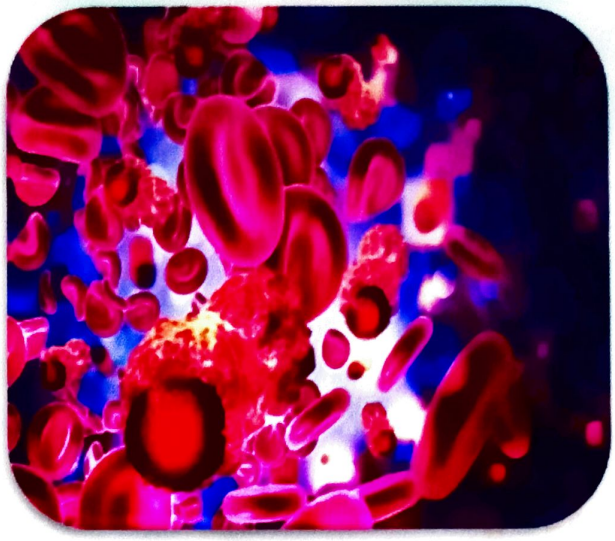
❖ Pharmacokinetics

i. It is rapidly and completely **absorbed from the gut.**

ii. Plasma **t½ is 0.3–1 hr.**

iii. Metabolised in **liver**

iv. Excreated in **urine**



❖ Adverse Effect

i. Skin rashes

ii. **Anaphylactic shock**

iii. **Blood dyscrasias**

❖ Uses

i. Treatment UTI

2. Bactericidal agent

i. Cotrimoxazole (Septran, Bactrim)

- This combination of **sulfamethoxazole and trimethoprim** is a potent and cost-effective bactericidal combination against many common urinary tract pathogens predominantly **E. coli** and **Proteus** species **but not Pseudomonas.**
- Cotrimoxazole may be used in **acute UTI** without bacteriological data including **chlamydia trachomatis**, are covered by **Cotrimoxazole.**
- **Given once daily at bed time,** Cotrimoxazole 480 mg used for prophylaxis of **recurrent cystitis** in women, as well as in catheterized patients.
- It should **not be used to treat UTI during pregnancy.**
- In **acute uncomplicated UTI**, it is used in the dose of **2 tablets twice a day for 7-10 days.**

- As trimethoprim has been reported to be **teratogenic in animals.**
- It should be **avoided during pregnancy.**
- Renal insufficiency leads to retention of trimethoprim and can alter the optimum **1:5 ratio of trimethoprim to sulfamethoxazole in urine**.
- In **smaller doses (as low as one tablet twice a week)** it has been showed to be effective in **eliminating chronic bacteriuria.**

ii. Ampicillin/Amoxicillin

- Ampicillin is effective both **orally and parenterally.**
- It is bactericidal **to E. Coli, Aerobacter** and certain strains of **proteus.**
- Pseudomonas is resistant to it and it is **ineffective against penicillinase producing strains of staph. Aureus.**
- It produces good tissue levels and is **excreted unchanged in the urine** in high concentrations.
- It is well tolerated.
- It is useful for treatment of **UTI in pregnant women.**
- Many infections with **E. Coli**, especially those acquired in the hospital, are found to be resistant to ampicillin.
- **Drug of first choice in UTI.**
- Many E. coli strains are now **ampicillin-resistant. Amoxicillin + clavulanic acid** is more frequently used.

iii. Carbenicillin

- Dose of **1 gm. four times a day**, it is useful in **pseudomonas pyocyanea infection** of the urinary tract in which it is **combined with gentamicin.**
- **They not be mixed in the same vial or syringe** because **carbenicillin inactivates gentamicin.**

iv. Piperacillin

- It has a **broad spectrum of activity against gram negative organisms**, especially **Ps. aeruginosa.**
- It is given IV daily, adult **doses of 4-8 g.** for moderate infections in persons with normal renal function; the dose is raised to **12-16 g/day** in life threatening infections.
- It can be **combined with gentamicin with synergistic effects**.
- It is use should be limited to severe, UTI with life threatening **septicemia.**
- **Piperacillin/Ticarcillin** antibiotics are used only in **serious Pseudomonas infection** in patients with **catheters or chronic urinary obstruction (prostatic hypertrophy)**

vi. Aminoglycoside antibiotics

- **Gentamicin and Amikacin** are the aminoglycosides commonly used in UTI.
- They are effective against **E. coli, Proteus and Pseudomonas.**

❖ Adverse effect

i. **Ototoxicity , Renal toxicity ,Nephrotoxicity**

- Their use should be reserved for **complicated UTI.**

vii. Fluoroquinolones

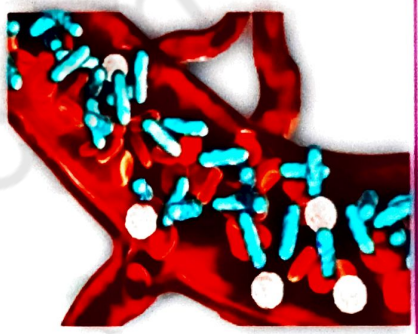
- Fluoroquinolones are considered ideal agents for **nosocomial pyelonephritis** and **complicated UTI.**
- The first generation FQs, especially **ciprofloxacin and Ofloxacin** are highly effective and currently the most popular drugs, because of potent action against **gram-negative bacilli and low cost.**
- Norfloxacin given for up to **12 weeks** may achieve cure in **chronic UTI.**
- The **FQs should not be given to pregnant women.**

viii. CEPHALOSPORINS

- These drugs are valuable in infections with **E. coli** and **Proteus** resistant to other antibiotics.
- They are the drugs of choice in **klebsiella infections.**
- The newer cephalosporins are particularly **effective against multi-resistant enterobacteria and Pseudomonas resistant to other antibiotics.**
- Cephalosporins are particularly indicated in **septicemic UTI.**

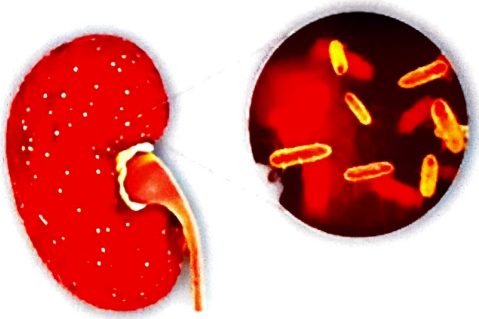
➢ **long-term suppressive treatment of lower UTI are:**

- **Nitrofurantoin 100 mg***
- **Norfloxacin 400 mg***
- **Cephalexin 250 mg**
- **All drugs are given once daily at bed time.**



❑ TREATMENT OF UTI

- **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 cranberry juice or use of ascorbic acid.



❖ Goals of therapy

i. **Elimination of infection**

ii. **Relief of acute symptoms**

iii. **Prevention of recurrence and long term complications**

❖ Principles of anti microbial therapy:

- **Levels of antibiotic in urine but not in blood**
- Blood levels of antibiotic-important in **pyelonephritis**
- **Penicillins & cephalosporins -drugs of choice for UTI with renal failure.**

❖ Anti-microbial therapy

❖ Treatment duration:

i. Single dose therapy

ii. 3 day course

iii. 7 day course

iv. 10-14 day course

➢ Single dose therapy:

- ✓ Trimethoprim- sulfamethaxole
- ✓ Amoxicillin- clavunate 500mg
- ✓ Amoxicillin 3gm
- ✓ Ciprofloxacin 500mg
- ✓ Norfloxacin 400mg

➢ 3 day therapy:

- Efficacy same as 7 day therapy with less adverse effects
- Drugs used include
  - ✓ Quinoline
  - ✓ TMP-SMZ
  - ✓ beta lactam antibiotics

➢ 7 day therapy:

- ✓ Cotrimoxazole 2 tab BID
- ✓ Ampicillin 250-500 mg
- ✓ Cephalexin 500 mg QID
- ✓ Trimethoprim 100 mg bid

- Used less for acute uncomplicated UTI
- Useful in
  a. Recurrent cases
  b. Pregnancy
  c. UTI with other risk factors

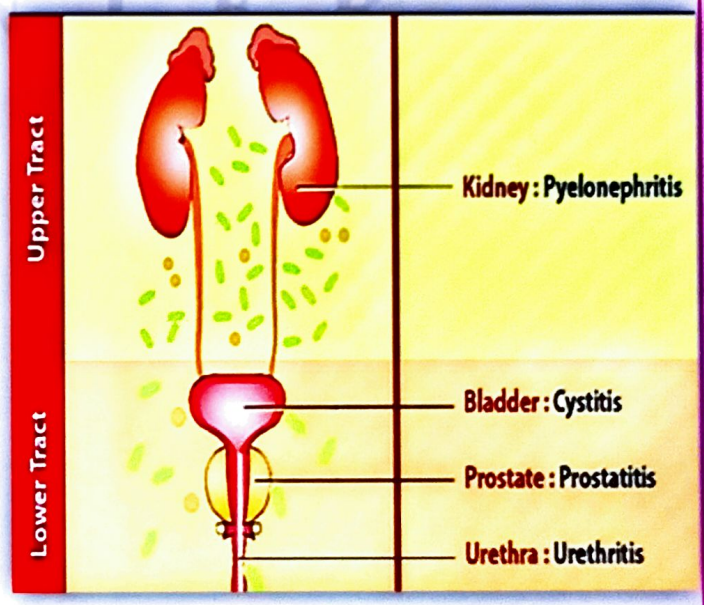
❖ Pathogen specific treatment

PATHOGEN	DRUG FOR TREATMENT
Escherichia coli	Ceftriaxone
Pseudomonas aeruginosa	Gentamycin
Klebsiella species Enterobacter species Proteus species	Ceftazidime
Enterococcus species	Ampicillin

❖ Infection specific treatment

❑ Lower UTI

- ➢ 3day therapy preferred
  - ✓ Trimethoprim
  - ✓ Nitrofurantoin
  - ✓ Ciprofloxacin –Norfloxacin
  - ✓ Amoxicillin
  - ✓ Cephalexin



❑ Acute pyelonephritis

- ➢ Parenteral antibiotics
  - ✓ Cefuroxime - 750mg I.V. Q8h
  - ✓ Gentamycin - 80-120g I.V. Q12h
  - ✓ Ciprofloxacin - 200mg I.V. Q12h
  - ✓ 10-14 days treatment Ceftazidime, Imipenem, ciprofloxacin for hospital acquired pyelonephritis

❑ Asymptomatic bacteriuria

- **Children :**

  Treatment same as symptomatic bacteriuria(No antibiotics)

- **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

- ✓ Cephalexin
- ✓ Nitrofurantoin
- ✓ Amoxicillin

Therapy continued at regular intervals of pregnancy.

❑ Relapsing UTI

7-10 day course

If fails – 2 week course /6 week course

Structural abnormalities corrected by surgery 6 week course:

i. Children

ii. Adults with continuous symptoms

iii. High risk of renal damage

❑ UPPER UTI

1. Acute uncomplicated pyelonephritis :

Drug regimen : Cotrimoxazole /Gentamicin with/without Ampicillin/ Cephalosporins

2. Complicated UTI:

- Minimal symptoms- Cipro. 500mg BD
- Severe illness :Inj. Cefotaxime 2g QID iv & Inj . Genta 5 mg/kg od iv) x 7-14 days

3. Chronic Pyelonephritis :- Choice of drug after AST cause to be searched.

❖ Antibacterial Prophylaxis for UTI

- Single dose of trimethoprim 100mg/nitrofurantoin 50mg
- Long term low dose prophylaxis(beneficial)

i. Phenazopyridine (pyridium, pyridacil)

- This azo dye is used in the dose of 200 mg. three times a day to relieve **pain, burning, urgency** and frequency associated with lower UTI (cystitis, prostatitis and urethritis).
- It does not act as a urinary antiseptic but can give symptomatic relief.
- The drug colours the urine red or orange and can stain clothing.
- Therapy with this drug is generally limited to one week.

❖ Prevention of urinary tract infection

1.Drink plenty of liquids, especially water.

- Drinking water helps dilute your urine and ensures that you'll urinate more frequently allowing bacteria to be flushed from your urinary tract before an infection can begin.

2. Drink cranberry juice.

- Although studies are not conclusive that cranberry juice prevents UTIs, it is likely not harmful

3. Wipe from front to back.

- Doing so after urinating and after a bowel movement helps prevent bacteria in the anal region from spreading to the vagina and urethra.

4. Empty your bladder soon after intercourse. Also, **drink a full glass of water** to help flush bacteria.

5. Avoid potentially irritating feminine products.

- Using deodorant sprays or other feminine products, such as **douches and powders**, in the genital area can irritate the urethra.

SEXUALLY TRANSMITTED DISEASE

Points to be covered in this topic

1. INTRODUCTION
2. CLASSIFICATION OF STD
3. TREATMENT OF STD

❑ INTRODUCTION

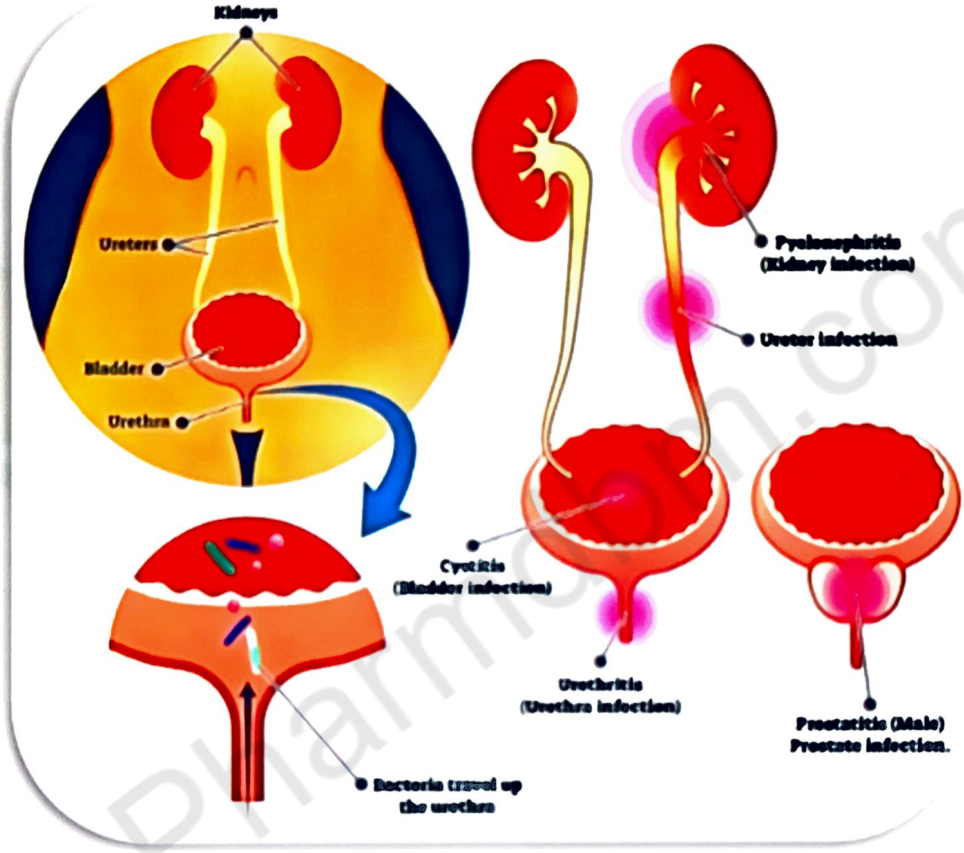
- Sexually transmitted diseases (STDs), or sexually transmitted infections (STIs), are infections that are **passed from one person to another through sexual contact.**
- The contact is usually vaginal, oral, or anal sex.
- Medicine which may treat STD which are caused by- **bacteria. Fungus, yeast** but there is **not yet treatment for virus generated STD** but **medicines** can help the **disease under control.**
- Correct usage of **latex condoms greatly reduces**, but does not completely eliminate, the risk of catching or spreading STDS.

❖ Sign & symptoms

i. **Pain while urination**
ii. **Lower abdominal pain specially in woman**
iii. **Genital discharge in women**
iv. **Discharge from the Genital parts in men**
v. **Pain during sexual intercourse in women**
vi. **Bleeding between periods in women**
vii. **Testicular pain in men**

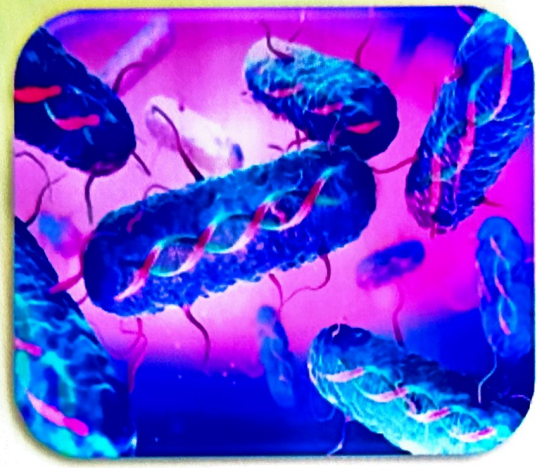
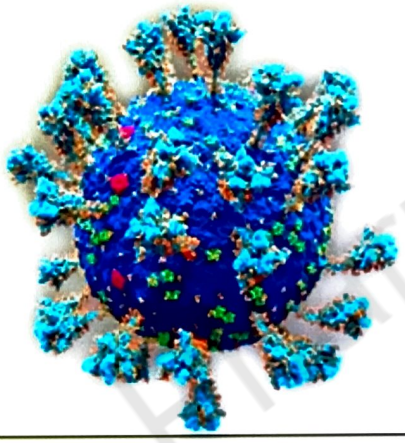
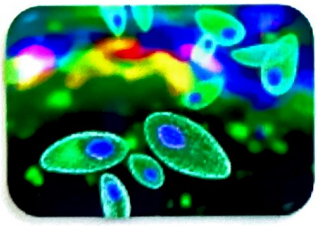
- "Clinical syndromes"
  - ✓ Genital ulcer
  - ✓ Urethral discharge (urethritis)
  - ✓ Vaginal discharge (vaginitis)
  - ✓ Lower abdominal pain (pelvic inflammatory disease)

Each syndrome is then treated with multiple drugs to cover multiple pathogens.



❖ THE IMPORTANT STD ARE

1. **Syphilis**
2. **Gonorrhea**
3. **Chancroid**
4. **Lymphogranuloma venereum**
5. **Granuloma of inguinale**
6. **Vaginitis**
7. **AIDS (acquired immune deficiency disease)**
8. **Non-gonococcal urethritis (NGU)**

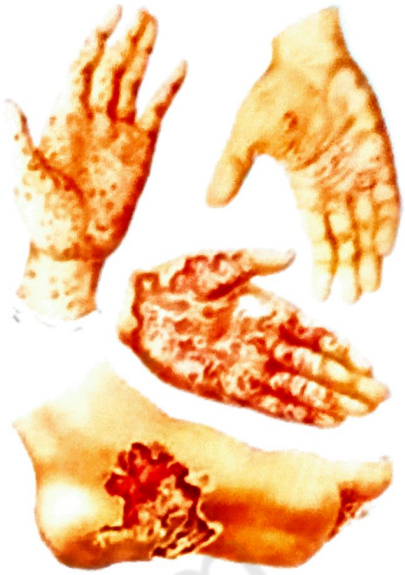
CAUSATIVE AGENTS OF STD	EXAMPLES
STDs caused by Bacteria 	Cancroid (Haemophilus ducreyi), Chlamydia (Chlamydia trachomatis) Gonorrhea (Neisseria gonorrhea). Granuloma inguinal (Calvmmato bacterium granulomatous). Lymph granuloma venereum (Chlamydia trachomatis), Syphilis(Treponema palladium)
STDs caused by Viruses 	Genital herpes (herpes simplex virus) Genital warts (human papillomavirus virus) Hepatitis B and D. (hepatitis viruses, types A-E) HIV/AIDS. Molluscum contagiosum(poxvirus)
STD caused by Protozoan 	Trichomoniasis (Trichomoniasis Vaginalis)
STD's caused by Parasites 	Pubic lice or crabs (Peliculosis pubis), Scabies Sarcoptex scabies

❑ CLASSIFICATION OF STD

Syphilis	Early < 1years	Benzathine penicillin , procaine penicillin , doxycycline & tetracycline if allergy to penicillin
	Late> 1 years	Benzathine penicillin procaine penicillin Increase
Chlamydia trachomatis	Non species urethritis	Azithromycin ,doxycycline , erythromycin
	Lymphogranuloma venereum	
Gonorrhoea (N-Gonorrhoeae)	Non Penicillinase producing	(Amoxicillin/Ampicillin Penicillinase)
	Penicillinase producing	Ceftriaxone , cefixime ,ciprofloxacin , Ofloxacin
Granuloma inguinale /Donovanasis (colymn granulomatis)	Tetracycline, sulfisoxazole, ampicillin ,Azithromycin ,Doxycycline	
Chancroid (H.ducreyi)	Ceftriaxone, azithromycin , erythromycin	
Genital herpes Simplex	Acyclovir, Valacyclovir, Famciclovir	
Trichomonas vaginitis	Metronidazole, Tinidazole, Chine	
Human Papillomavirus(veneral parts)	Imiquimod, Podophyllin, Podofilos, Fluorouracil (5-FU), Trichloroacetic Acid (TCA), Interferon	
HIV/AIDS	Abacavir, Didamosine. Lamivudine, Stavadine , Zalcitabine, Zidovadine, Indinavir, Nelfinavit . Ritonavir, Saquinavir, Lopinavir Plus Ritonavit, Delavindine, Elvirenz, Nevirapine	

Drug Therapy of Syphilis

- Syphilis is caused by the spirochete **Treponema Pallidum.**
- **Penicillin** is the drug of choice in the therapy of all stages of syphilis.
- Penicillin resistant **T. Pallidum** is so far unknown.
- The classic **Oslo studies (1891-1951)** helped to divide the natural history of untreated syphilis into **'Early' and 'late' stages.**



➢ Syphilis can present in one of four different stages: **primary, secondary, latent, and tertiary.** It may also occur congenitally.

1.Primary Syphilis: (3-90 days after the initial exposure)

- A skin lesion appears at the point of contact called a **chancre (single firm, painless, non itchy skin ulceration)**. Lesions outside of the genitals may be painful.

2. Secondary Syphilis: (4-10 weeks after the primary infection)

- **Reddish-pink non-itchy rash** on the trunk and extremities including the **palms and soles**. Other symptoms may include **fever, sore throat, malaise, weight loss , hair loss, and headache.**

3. Tertiary Syphilis: (3-15 years after the initial infection)

- Divided into three different forms: late **neurosyphilis, cardiovascular syphilis, and gummatous syphilis** (soft, tumor-like balls of inflammation).

4.Congenital Syphilis:

- May occur during pregnancy or during the birth process. Common symptoms include:
- **Hepatosplenomegaly ,**
- **Rash, fever, neurosyphilis , and pneumonitis.**

- **Primary and secondary syphilis and latent syphilis of less than one year's duration**:
  - **Procaine penicillin 600,000 units** IM daily for 8 days;
  - **Benzathine penicillin 2.4 mega units IM** (1.2 mega units in each buttock) in a single dose. Benzathine penicillin is likely to be painful.
  - Patients who are allergic to penicillin should be treated with **tetracycline or erythromycin 500 mg.** orally, four times a day, on empty stomach, or with **doxycycline 100 mg.** twice a day for 15 days.
- **Syphilis (except neurosyphilis) of more than one year's duration (latent, cardiovascular or late benign):**

  (a)Procaine penicillin 600,000 units IM daily for 15 days;

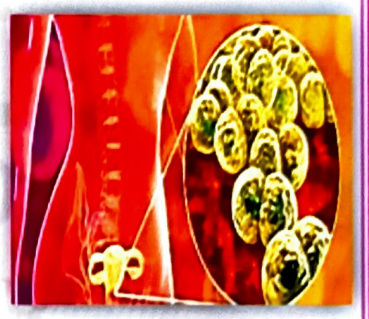
  (b)Benzathine penicillin 2.4 mega units I Monce a week for 3 weeks.

  (C) Patients allergic to penicillin should be treated with **tetracycline or erythromycin, 500 mg.** orally, **four times a day**, on empty stomach or with doxycycline 100 mg. twice a day for 30 days.
- **Pregnancy and syphilis**
  - Congenital syphilis is a completely preventable disease. Hence, syphilis detected during pregnancy should be treated with any of the **regimes of penicillin.**
  - **Patients allergic to penicillin** should be treated with **erythromycin** but not with **tetracycline.**
- **Congenital syphilis** detected in **infants and children** can be treated by injecting procaine **penicillin in the dose of 100,000 units** daily for 10 days
- **Jarish-Herxheimer reaction**
  - Jarisch Herxheimer reaction (JHR) is **a transient clinical phenomenon that occurs in patients infected by spirochetes who undergo antibiotic treatment.**
  - The reaction occurs within 24 hours of antibiotic treatment of spirochete infections, including syphilis, leptospirosis, Lyme disease, and relapsing fever.

- In **cardiovascular and neurosyphilis**, however, a **Herxheimer reaction** may precipitate **severe angina or congestive cardiac failure**; and **psychosis, convulsions, coma or optic atrophy** respectively..

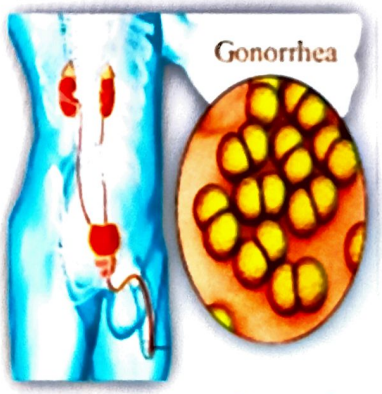
Drug Therapy of Gonorrhea

- Gonorrhoea is caused by **gonococci**, most strains of which remain **sensitive to penicillin**; however some strains are **resistant to penicillin** (penicillinase-producing N.gonorrhoeae, PPNG), to **tetracycline** (tetracycline-resistant gonorrhoeae, TRNG), or to **penicillin, tetracycline, spectinomycin and/or others** (chromo somally mediated resistant N.gonorrhoeae, CMRNG).
- Eradication of acute, uncomplicated gonococcal infection caused by penicillin sensitive organisms is easy.



❖ Symptoms of gonorrhea

- **Greater frequency or urgency of urination.**
- **A pus-like discharge or drip from your penis (this discharge could be yellow, white, beige, or greenish)**
- **Discoloration and swelling at the penis opening.**
- **Testicular swelling or pain.**
- **Itching and soreness in your anus.**
- **Rectal bleeding or discharge.**



- Gonococcal infection is **more difficult to diagnose** and treat in **females than in males.**
- Acute pelvic inflammatory disease **(PID)** may be caused by other **organisms (chlamydia trachomatis, mycoplasma hominins, vaginal flora including anaerobes, gram-negative organisms such as E.Coli, and group B streptococci.)**

❖ **Acute uncomplicated cases :**

- The response to treatment is usually **prompt and dramatic.**
- **7 day course of doxycycline 100 mg. twice a day.**

❖ **Antimicrobial regimens for acute uncomplicated gonorrhoea**

- **Penicillin G** (aqueous) 4.8 mega units, injected in two divided doses, at two different sites, at one visit, 30 minutes after 1 g. of probenecid orally.
- **Ampicillin** 3.5 g. orally, a single dose preceded by 1 g. of **probenecid.**
- **Procaine penicillin** 1.2 mega units plus penicillin G 1 mega units IM, followed by two similar injections, 24 hours apart.
- **Cotrimoxazole** 2 tablets twice daily for 5 days, or 4 tablets twice daily for two days. It does not mask syphilis.
- **Ciprofloxacin** 500 mg. orally, single dose.
- **Ceftriaxone** 125-250 mg. IM, single dose.
- **Cefixime** 400 mg, orally, single dose;.
- **Spectinomycin** 2 g. IM, single dose.

❖ **Complicated cases :** The other measures that may be needed in these patients are **surgery, local irrigation with antiseptic lotions, local heat** and **prostatic massage**

❖ **Antimicrobial regimens for complicated gonorrhoea**

- **Procaine penicillin 2 mega units** daily for 10 days **plus tetracycline 0.5 g. QID (or doxycycline 100 mg. BID) for 14 days.**
- **Cefoxitin** IV 2 g. every 6 hours plus **doxycycline IV 100 mg.** every 12 hours; continue drugs IV for at least 48 hours after substantial clinical improvement; then, **continue doxycycline orally 100 mg. BID** to **complete 14 days of total treatment.**

- **Gentamicin IV or IM 2 mg/kg** (loading dose) followed by 1.5 mg/kg every 8 hours (in patients with normal renal function) + **clindamycin 900 mg.** IV every 8 hours; 48 hours after the patient shows substantial clinical improvement, change over to oral doxycycline 100 mg. 12 hourly, to complete 14 days of total treatment.
- **Ofloxacin orally 400 mg. BID** for 14 days + **clindamycin orally 450 mg.** QID for 14 days (or metronidazole orally 500 mg. BID for 14 days).

Drug Therapy of Chancroid

- Chancroid or soft sore is caused by **H.ducrei .**
- The diagnosis is made by clinical findings and a specific **skin test.**
- The treatment of choice is **erythromycin 500 mg. orally four times a day for 7-10 days.**
- Alternative regimens are **Cotrimoxazole 2 tablets twice a day for 7 days**; **ciprofloxacin 500 mg. orally twice a day for 3 days**; and **ceftriaxone 250 mg. IM single dose.**

Drug Therapy of Lymphogranuloma Venereum

- Disease is caused by **chlamydia.**
- **Tetracycline 0.5 g. six hourly or doxycycline 100 mg twice a day for 21 days** is effective in curing the **acute inguinal disease.**
- **Chronic hypertrophic type, surgery may be needed** in addition to **tetracyclines for 6-8 weeks.**
- **Sulfonamides** are also as effective as tetracyclines in this infection. Alternatively, erythromycin may be used.

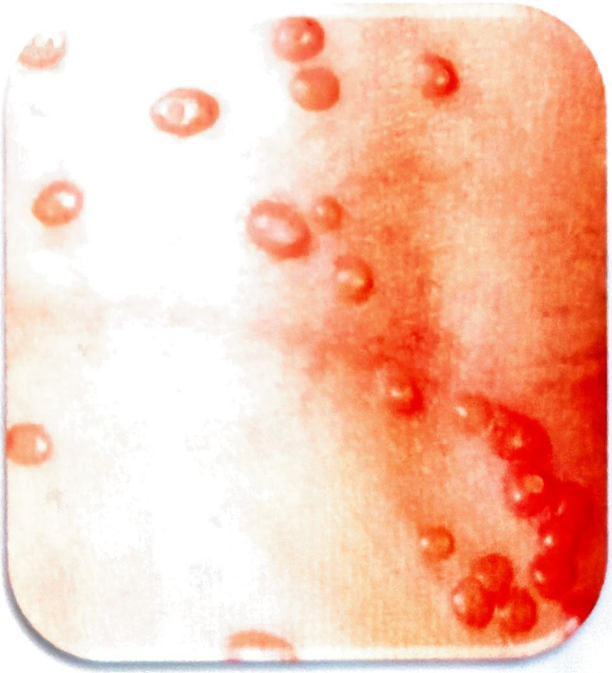
Drug Therapy of Granuloma Inguinale

- Granuloma inguinale is caused by **Donovania granulomates.**
- This infection responds well to **tetracycline, sulfisoxazole or ampicillin** orally in the dose of **500 mg.** 6 hourly for 3-4 weeks; and to **Cotrimoxazole 2 tablets twice daily.**

Drug Therapy of Venereal Warts

- The warts grow rapidly in the **presence of moisture** and are **inhibited by dryness.**
- The surrounding skin must be **protected from podophyllum by application of soft paraffin.**
- **Cryotherapy with liquid nitrogen** is also effective.
- **Imiquimod 5 % cream,** applied three times a week has been shown to eradicate about 50% of these anogenital warts.

- It acts by inducing the local production of **interferon alpha** alone with pro-inflammatory **cytokines interleukines 1, 6 and 8, and TNF alpha.**
- **Imiquimod (1% cream) applied three times a day for 5 days** a week also resolves the lesions of **Molluscum contagiosum .**



Vaginitis Drug Therapy

This is a common condition predominantly caused by 3 types of organisms

- ✓ **C. albicans (yeast)**
- ✓ **T. vaginalis (Trichomonas)**
- ✓ **Gardenerlla vaginalis (bacteria)**

➢ **Single dose regimens for treatment of STDs**

- **Syphilis (early) :- Benzathine penicillin 2.4 mega units** in two IM injections, one on each buttock, during one clinic visit
- **Gonorrhoea** :- complicated & non complicated
- **Chlamydial NGU :- Azithromycin 1 gm orally.**
- **Chancroid :- Azithromycin 1 gm or Ciprofloxacin 500 mg** orally OR **Ceftriaxone 250 mg IM.**
- **Trichomonias:- Metronidazole 2 gm orally.**

Single dose regimen is not recommended for: **lymphogranuloma venereum** and **granuloma inguinale.**

Drug Therapy of Non- gonococcal Urethritis (NGU)

- STD is caused by **Chlamydia trachomatis.**
- The treatment of choice is **doxycycline 100 mg. twice a day** or **tetracycline 500 mg. six hourly, for 7 - 14 days.**
- **Erythromycin 500 mg. six hourly, for 7 days** may also be effective but is likely to be inadequate for gonorrhoea.

AIDS-Drug Therapy

- **Acquired immunodeficiency syndrome (AIDS)** results from infection with **human immunodeficiency virus (HIV)—a retrovirus.**
- These are drugs active against human immunodeficiency virus (HIV) which is a retrovirus.

CLASS	DRUGS
Nucleoside reverse transcriptase Inhibitors (NRTIs)	Zidovudine, Didanosine, Stavudine, Lamivudine, Abacavir, Emtricitabine, Tenofovir
Non-nucleoside reverse transcriptase Inhibitors (NNRTIs)	Nevirapine, Efavirenz, Delavirdine, Etravirine, Rilpivirine
Protease inhibitors (Pls)	Ritonavir, Atazanavir, Indinavir, Nelfinavir, Saquinavir Fosamprenavir, Lopinavir, Darunavir

1.Nucleoside reverse transcriptase Inhibitors (NRTIs)

- These **drugs after entering.**
- HIV infected cells, are **converted to active triphosphate ZIDOVUDINE formed by cellular kinase** and **competitively inhibits HIV reverse transcriptase.**
- They get incorporated into **the growing viral DNA** and cause **termination of chain elongation of proviral DNA.**

1. Zidovudine

- Zidovudine was the **first antiretroviral drug** approved for the treatment of **HIV infection.**
- It is the **prototype drug of NRTIs.**
- Zidovudine is **effective against HIV-1 and HIV-2.**
- It protects the **uninfected cells from HIV**, but has **no effect on HIV-infected cells.**
- Zidovudine is a **thymidine analog, active against HIV infections** and other retroviruses.

❖ Mechanism of action

- Zidovudine phosphorylated in **the host cell -zidovudine triphosphate** selectively **inhibits viral reverse transcriptase** in preference to **cellular DNA polymerase.**

- **MOA of Tenofovir is a nucleotide analog** and **competitively inhibits HIV reverse transcriptase** similar to nucleoside analogs.

❖ Pharmacokinetics

- Oral absorption of AZT is rapid, but **bioavailability is ~65%.**
- Cleared by **hepatic glucuronidation (t½ 1 hr)**

- **Excreted in urine- Plasma protein binding is 30%** and CSF level is ~50% of that in plasma.
- It crosses **placenta** and is found in **milk**

❖ Adverse effect

i. **Anaemia,**

ii. **Granulocytopenia**

iii. **Myopathy, peripheral neuropathy and pancreatitis.**

iv. **Lactic acidosis** and **hepatic steatosis** are rare but can be fatal.

v. Toxicity is due to **inhibition of DNA polymerase in human cells** though to a small extent

vi. **Bone marrow suppression**

❖ Uses

i. Zidovudine is used in **combination with other antiretroviral drugs** for the **treatment of AIDS.**

ii. It is also used for **post-exposure prophylaxis (PEP)** and to prevent vertical transmission of HIV.

ii. Didanosine

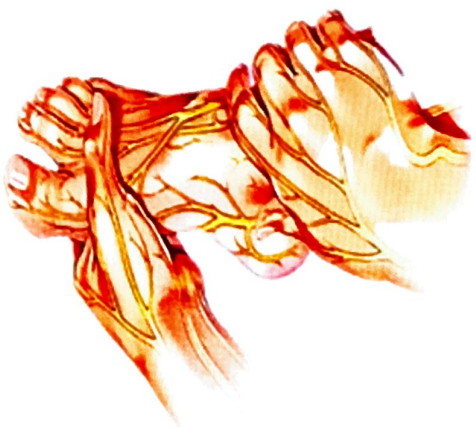
- It is a **purine nucleoside** analogue which after **intracellular conversion to didanosine triphosphate competes with ATP** for incorporation into viral DNA,
- **Inhibits HIV reverse transcriptase** and terminates proviral DNA.
- Mutational resistance develops, but only few AZT **resistant mutants are non-responsive to didanosine** also.
- It is infrequently used now due to **higher toxicity than other NRTIs.**
- It can be given **once daily** because the drug remains intracellularly for a long time.

IV. Lamivudine (3TC)

- This **deoxycytidine analogue** is **phosphorylated intracellularly** and **inhibits HIV reverse transcriptase** as well as **HBV DNA polymerase.**
- Its incorporation into viral DNA results in **chain termination.**
- Most human **DNA polymerases** are not affected and systemic toxicity of 3TC is low. Point mutation in **HIV-reverse transcriptase and HBV-DNA polymerase** gives rise to rapid lamivudine resistance.

❖ Pharmacokinetics

i. **Oral bioavailability** of 3TC is high
ii. **plasma t½ longer (6–8 hours).**
iii. Intracellular t½ is still longer (> 12 hr).
iv. It is mainly excreted unchanged in **urine.**



❖ Adverse effects

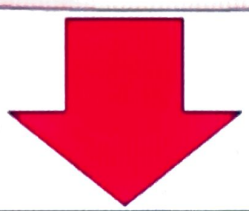
i. **Peripheral neuritis**
ii. **Pancreatitis**
iii. **Gastrointestinal disturbances, Lactic acidosis, Skin rashes**

2. Non-nucleoside reverse transcriptase Inhibitors (NNRTIs)

- NNRTIs are **highly active against HIV-1** but have **no effect on HIV-2.**
- There is **no cross-resistance with the NRTIs.**
- They are used in combination with **NRTIs in the treatment of AIDS.**

❖ Mechanism of action

Nevirapine, Delavirdine Efavirenz



Bind directly to reverse transcriptase enzyme and inhibit their function(Do not require intracellular phosphorylation)

i.Nevirapine (NPV)

❖ Pharmacokinetics

- It is **well absorbed orally >90% bioavailability**, attains high levels in CSFAnd has a **long t½.**
- Fatty food enhances the absorption and also toxicity hence, it should be taken on empty stomach.
- It is metabolised by the microsomal enzymes **CYP3A4** in the liver.

❖ Adverse effect

- **Allergic reactions ranging from skin rashes**
- **Pruritus**
- **stevens-johnson syndrome**
- **toxic epidermal necrolysis** can Occur.

❖ Uses

i. Nevirapine is used in the **treatment of HIV-1 infections** in combination with other drugs.

ii. Nevirapine is effective in a single dose (200 mg) at the onset of labour and in newborn 2 mg/kg single dose within 3 days of **birth to prevent vertical transmission from the mother to the newborn.**

ii. Efavirenz

❖ Pharmacokinetics

- It has an **oral bioavailability of 50%.**
- It is **99% bound to plasma proteins.**
- It is **metabolised by the microsomal enzymes.**

❖ Side effects

i. **Headache, dizziness, drowsiness, nightmares, confusion, vomiting**

ii. **Diarrhoea and skin rashes.**

iii. Efavirenz has **teratogenic effects in monkeys** and is **contraindicated in pregnant women.**

❖ Uses

- Efavirenz is used in the treatment of **HIV-1 infection** in combination with other antiretroviral drug

iii. Etravirine

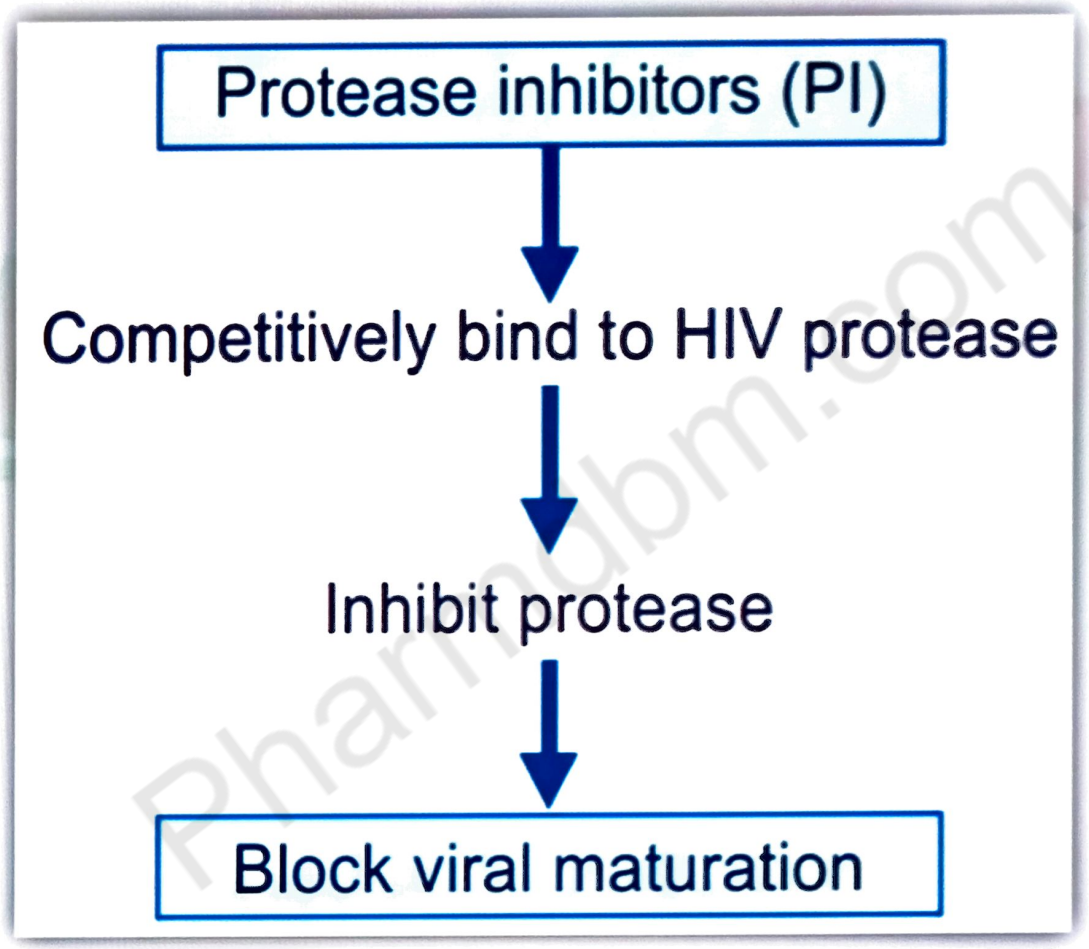
- It is effective in **HIV-1 that is resistant to other NNRTIs.**
- It is well tolerated—can cause **nausea, diarrhoea, skin rashes and raised liver enzymes.**
- Etravirine is also metabolised by **microsomal enzymes**, **inhibits some (like CYP 2C9 and CYP 2C19) and induces some others like CYP3A4**

3. Protease inhibitors (PIs)

Ritonavir, Atazanavir, Indinavir, Nelfinavir, Saquinavir Fosamprenavir, Lopinavir, Darunavir

- Protease inhibitors have been used with other antiretroviral drugs.
- **Saquinavir** is the first agent to be used in this group

❖ Mechanism of action



- They competitively **inhibit the HIV protease enzyme** ⟶ **prevent cleavage of viral poly proteins** to the final functional, structural and enzymatic components of HIV ⟶ **immature and non infectious** viral particles are produced.

✓ **Cross-resistance** is common among the PIs, but there is no cross-resistance with reverse transcriptase inhibitors.

- PIs are used orally with **reverse transcriptase inhibitors** in patients with AIDS.

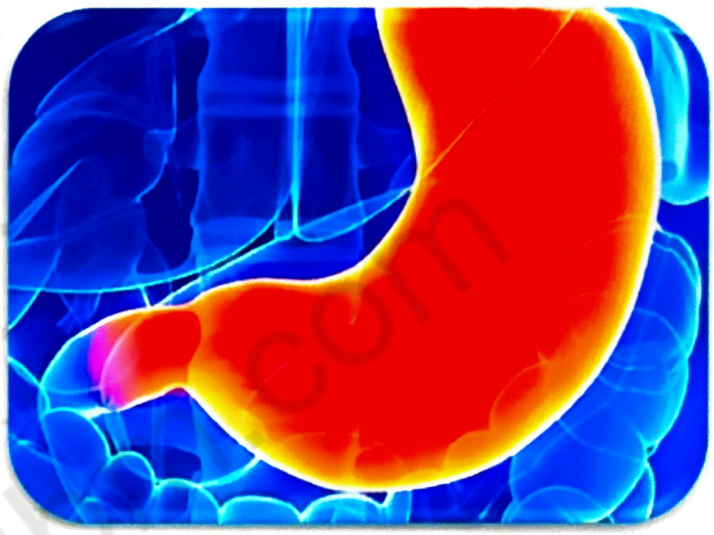
i. Ritonavir (RTV)

❖ Pharmacokinetics

- It is well absorbed and metabolised by microsomal enzymes like **CYP3A4.**
- It is a powerful **enzyme inhibitor.**

❖ Adverse effect

- **Gastrointestinal disturbances**
- **Nausea**
- **Diarrhoea**
- **Paresthesias , fatigue**
- **Lipid abnormalities**



ii. Atazanavir (ATV)

❖ Pharmacokinetics

- This PI is administered with **light meal which improves absorption,** while acid suppressant drugs decrease its absorption.
- ATV is **metabolized primarily by CYP3A4**, which is also moderately inhibited by it.
- Bioavailability and efficacy of ATV is improved by combining with RTV.
- **t½ is 6–8 hours.**

❖ Side effects:- **Loose motions, nausea and abdominal pain.**

iii. Indinavir(INV)

- Indinavir is absorbed in **presence of acidic medium** and should be given on an **empty stomach.**
- It can cause **GI disturbances and renal stones** —enough water intake needed.

iv. Nelfinavir (NFV)

- It is to be taken with meals, since **food increases absorption**, but **bioavailability is erratic.**
- NFV is mainly **metabolized by CYP2C19.**

❖ **Side effect :- Diarrhoea and flatulence.**

v. Saquinavir (SQV)

- Its **oral bioavailability is low**, the tablet.
- But **fatty food increases absorption by >5 times**
- It is a **weak inhibitor of CYP3A4.**

❖ **Side effects :-**

i. **Photosensitivity**

ii. **GI disturbances**

vi. Fosamprenavir (FPV)

- It is a **phosphorylated prodrug** of amprenavir that has better **oral bioavailability** and better tolerability than the parent drug.
- As such, it has **replaced amprenavir.**
- Fosamprenavir is **active against both HIV-1 and HIV-2**, and is effective in treatment-naive as well as previously PI treated patients.

❖ **Pharmacokinetic**

- It is extensively metabolized, mainly by **CYP3A4** and is a moderate inhibitor of CYP3A4.
- The plasma t½ is ~8 hours.

❖ **Side effects**

i. **Nausea**

ii. **Diarrhoea**

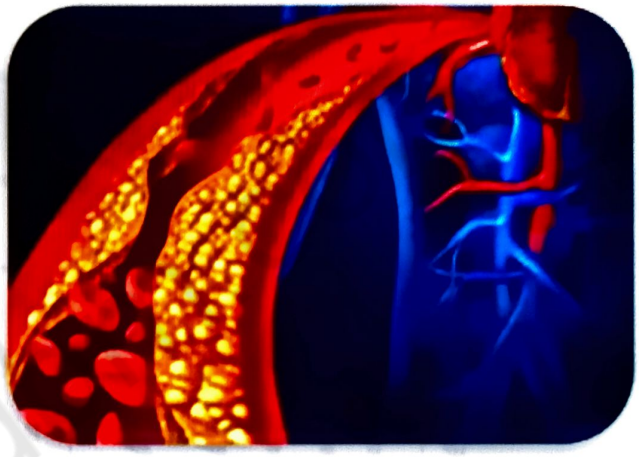
iii. **Fatigue and Rashes**

vii. Lopinavir(LPV)

- Lopinavir is given along with **ritonavir (LPV/r)—effective against both HIV-1 and HIV-2.**
- CYP3A4 inhibitor.
- It should be given with food.
- Lopinavir **should not be** given concurrently with **fosamprenavir, rifampicin and alcohol**
- **Lopinavir + Ritonavir ⟶ improve bioavailability**

❖ Side effect

i. **Diarrhoea**
ii. **Abdominal pain**
iii. **Nausea**
iv. **Dyslipidaemias**



viii. Darunavir

- **Darunavir** is a potent newer PI **active against both HIV-1 and HIV-2,** including several strains resistant to other PIs.

❖ Pharmacokinetics

- First pass metabolism as well as systemic clearance by inhibiting CYP3A4.
- It is metabolized extensively by **CYP3A4** and **excreted in urine** with a **t½ of 15 hrs.**

❖ Side effect

- **Diarrhoea**
- **Rise in hepatic enzymes**
- **Rashes**
- **Allergic reactions**

❑ PREVENTION OF SEXUALLY TRANSMITTED DISEASE

- **Practice safe sex**: This simply means the use **latex condoms** or other barrier methods as this **prevents you from contacting infections**.
- Get Tested Regularly, and Encourage Your Partners to Do the Same.(syphilis blood test) repeat test **6 weeks after the first test**.
- **Limit or eliminate drug and alcohol** use before and during sex.
- Stay with one uninfected partner.
- **Bath before and after sex.**
- Do not practice **oral sex 2 hours after brushing your mouth.**
- Abstinence
- Get an HIV blood test, to find out if you've been infected with HIV.
- Get vaccination for **Hepatitis B or A.**
- **Do not donate blood,** unless you know you have never been infected with **HIV, hepatitis or syphilis.**
- Get Treated also encourage your partner to do so and **avoid sex** until **treatment is completed** to avoid re-infecting your partner.

❖ Chemoprophylaxis of STD:

- Intramuscular injection of **procaine penicillin, 2.4 mega units** into each **buttock (a total of 4.8 mega units),** preceded by **1 g. of probenecid,** helps to **prevent both gonorrhoea and syphilis.**
- It is **more effective** in **preventing gonorrhoea than syphilis.**
- In patients allergic to penicillin, tetracycline may be used in the dose of 0.5 g. orally, four times a day, on empty stomach, for 15 days.
- **Basic therapy (for 4 weeks) in persons** with **non-intact skin or mucosa** contaminated with **small or large volumes** of infected material.

- **Expanded regimen (for 4 weeks) in persons with deep puncture wounds with hollow needles (severe exposure).**

Drugs used in common sexually transmitted disease

STD	TREATMENT		ALTERNATIVE
Syphilis	PP 6L units IM daily x 10 days B. Penicillin 2.4 MU IM single dose e		Doxycycline 100 mg BD * 15 days Erythromycin 500 mg QID x 15 days
Gonorrhoea	a. Uncomplicated	Ciprofloxacin 500 mg oral single dose Ceftriaxone 250 mg IM single dose Cefixime 400 mg oral single dose	Levofloxacin 250 mg oral single dose Spectinomycin 2 g IM single dose Cotrimoxazole 2 tab BD x 5 days
	b. Complicated	Ofloxacin 400 mg BD x 14 days Clindamycin 450 mg QID x 14 days	Procaine penicillin 2MU M * 10 days +Doxy 100 mg BD x 14 days
Lymphogranuloma venereum	Doxycycline 100 mg BD, oral x 21 days, Azithromycin 1 g oral single dose		Tetracycline 500 mg QID x 21 days
Chancroid	Azithromycin 1g oral single dose Erythromycin 500 mg QID x 7-10 days Ceftriaxone 250 mg IM single dose		Ciprofloxacin 500 mg BD * 3 days Cotrimoxazole 2 BD for 7 days
Granuloma inguinale	Doxycycline 100 mg BD x 3-4 wks Azithromycin 1 g once a wk x 4 wks		Cotrimoxazole 2BD * 3 - 4 wks
6. Trichomoniasis	Metronidazole 2 g oral single dose		Secnidazole 2 g single dose