

PHARMACOLOGY-III

UNIT 4 NOTES

CHEMOTHERAPY

- URINARY TRACT INFECTIONS
- CHEMOTHERAPY OF MALIGNANCY

IMMUNOPHARMACOLOGY

- IMMUNOSTIMULANTS
- IMMUNOSUPPRESSANTS



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CHEMOTHERAPY

URINARY TRACT INFECTIONS (UTIs)

- UTIs are infections that affect any part of the urinary system, including kidneys, ureters, bladder and urethra.
- The majority of UTIs are caused by bacteria with *Escherichia coli* (E.coli) being the most common pathogen.
- The most common type of UTI is a bladder infection (cystitis), which affects the lower urinary tract.
- Women are more prone of UTIs than men, but both genders can experience them.

CAUSES

- E. coli bacteria (common cause)
- Poor hygiene (from anus to urethra)
- Sexual intercourse
- Urinary retention
- Long-term catheter use
- Weak immune system (HIV, AIDS, Diabetes or Cancer treatment)
- Hormonal changes during pregnancy
- Due to menopause (Lower estrogen levels) etc.

SYMPTOMS

- Burning sensation during urination
- Strong-smelling urine
- Pelvic pain
- Pain or pressure in lower abdomen
- Feeling tired or fatigued
- Fever or chills
- Increased urgency
- Back pain, Nausea, Vomiting etc.

UTI may occur in mainly two forms :

i) Acute infection -

- They are sudden onset bacterial infection of urinary tract.
- It can affect lower urinary tract (bladder & urethra), with upper UTIs often presenting with fever, flank pain and Nausea.

ii) Chronic Infection -

- They refer to persistent bacterial infection of urinary tract, often lasting for weeks or recurring multiple times.
- They are characterized by dysuria, frequency and urgency, often due to underlying condition like urinary tract abnormalities, bladder outlet obstruction or incomplete bladder emptying.

PATHOPHYSIOLOGY

Germs enter the urinary tract (mainly through urethra)



Bacteria stick to the walls of the bladder or urethra.



They start to grow & multiply, causing infection in urinary system



Body reacts by sending WBC to fight with infection



Causes symptoms like burning while peeing, needing to pee often and lower belly pain (Acute UTIs)



If not treated, the infection can travel up to the kidneys and cause more serious illness (Chronic UTIs)

TREATMENT

BACTERIOSTATIC AGENT

Nitrofurantoin
Sulfonamides
Tetracyclines

BACTERICIDAL AGENTS

Cotrimoxazole
Ampicillin
Aminoglycosides
Cephalosporins
Fluoroquinolones

URINARY ANTISEPTICS

Nalidixic Acid
Nitrofurantoin
Methanamine
- mandelate

① BACTERIOSTATIC AGENT

- They are agents that inhibit the growth and reproduction of bacteria without killing them.

Nitrofurantoin

- It is an antibiotic (bacteriostatic) used to treat primary UTIs.
- It works by inhibiting bacterial enzymes and disrupting bacteria's ability to reproduce.
- It is mainly effective and commonly used to treat E. coli bacteria.

Pharmacokinetics

- Absorption - Rapidly absorbed from GIT.
- Distribution - Widely distributed, but its plasma concentration is low, mainly concentrated in urine (most effective).
- Metabolism - Mainly metabolized in liver, but most of the drug excreted unchanged form in urine.
- Excretion - Primarily excreted in urine (but 40-50% drug being unchanged in urine).
- Half time - About 20 minutes - 1 hours.

Adverse effects

- Nausea, Vomitting
- Diarrhea
- Headache
- Rash
- Hepatotoxicity
- Hemolysis etc.

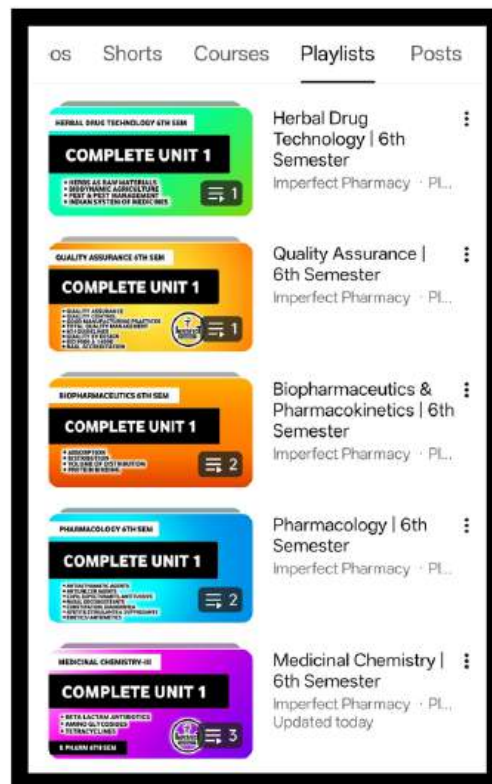
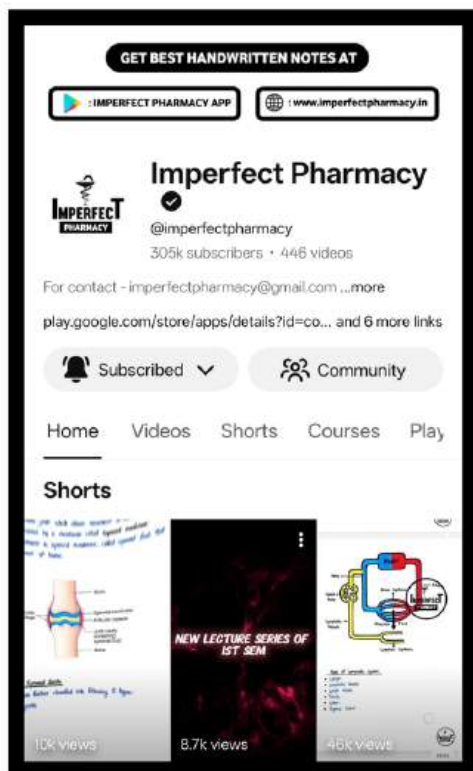
Therapeutic Uses

- Cystitis
- Urethritis
- Prostatitis
- Pyelonephritis
- UTIs etc.

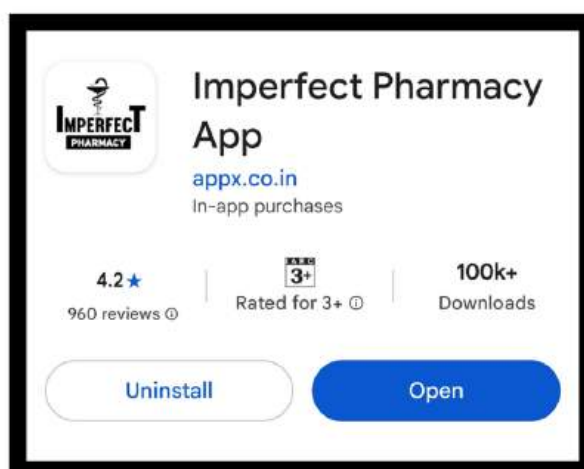
② BACTERICIDAL AGENT

- These are agents that kill the bacteria directly, rather than inhibiting their growth.
- These agents effective against eradicating bacterial infections by destroying the bacteria or disrupting essential process within bacterial cells.

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Cotrimoxazole

- It is combination antibiotic, which has sulfamethoxazole and trimethoprim.
- This combination works to inhibit the growth of bacteria, making it effective treatment for variety of bacterial infections.

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- These two drugs combination works jointly to inhibit continuously bacterial folic acid synthesis pathway, and effective most instead of using drug alone.

Pharmacokinetics

- Absorption- Rapidly absorbed after oral administration.
- Distribution- Widely distributed in tissues and body fluids, including lungs, kidneys and urine, making it effective for treating infections in these areas.
- Metabolism- Mainly metabolized in liver.
- Excretion- Both components primarily excreted via kidneys.
- Half time- 8-10 hours (trimethoprim), 8-10 (Sulfamethoxazole).

Adverse Effects

- Diarrhea
- Nausea, Vomiting
- Headache
- Hepatotoxicity
- Nephrotoxicity
- Photosensitivity etc.

Therapeutic Uses

- Pneumonia
- UTI
- Diarrhea
- Meningitis
- Otitis
- Malaria
- Sinusitis etc.

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SEXUALLY TRANSMITTED DISEASE (STDs)

- They are infections that are primarily transmitted through sexual contact.
- It can be also spread through non-sexual means such as blood transfusions, sharing needles or during childbirth or breastfeeding.
- These diseases are caused by bacteria, virus or parasites and are typically transmitted through vaginal, anal or oral sex.

TYPES OF STDs

- STD can be caused by various pathogens :

① BACTERIAL STDs

- i) Chlamydia -
 - It is bacterial infection caused by *Chlamydia Trachomatis*.
 - It can affect men and women both genders, primarily affecting genital tract, but it can also affect throat, eyes, and rectum.
 - Mainly it has no symptoms but if it has then include abnormal discharge from genital, burning during urination and pain during pee.
- ii) Gonorrhea -
 - It is caused by bacteria *Neisseria Gonorrhoeae*.
 - It can infect both genders, typically affecting genital tract, but it can also affect the throat, eyes and rectum.
 - It is unlike Chlamydia, Gonorrhea can be also asymptomatic (no symptoms), means many people may not know that they are infected.
 - But if have symptoms includes: Increased vaginal discharge, painful urination, pelvic pain (in women), discharge during urination (in men), sometimes swollen or painful testicles.

- iii) Syphilis -
- Syphilis is STD, which caused by bacteria *Treponema Palladium*.
 - It progress in stages- Primary stage, Secondary stage, Latent stage, Tertiary stages and can cause serious health complications if left untreated.
 - Symptoms are involved painless sore or ulcer (chancere) on the site of infection typically genital, anal or orally and rashes, mucous mebrane lesions, fever, swollen lymph nodes and sore throat (Secondary stage) and Organ issues such as heart, brain and nerves, leading to serious complications like neurological problems, Cardiovascular issues and organ failure (In Tertiary stage).

② VIRAL STDs - They are often chronic and may not have cure, through treatment can help manage the symptoms.

i) HIV/AIDS - It attacks the immune system and leading to AIDS (Aquire Immunodeficiency Syndrome), where the immune system is severely weakened.

ii) (HSV) Herpes - Two types Of Herpes Simplex Virus (Hsv): HSV-1 and HSV-2. HSV-1 typically causes oral sores (cold sores), while HSV-2 is more common cause of genital herpes.

iii) HPV (Human Papillomavirus) - A group of related viruses, some of which can lead to genital warts and are associated with cancer such as cervical cancer.

③ PARASITIC STDs - They are caused by parasites, which are organisms that live on or inside the host.

i) Trichomoniasis - It is caused by parasite, *Trichomonas vaginalis* and can result in vaginal infections and discomfort during urination.

TREATMENT

i) Bacterial STDs : • They can be treated by antibiotic like doxycyclines, azithromycin, tetracyclines and Penicillins.
• Early treatment is crucial to prevent long-term complications.

ii) Viral STDs : • They can be managed and reduced with antiviral drugs because they are not totally curable. HIV treatment with antiretroviral therapy (ART) can suppress the virus, allowing individuals to live-long, healthy lives.

iii) Parasitic STDs : • They are treated with antiparasitic medications.

IMMUNOPHARMACOLOGY

- Immunopharmacology is a specialized branch of pharmacology that studies the interaction between drugs and the immune system.
- It focuses on understanding how certain drugs can enhance or suppress immune responses, which is crucial in treating diseases like autoimmune disorders, allergies, infections and in organ transplantation.

- Types of immunopharmacology:

- i) Immunostimulants
- ii) Immunosuppressants

- IMMUNITY

- Immunity is the body's ability to protect itself from harmful things like germs, viruses, bacteria and toxins that can cause sickness.
- When your immune system is strong, it can stop you from getting sick or help you get better faster.
- There are two types of immunity:
 - i) Innate immunity
 - ii) Adaptive immunity

- ① Innate immunity

- This is the first line of defense from birth.
- It provides immediate but non-specific protection against a wide range of pathogens.

② Adaptive immunity

This type of immunity learns to recognise specific germs.

When you get sick, get a vaccine, your body creates "memory" so it can fight the germ faster next time.

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IMMUNOSTIMULANTS

- Immunostimulants are substances that enhance or stimulate the body's immune system to produce a stronger immune response.
- They work by activating various components of immune system, such as WBCs, antibodies and other immune mediators, to defend against infections, diseases and other harmful pathogens or agents.

CLASSIFICATION

- i) Specific immunostimulants
- ii) Non-specific immunostimulants

① Specific Immunostimulants : A specific immunostimulants is that helps the immune system get stronger and better at fighting specific germs like viruses or bacteria. It teaches your body to how to defend against certain disease.
Ex- vaccines etc.

② Non-specific Immunostimulants : It is that boosts your immune system in general, helping it fight off many types of germs/ diseases, not just one specific disease.
Ex- Immuglobulins etc.

Different types of Immunostimulants

- i) Vaccines –
 - BCG
 - Rota virus vaccines
 - Polio myelitis vaccine
 - Viral vaccines
- ii) Thalidomide
- iii) Levamisole
- iv) Interferons
- v) Colony stimulating factors
- vi) Cytokines etc.

① VACCINES

- The vaccines made from bacteria or part of bacteria that help develop immunity against bacterial infections.
- These vaccines either use to killed bacteria, weakened bacteria or pieces of bacteria (like proteins) to trigger an immune response without causing disease.
- Ex - BCG vaccines (Bacillus Calmette- Guerin) helps protect against tuberculosis (TB). It's made from a weakened form of the bacteria that cause TB.

② THALIDOMIDE

- Thalidomide is a medication originally used as a sedative but later found that it has immunostimulants properties.
- In immunostimulants, it helps to regulate the immune system by reducing inflammation and promoting immune response.
- It is used in treating conditions like leprosy and multiple myeloma, and it must be used carefully due to its side effects.

LEVAMISOLE

- Levamisole is a medication that stimulates the immune system.
- It was originally used as deworming agent but is now sometimes used in treating autoimmune disorders and cancer.
- It works by boosting the activity of certain WBCs, helping the body fight infections and diseases.

INTERFERONS

- Interferons are proteins produced by the body that help boost the immune system.
- They work by interfering with the ability of viruses to spread and by stimulating immune cells to fight infections.
- Interferons are used to treat diseases like hepatitis and certain cancers.

COLONY STIMULATING FACTORS

- Colony stimulating factors (CSFs) are proteins that help stimulate the production of white blood cells in the bone marrow.
- They are used as immunostimulants to boost the immune system, especially in the people with low WBCs counts due to conditions like cancer or infections.

CYTOKINES

- Cytokines are small proteins that help regulate the immune system.
- They act as messengers between cells, helping to control inflammation and immune responses.
- In immunostimulants, cytokines are used to treat/boost the immune systems and help fight infections or diseases like cancer.

IMMUNOSUPPRESSANTS

- Immunosuppressants are group of medications or substances that reduce the activity of the immune system.
- The immune system normally protects the body from infections and foreign pathogens/ infections, but in certain situation, the immune system can become overactive or attack the body's own tissues.
- Immunosuppressants help control these reaction by weakening or suppressing the immune response.

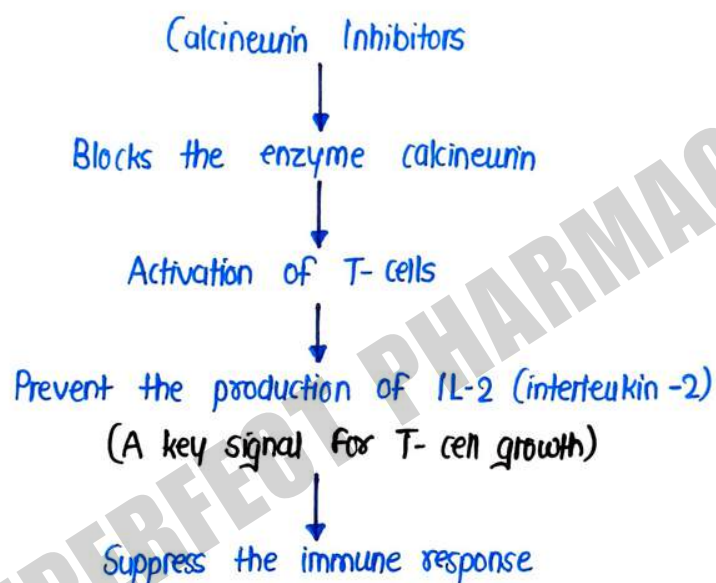
CLASSIFICATION

- i) Calcineurin Inhibitors Cyclosporine (Cyclosporin), Tacrolimus
- ii) m-TOR Inhibitors Sirolimus, Everolimus, Temsirolimus
- iii) Antiproliferative drugs Azathioprine, Methotrexate, Cyclophosphamide etc.
- iv) Glucocorticoids Prednisolone (others)
- v) Biological agents
 - TNF α inhibitors Entanercept, Infliximab, Adalimumab
 - IL-1 receptor antagonists Anakinra
 - IL-2 receptor antagonists Basiliximab, Daclizumab
 - Anti-CD3 antibody Muromonab CD3
 - Polyclonal antibodies Anti-thymocyte antibody (ATG), Rho(D) immuno globulin

① CALCINEURIN INHIBITORS

- They are class of immunosuppressants drugs that block the activity of calcineurin, a protein phosphate involved in activating T- cells of the immune system.
- Ex- Cyclosporine etc.

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Adverse Effects

- Nephrotoxicity
- Hypertension
- Neurotoxicity
- Infection
- Hyperlipidemia etc.

Therapeutic Uses

- Organ transplant
- Autoimmune disorders
- Psoriasis
- Inflammatory Bowel Disease
- Hepatitis etc.

② m - TOR INHIBITORS

- m-TOR inhibitors are drug that block the mammalian target of rapamycin (m-TOR), a protein that controls cell growth, proliferation and survival.
- By inhibiting, mTOR, these drugs suppress the immune system and slow down the cell division.
- Ex- Sirolimus (Rapamycin) etc.

Adverse Effects

- Mouth Ulcers
- Hyperlipidemia
- Immunosuppression
- Anemia
- Hypertension etc.

Therapeutic Uses

- Organ transplant
- Cancer
- Autoimmune Disorders
- Renal Disease
- Asthma
- Atherosclerosis

③ ANTIPROLIFERATIVE DRUGS

- They are medications that slow down or stop the multiplication of cells, especially immune cells like T-cells and B Lymphocytes.
- They are commonly used to prevent organ transplant rejection and to treat autoimmune diseases and some cancers and other diseases.
- Ex - Azathioprine, Methotrexate etc.

Adverse Effects

- Nausea
- Infection
- Myelosuppression
- Hair loss
- Mucosal Ulcers etc.

Therapeutic uses

- Cancer
- Organ transplant
- IBS
- Autoimmune disorders
- Psoriasis
- Rheumatoid arthritis etc.

④ GLUCOCORTICOIDS

- They are type of steroid hormone that reduce inflammation and suppress the immune system.
- They are used to treat many conditions like allergies, autoimmune disorders and during & after organ transplant.
- Ex - Prednisolone, Dexamethasone etc.

Adverse Effects

- Hypertension
- Hyperglycemia
- Osteoporosis
- Weight gain
- Mood changes
- Insomnia etc.

Therapeutic uses

- Inflammation
- Allergies
- Autoimmune disorders
- Cancer
- Arthritis
- Organ transplant etc.

⑤ BIOLOGICAL AGENTS

1) TNF- α Inhibitors

- They are block Tumor Necrosis factors - α (TNF- α), a substance in the body that causes inflammation.
- By blocking TNF - α , these drugs helps reduce inflammation and immune system activity.
- Ex- Infliximab, Adalimumab etc.

Uses : Rheumatoid arthritis, Crohns Disease, Psoriasis etc.

ii) IL-1 receptor antagonists

- They are drugs that block interleukin -1 receptor, preventing IL-1 from attaching to receptor and triggering inflammation.
- This helps to reduce inflammation and immune response in the body.
- Ex. Anakinra etc.

Uses : Autoimmune disorders like Rheumatoid arthritis etc.

iii) IL-2 receptor antagonists

- They block interleukin -2 (IL-2) on T-cells, preventing IL-2 from activating them (T-cells).
- This reduces T-cells growth and immune response.
- Ex- Basiliximab, Daclizumab etc.

Uses : Preventing Organ Transplant Rejection etc.

iv) Anti-CD3 antibody

- An Anti-CD3 antibody is a type of monoclonal antibody that binds with CD3 receptor on T-cells, blocking their activation and reducing the immune response.
- Ex- Muromonab-CD3 (OKT3) etc.

Uses : Organ transplant rejection and some autoimmune disorders etc.

⑤ Polyclonal Antibodies

- They are the mixture of antibodies that target multiple sites (epitopes) on the same antigen.
- They are produced by different B-cells clones in the body.
- Ex- Antithyomocyte Globulin (ATG)

Uses : Suppressing the immune system, especially in organ transplant and treating immune related disorders.

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