PHARMACOLOGY

STUDENT BOOK
SENIOR 6

ASSOCIATE NURSING PROGRAM

First Edition

FOREWORD

Dear Student,

The Rwanda Basic Education Board is pleased to introduce this Associate Nursing Program textbook of Pharmacology. This resource is crafted to support competence-based teaching and learning, ensuring a uniform approach to mastering the Fundamentals of Nursing. Our educational philosophy is designed to help you realize your full potential at each level of your education, equipping you to integrate effectively into society and seize career opportunities.

The Rwandan government emphasizes the alignment of educational materials with the syllabus to enhance your learning experience. Instructional materials, activities, and engagement play a crucial role in shaping how well you learn. This textbook focuses on activities that promote idea development and discovery, whether done individually or in groups.

In a competence-based curriculum, learning is an active process where knowledge, skills, and attitude and values are developed through practical activities and real-life scenarios. To fully benefit from this textbook, you should:

- Engage in activities and laboratory experiments to build your skills.
- Share information through presentations, discussions, and collaborative work.
- Take ownership of your learning and draw insights from your activities.

I extend my gratitude to all those who contributed to the creation of this book, including the Ministry of Health, University of Rwanda, and other institutions. Special thanks go to the dedicated faculty members, nurses, midwives, teachers, illustrators, and designers who worked diligently on this project.

Dr. MBARUSHIMANA Nelson

Director General, REB

ACKNOWLEDGMENT

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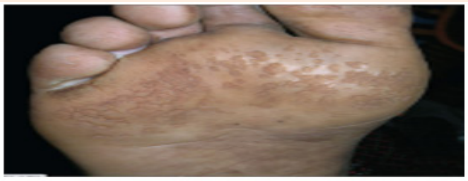
UNIT 1 ANTIFUNGAL DRUGS

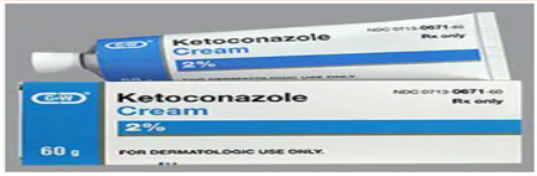
Key Unit Competence

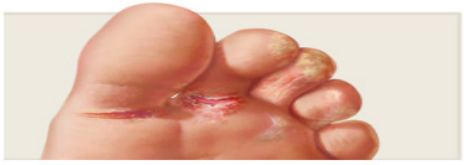
Utilize appropriately antifungal medications to manage different health condition at the primary healthcare settings.

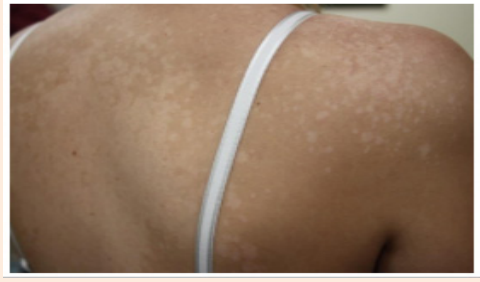
Introductory activity 1.0

The images below show different patients with fungal infections and they are being treated with different medications.









1) Have you ever seen some of the medical conditions above?
2) Which types of medications have you seen being used for these medical conditions above?
3) Have you ever seen these medications in the images above?

1.1 Definition and classification of antifungal drugs

Learning Activity 1.1

Read the scenario below:

A 35-year-old male patient is on drugs that he applies as a cream between his toes. The only explanations he got from the prescribers is to apply the cream as prescribed and dry the area before application of the drug. He has limited information regarding the intent of the drug, and what he only knows is that the drug was prescribed for an infectious disease. He then doubts whether he is taking an antibiotic or antifungal or any other drug. He wants you to provide detailed information. Answer the following questions to provide explanations to him:

a) Explain what an antifungal drug is.

b) What are different classes of antifungal drugs according to where they exert their effects?

CONTENT SUMMARY

Fungal infections in humans range from conditions such as the annoying “athlete’s foot” to potentially fatal systemic infections. An infection caused by a fungus is called a mycosis. Fungi differ from bacteria in that the fungus has a rigid cell wall that is made up of chitin and various polysaccharides and a cell membrane that contains ergosterol. The composition of the protective layers of the fungal cell makes the organism resistant to antibiotics. Conversely, because of their cellular makeup, bacteria are resistant to antifungal drugs.

The incidence of fungal infections has increased with the rising number of immunocompromised individuals-patients with acquired immune deficiency syndrome (AIDS) and AIDS-related complex, those taking immunosuppressant drugs, those who have undergone transplantation surgery or cancer treatment, and members of the increasingly large elderly population, whose body is no longer able to protect itself from many fungi that are found throughout the environment. For example, Candida, a fungus that is normally found on mucous membranes, can cause yeast infections or “thrush” in the gastrointestinal (GI) tract and yeast infections or “vaginitis” in the vagina.

Continued advancement of medical science offers life-saving treatment options for a variety of hematologic, oncologic, and rheumatologic conditions. Immunosuppression, a common therapeutic side-effect, predisposes patients to invasive fungal infections, which are escalating in prevalence. The development of effective, well tolerated antifungals has lagged behind the advances of antibacterial therapy. Amphotericin B deoxycholate, an antifungal developed in the 1950s,

marked a major therapeutic advance. Although very effective for the treatment of numerous invasive fungal infections, it is not without cost, and its side-effects often limit its use.

Antifungal drug can simply be defined as a drug used to treat fungal infections.

An antifungal agent is a drug that selectively eliminates fungal pathogens from a host with minimal toxicity to the host.

Antifungal agents are classified according to either their mechanism of action/ structure or where they exert their effect.

According to where they exert their effects, the antifungal drugs may be classified as systemic antifungals or topical antifungals

Most antifungal drugs interfere with biosynthesis or integrity of ergosterol, the major sterol in the fungal cell membrane. Others cause disruption of the fungal cell wall.

According to their mechanism of action or structure, antifungals are categorized in 4 main classes. These are azole antifungal drugs, polyene antifungal drugs, allylamine and morpholine antifungal drugs, and echinocandin antifungal drugs.

The azoles are a large group of antifungals used to treat systemic and topical fungal infections. The azoles include fluconazole, itraconazole, ketoconazole (Nizoral), posaconazole, and voriconazole. Although azoles are considered less toxic than some other antifungals, such as amphotericin B, they may also be less effective in very severe and progressive infections.

The polyene antifungal drugs include amphotericin, nystatin, and pimaricin. They interact with sterols in the cell membrane (ergosterol in fungi, cholesterol in humans) to form channels through which small molecules leak from the inside of the fungal cell to the outside.

Allylamines (naftifine, terbinafine) inhibit ergosterol biosynthesis at the level of squalene epoxidase. The morpholine drug, amorolfine, inhibits the same pathway at a later step.

The echinocandin antifungals are another group of antifungals. Drugs in this class include anidulafungin, caspofungin, and micafungin.

Self-assessment 1.1

1) You have a colleague of class in the associate nursing program who tells you that she has an onychomycosis (fungal infection of the nails). She has been prescribed an antifungal drug, and the prescribing person told her that there are 4 main classes of antifungal drugs according to their structure/mechanism of action, with specifications that the drug prescribed belongs to one of the classes. However, she does not remember these classes of antifungal drugs, and needs your assistance to remind her. Which classes of antifungal drugs will you tell your colleague?

2) A patient with a fungal infection asks the nurse why she cannot take antibiotics. The nurse explains that the reason for this is that a fungus is resistant to antibiotics because:

a) A fungal cell wall has fewer but more selective protective layers.

b) The composition of the fungal cell wall is highly rigid and protective.

c) A fungus does not reproduce by the usual methods of cell division.

d) Antibiotics are developed to affect only bacterial cell walls.

1.2 Antifungal drugs available at the primary health care settings

1.2.1 Systemic antifungals: azole and echinocandin antifungals

Learning Activity 1.2.1

1) Read carefully the scenario below:

A 50-year-old female patient is admitted at the healthcare facility with features of a fungal infection. The thorough assessment reveals that the patient has an infection that can be treated by antifungals for systemic use. You decide to avoid using an antifungal for topical use because you think it cannot work appropriately for this specific patient. Read the pharmacology book on systemic antifungals, with focus on focus on azoles and echinocandin antifungals and come up with at least 5 examples of antifungals for systemic use, belonging to these categories.

Guidance: Read the book of pharmacology brought by the teacher in class, on topic of antifungal drugs (focus on azoles and echinocandin antifungals).

CONTENT SUMMARY

The drugs used to treat systemic fungal infections can be toxic to the host and are not to be used indiscriminately. It is important to get a culture of the fungus causing the infection to ensure that the right drug is being used so that the patient is not put at additional risk from the toxic adverse effects associated with these drugs.

I. AZOLE ANTIFUNGALS

The azoles are a large group of antifungals used to treat systemic and topical fungal infections. The azoles include fluconazole, itraconazole, ketoconazole, posaconazole, and voriconazole (Vfend). Although azoles are considered less toxic than some other antifungals, such as amphotericin B, they may also be less effective in very severe and progressive infections.

1) Therapeutic Actions and Indications

These drugs bind to sterols and can cause cell death (a fungicidal effect) or interfere with cell replication (a fungistatic effect), depending on the type of fungus being affected and the concentration of the drug. Ketoconazole, fluconazole, and itraconazole work by blocking the activity of a sterol in the fungal wall. In addition, they may block the activity of human steroids, including testosterone and cortisol.

Posaconazole is one of the newest antifungals. This drug and voriconazole inhibit the synthesis of ergosterol, which leads to the inability of the fungus to form a cell wall, which results in cell death.

Fluconazole is indicated in the treatment of candidiasis, cryptococcal meningitis, other systemic fungal infections; prophylaxis for reducing the incidence of candidiasis in bone marrow transplant recipients.

Its usual dosage is:

- Adults: 200–400 mg PO on day 1, followed by 100 mg/d PO; IV route can be used, but do not exceed 200 mg/h,
- Paediatric population: 3–6 mg/kg PO; do not exceed 12 mg/kg.

Ketoconazole (Nizoral) is indicated in the treatment of aspergillosis, leishmaniasis, cryptococcosis, blastomycosis, moniliasis, coccidioidomycosis, histoplasmosis, and mucormycosis; topical treatment of mycoses (cream), and to reduce the scaling of dandruff (shampoo).

Its usual dosage is:

- Adult: 200 mg/d PO, up to 400 mg/d PO in severe cases
- Paediatric population (≥2 y): 3.3–6.6 mg/kg/d PO
- Paediatric (<2 y): Safety has not been established.
- Topical: as a shampoo and topical agents

Other indications of the azoles for systemic use include treatment of blastomycosis, histoplasmosis, and aspergillosis; prophylaxis of invasive Aspergillus and Candida infections in adults and children >13 y who are immunosuppressed secondary to antineoplastic, chemotherapy, graft-vs.-host disease following transplants, or hematological malignancies.

2) Pharmacokinetics

Ketoconazole, itraconazole and posaconazole are administered orally. Ketoconazole is also available as a shampoo and a cream. Fluconazole and voriconazole are available in oral and intravenous (IV) preparations, making it possible to start the drug intravenously for a serious infection and then switch to an oral form when the patient's condition improves and he or she is able to take oral medications. Ketoconazole is absorbed rapidly from the GI tract, with peak levels occurring within 1 to 3 hours. It is extensively metabolized in the liver and excreted through the feces.

Fluconazole reaches peak levels within 1 to 2 hours after administration. Most of the drug is excreted unchanged in the urine, so extreme caution should be used in the presence of renal dysfunction. Itraconazole is slowly absorbed from the GI tract and is metabolized in the liver by the CYP450 system. It is excreted in the urine and feces. Posaconazole is given orally, has a rapid onset of action, and peaks within 3 to 5 hours. It is metabolized in the liver and excreted in the feces. Voriconazole reaches peak levels in 1 to 2 hours if given orally, and at the onset of the infusion if given IV. It is metabolized in the liver with a half-life of 24 hours and is excreted in the urine.

3) Contraindications and Cautions

Ketoconazole has been associated with severe hepatic toxicity and should be avoided in patients with hepatic dysfunction to prevent serious hepatic toxicity. In addition, ketoconazole is not the drug of choice for patients with endocrine or fertility problems because of its effects on these processes. Although fluconazole should be used with caution in the presence of liver or renal impairment, because it could cause liver or renal toxicity, fluconazole is not associated with the endocrine problems seen with ketoconazole.

Because itraconazole has been associated with hepatic failure, should not be used in patients with hepatic failure, and should be used with caution in those with hepatic impairment. It is not known whether posaconazole crosses the placenta or enters breast milk, so it should not be used during pregnancy or lactation unless the benefi ts clearly outweigh the potential risks. Caution should be used if posaconazole is used in the presence of liver impairment because it can cause liver toxicity. Carefully monitor patients for bone marrow suppression and GI and liver toxicity if using this drug.

Voriconazole should not be used with any other drugs that prolong the QTc interval because that could be worsened and can cause ergotism if taken with ergot alkaloid; so it should not be combined with ergots.

4) Adverse Effects

Many of the azoles are associated with liver toxicity and can cause severe effects on a fetus or a nursing baby.

5) Clinically Important Drug–Drug Interactions

Ketoconazole and fluconazole strongly inhibit the CYP450 enzyme system in the liver and are associated with many drug–drug interactions, such as increased serum levels of the following agents: cyclosporine, digoxin, oral hypoglycemics, warfarin, oral anticoagulants, and phenytoin. If these combinations cannot be avoided, closely monitor patients and anticipate the need for dose adjustments. A drug guide should be consulted any time one of these drugs is added to or removed from a drug regimen. Itraconazole has a black box warning regarding the potential for serious cardiovascular effects if it is given with lovastatin, simvastatin, triazolam, midazolam, pimozide, or dofetilide. These combinations should be avoided. Voriconazole and posaconazole should not be used with any other drugs that prolong the QTc interval and can cause ergotism if taken with ergot alkaloids.

II. ECHINOCANDIN ANTIFUNGALS

The echinocandin antifungals are another group of antifungals. Drugs in this class include anidulafungin, caspofungin, and micafungin.

1) Therapeutic Actions and Indications

The echinocandins work by inhibiting glucan synthesis. Glucan is an enzyme that is present in the fungal cell well but not in human cell walls. If this enzyme is inhibited, the fungal cell wall cannot form, leading to death of the cell wall.

The echinocandins are mainly used in the treatment of candidemia (infection of the blood stream) and other forms of Candida infection, intraabdominal infections, and esophageal candidiasis.

They are also used in the treatment of invasive aspergillosis in patients who do not respond or are intolerant to other therapies.

Finally, they can be used in the treatment of patients with esophageal candidiasis; prophylaxis of Candida infections in patients with hematopoietic stem cell transplant.

The usual dosage of anidulafungin is 100–200 mg IV on day 1, then 50–100 mg/d IV for 14 d; with the dose varying with infection being treated.

2) Pharmacokinetics

Anidulafungin is given as a daily IV infusion for at least 14 days. It has a rapid onset of action, is metabolized by degradation, and has half-life of 40 to 50 hours. This drug is excreted in the feces. Caspofungin is available for IV use. This drug is slowly metabolized in the liver, with half-lives of 9 to 11 hours, then 6 to 48 hours, and then 40 to 50 hours. It is bound to protein and widely distributed throughout the body. It is excreted through the urine. Micafungin is an IV drug. It has a rapid onset, a half-life of 14 to 17 hours, and is excreted in the urine.

3) Contraindications and Cautions

Anidulafungin may cross the placenta and enter breast milk and should not be used by pregnant or lactating women. Caution must be used in the presence of hepatic impairment because it can be toxic to the liver. Caspofungin can be toxic to the liver; therefore, reduced doses must be used if a patient has known hepatic impairment. Caspofungin is embryotoxic in animal studies and is known to enter breast milk; therefore, it should be used with great caution during pregnancy and lactation. Because of the potential for adverse reactions in the fetus or the neonate, micafungin should be used during pregnancy and lactation only if the benefits clearly outweigh the risks.

4) Adverse Effects

Anidulafungin and caspofungin are associated with hepatic toxicity, and liver function should be monitored closely when using these drugs. Potentially serious hypersensitivity reactions have occurred with micafungin. In addition, bone marrow suppression can occur; monitor patients closely.

5) Clinically Important Drug-Drug Interactions

Concurrent use of cyclosporine with caspofungin is contraindicated unless the benefit clearly outweighs the risk of hepatic injury.

Self-assessment 1.2.1

1) The antifungal drugs for systemic use are more likely to be less toxic compared to the antifungal drugs for topical use. TRUE or FALSE
2) Ketoconazole is an echinocandin antifungal for systemic use. TRUE or FALSE
3) Anidulafungin and caspofungin are associated with hepatic toxicity, and liver function should be monitored closely when using these drugs. TRUE or FALSE

1.2.2 Systemic antifungals: other antifungal agents

Learning Activity 1.2.2

Read carefully the scenario below:

A 5-year-old male patient consults the healthcare facility where you are carrying out the clinical practice. He has mouth and tongue ulcerations following long-term use of cephalosporins of third generation. You decide that the patient has a fungal condition that requires to be treated with an antifungal known as “nystatin”. You then decide to prescribe that antifungal agent.

a) What are the main indications of nystatin?

b) What is the usual dosage of nystatin?

Guidance: Read the book of pharmacology brought by the teacher in class, on topic of antifungal drugs.

CONTENT SUMMARY

Other antifungal drugs that are available do not fit into either of these classes. These include amphotericin B, flucytosine, griseofulvin, and nystatin.

1) Therapeutic Actions and Indications

Other antifungal agents work to cause fungal cell death or to prevent fungal cell reproduction. **Amphotericin B** is a very potent drug with many unpleasant adverse effects. The drug binds to the sterols in the fungus cell wall, changing cell wall permeability. This change can lead to cell death (fungicidal effect) or prevent the fungal cells from reproducing (fungistatic effect). Because of the many adverse effects associated with this agent, its use is reserved for progressive, potentially fatal infections.

Amphotericin B is mainly used in the treatment of aspergillosis, leishmaniasis, cryptococcosis, blastomycosis, moniliasis, coccidioidomycosis, histoplasmosis and mucormycosis; use is reserved for progressive, potential fatal infections due to many associated adverse effects.

The usual dosage for amphotericin B is 0.25–1.5 mg/kg/d IV based on the infection being treated.

Flucytosine is a less toxic drug that alters the cell membrane of susceptible fungi, causing cell death. The uses of flucytosine are limited to the treatment of systemic infections caused by Candida or Cryptococcus. Its usual dosage is 50–150 mg/kg/d PO in divided doses at 6-h intervals.

Griseofulvin is an older antifungal that acts in much the same way, changing cell membrane permeability and causing cell death. Griseofulvin is usually indicated in the treatment of variety of ringworm or tinea infections caused by susceptible Trichophyton species, including tinea corporis, tinea pedis, tinea cruris, tinea barbae, tinea capitis, and tinea unguium.

The dosage of griseofulvin is as follows:

Tinea corporis, tinea cruris, and tinea capitis:

Adult: 500 mg (microsize) or 330–375 mg/d (ultramicrosize) PO

Tinea pedis and tinea unguium:

Adult: 0.75–1 g (microsize) or 660–750 mg (ultramicrosize) PO daily

Paediatric population: (>2 y): 11 mg/kg/d (microsize) or 7.3 mg (ultramicrosize) PO daily (not recommended for children ≤2 y)

Nystatin binds to sterols in the cell wall, changing membrane permeability and allowing leaking of the cellular components, which will result in cell death. Nystatin is usually indicated in the treatment of candidiasis (oral form); treatment of local candidiasis, vaginal candidiasis, and cutaneous and mucocutaneous infections caused by Candida species.

Its usual dosage is 500,000–1,000,000 units t.i.d. PO; continue for 48 h after resolution to prevent relapse; also used topically.

1) Pharmacokinetics

Amphotericin B and flucytosine are available in IV form. They are excreted in the urine, with an initial half-life of 24 hours and then a 15-day half-life. Their metabolism is not fully understood. Flucytosine is well absorbed from the GI tract, with peak levels occurring in 2 hours. Most of the drug is excreted unchanged in the urine and a small amount in the feces, with a half-life of 2.4 to 4.8 hours. Griseofulvin is administered orally and reaches peak levels in around 4 hours. It is metabolized in the liver and excreted in the urine with a half-life of 24 hours. Nystatin is not absorbed from the GI tract and passes unchanged in the stool.

2) Contraindications and Cautions

Amphotericin B has been used successfully during pregnancy, but it should be used cautiously. It crosses into breast milk and should not be used during lactation because of the potential risk to the neonate. Because flucytosine is excreted primarily in the urine, extreme caution is needed in the presence of renal impairment because drug accumulation and toxicity can occur. Toxicity is associated with serum levels higher than 100 mcg/mL. Because of the potential for adverse reactions in the fetus or neonate, flucytosine should be used during pregnancy and lactation only

if the benefits clearly outweigh the risks. It is not known whether nystatin crosses the placenta or enters breast milk, so it should not be used during pregnancy or lactation unless the benefits clearly outweigh the potential risks.

3) Adverse Effects

Adverse effects of these drugs are related to their toxic effects on the liver and kidneys. Patients should be monitored closely for any changes in liver or kidney functions. Bone marrow suppression has also been reported with the use of these drugs. Rash and dermatological changes have been reported with these antifungals. Amphotericin B is associated with severe renal impairment, bone marrow suppression, GI irritation with nausea, vomiting, and potentially severe diarrhea, anorexia and weight loss, and pain at the injection site with the possibility of phlebitis or thrombophlebitis. Adverse effects of griseofulvin are relatively mild, with headache and central nervous system (CNS) changes occurring most frequently.

4) Clinically Important Drug-Drug Interactions

Patients who receive amphotericin B should not take other nephrotoxic drugs such as nephrotoxic antibiotics or antineoplastics, cyclosporine, or corticosteroids unless absolutely necessary because of the increased risk of severe renal toxicity.

Self-assessment 1.2.2

A 55-year-old male patient is being treated for cryptococcal meningitis following his immunosuppression with AIDS. The treating team decides to prescribe amphotericin B because they judge it may be beneficial for this patient.

a) What are other indications of amphotericin B?

b) What are the adverse effects of amphotericin B?

1.2.3 Topical antifungal agents

Learning Activity 1.2.3

A 20-year-old female patient consults the healthcare facility where you are carrying out your clinical practice as an associate nurse student. The patient complains of ulcerations between toes, itching and pain. He reports that she does not usually taker care of her toes properly, and most of the time she does not dry her feet adequately after bath, as she rushes for work early morning.

On your physical examination, you realize that the patient has athlete's foot, and you decide to prescribe a topical antifungal agent.

a) Give any three examples of topical azole-type antifungals

b) What are the nursing considerations would you take into account while prescribing topical antifungals?

Guidance: Use the book of pharmacology brought by the teacher in class, and read on topic of antifungals, subtopic of topical antifungals

CONTENT SUMMARY

Some antifungal drugs are available only in topical forms for treating a variety of mycoses of the skin and mucous membranes. Some of the systemic antifungals are also available in topical forms. Fungi that cause these mycoses are called dermatophytes. These diseases include a variety of tinea infections, which are often referred to as ringworm, although the causal organism is a fungus, not a worm.

These mycoses include tinea infections such as athlete's foot (tinea pedis), jock itch (tinea cruris), and yeast infections of the mouth and vagina often caused by Candida. Because the antifungal drugs reserved for use as topical agents are often too toxic for systemic administration, care is necessary when using them near open or draining wounds that might permit systemic absorption.

Topical antifungals include the azole-type antifungals such as butoconazole, clotrimazole, econazole, ketoconazole, miconazole, oxiconazole, sertaconazole nitrate, sulconazole, terconazole, and tioconazole. Topical antifungals also include other antifungals such as butenafine, ciclopirox, gentian violet, naftifine, tolnaftate, and undecylenic acid.

1) Therapeutic Actions and Indications

The topical antifungal drugs work to alter the cell permeability of the fungus, causing prevention of replication and fungal death. They are indicated only for local treatment of mycoses, including tinea infections.

Butoconazole is available as vaginal cream; applied only once a day for 4 wk. It is available over the counter (OTC) for treatment of vaginal Candida infections.

Clotrimazole is available OTC as a cream, lotion, or solution; applied as a thin layer twice a day for 2–4 wk. It is used in the treatment of oral and vaginal Candida infections; tinea infections.

Ketoconazole is available in cream, gel, foam, and shampoo form; applied once to twice daily for 2–4 wk. It is used in the treatment of seborrheic dermatitis, tinea corporis, tinea cruris, tinea pedis.

Miconazole is available as an OTC product in several topical forms (vaginal suppository, cream, powder, solution, ointment, gel and spray); applied twice daily for 2–4 wk. It is used in the treatment of local, topical mycoses, including bladder and vaginal infections and athlete's foot.

Terbinafine is available as a cream or gel; used for 1–4 wk; applied twice daily. It is used in the short-term (1–4 wk) treatment of topical mycosis; treatment of tinea infections.

Gentian violet is available as a topical solution; applied twice a day to affected area. It is used in the treatment of topical mycosis.

Naftifine is available as a cream or gel; applied twice a day for up to 4 wk. hort-term treatment of severe topical mycosis (up to 4 wk). It is used in the short-term treatment of severe topical mycosis (up to 4 wk).

2) Pharmacokinetics

These drugs are not absorbed systemically and do not undergo metabolism or excretion in the body.

3) Contraindications and Cautions

Because these drugs are not absorbed systemically, contraindications are limited to a known allergy to any of these drugs and open lesions. Econazole can cause intense, local burning and irritation and should be discontinued if these conditions become severe. Gentian violet stains skin and clothing bright purple; in addition, it is very toxic when absorbed, so it cannot be used near active lesions. Naftifine, oxiconazole, and sertaconazole nitrate should not be used for longer than 4 weeks due to the risk of adverse effects and possible emergence of resistant strains of fungi. Sulconazole should not be used for longer than 6 weeks due to the risk of adverse effects and possible emergence of resistant strains of fungi. Terbinafine should not be used for longer than 4 weeks. This drug should be stopped when the fungal condition appears to be improved or if local irritation and pain become too great to avoid toxic effects.

4) Adverse Effects

When these drugs are applied locally as a cream, lotion, or spray, local effects include irritation, burning, rash, and swelling. When they are taken as a suppository or troche, adverse effects include nausea, vomiting, and hepatic dysfunction (related to absorption of some of the drug by the GI tract) or urinary frequency, burning, and change in sexual activity (related to local absorption in the vagina).

Self-assessment 1.2.3

After going through the session of topical antifungals, answer the following questions:

1) What are the adverse effects of topical antifungals used as suppositories?
2) Give the indications of topical clotrimazole.

End unit assessment 1

1) The order reads, “Give nystatin (Mycostatin) suspension, 500,000 units by mouth (swish and swallow) 4 times a day for 1 week.” The medication is available in a suspension of 100,000 units per mL. How many milliliters will the nurse give per dose?

2) The nurse notes in a patient’s medication history that the patient is taking terbinafine (Lamisil). Based on this finding, the nurse interprets that the patient has which disorder?

a) Vaginal candidiasis

b) Cryptococcal meningitis

c) Invasive aspergillosis

d) Fungal infection of toenails or fingernails

3) What are the adverse effects of topical antifungal agents?

4) Terbinafine cream should be used in the long-term (at least 10 weeks) treatment of topical mycosis in order to get the result. TRUE or FALSE

5) Antifungals in topical forms are used to treat a variety of systemic mycoses of the internal body organs. True or False

UNIT 2 DRUGS ACTING ON GASTROINTESTINAL TRACT

Key Unit competence

To provide appropriate medications for common gastrointestinal medical conditions management.

Introductory activity 2.0

Observe the picture below and respond to the following questions.

A

B

C

D

1. What do you observe on images A, B, C and D?

2.1. Definition and classification of drugs acting on gastrointestinal tract:

Learning Activity 2.1

A 22-years old male patient consults a health facility where you are placed in the clinical practicum. He complains of lower abdominal pain, diarrhoea and vomiting. On the arrival, you find that the patient has lost fluids, and requires intravenous fluids. Your colleague needs you to advise him on the medications you may use to manage his pain and vomiting.

1. Using the library textbooks, list the categories of drugs acting on the gastrointestinal tract.
2. How can you define an antiemetic drug?
3. What are the main reasons for using the drugs acting on the gastrointestinal tract?

CONTENT SUMMARY

The anatomic structures of GI include the oral cavity, pharynx, oesophagus, stomach, small intestine, and large intestine the digestive tract plays a role of bringing life sustaining elements into the body, and taking waste products out of it, accessory organs (e.g., liver, gall bladder, salivary glands, and pancreas). Regulation of these actions is controlled by many mechanisms. One control mechanism of the GI tract is the autonomic nervous system (ANS), which consists of the sympathetic branch (fight-or flight response) and the parasympathetic branch (homeostatic response).

Parasympathetic stimulation increases intestinal motility and GI secretions and relaxes sphincters. Cholinergic drugs simulate these actions. Anticholinergic drugs inhibit these actions. Sympathetic stimulation decreases intestinal motility, decreases intestinal secretions, and inhibits the action of sphincters. Sympathetic drugs simulate these actions.

Gastrointestinal drugs can be administered for a **variety of reasons.** Some gastrointestinal drugs encourage peristalsis, suppress it, or reduce its undesirable by-products. Other GI drugs decrease the flow of saliva, control vomiting and diarrhoea, loosen stool, cause vomiting, protect the GI tract, decrease acid production, or re-establish GI normal flora.

These medications can be classified into the following categories based on their use:

- Drugs for gastritis and peptic ulcer diseases
- Antiemetic drugs

- Oral rehydration salts (ORS)
- Intravenous fluids
- Antispasmodic drugs
- Laxative drugs

Drugs that are used for gastritis and peptic ulcer disease management usually include **proton pump inhibitors, H2 receptor antagonists, antacids, and others such antibiotics or miscellaneous drugs. Antiemetic drugs** are the medications used for management of nausea and vomiting. Dehydration can be prevented or managed using either **oral rehydration salts** which are prepared solutions administered orally or intravenous fluids. **Antispasmodic dugs** are medications used in the management of different categories of visceral pain, including the pain of gastrointestinal tract such as the pain in intestines or stomach. Finally, **laxatives** are used to stimulate or facilitate evacuation of the bowels, for example in a case of constipation.

Self assessment 2.1

A 30-year-old female patient consults a health facility where you are placed in the clinical attachment with complaints of epigastric pain. She also complains of nausea and vomiting associated with diarrhea. On the arrival, you find that the patient has lost fluids, and requires intravenous fluids. Your colleague needs you to advise him on the medications you may use to manage his pain and vomiting.

1. Which of the following classes of drugs you think may help for this patient on pain relief?
    A. Antispasmodics
    B. Antiemetics
    C. Laxative drugs
    D. Antiulcer drugs
2. Which of the following categories of drugs you think may be helpful for this patient?
    A. Antispasmodics and Laxative drugs
    B. Laxative drugs and Antiemetics
    C. Antiulcer drugs and Laxative drugs
    D. Antiemetics and Antispasmodics
3. Your colleague attempts to administer a laxative to the patient but needs to get your view about this decision. What can you advise him/her?

2.2. Introduction to drugs for gastritis and peptic ulcer disease

Learning Activity 2.2

Mr. MM is a middle age man who likes smoking 15 cigarettes per day. He has history of arthritis, and for this, he used to take frequently diclofenac over the counter to relieve his pain. Since last week, he started complaining of moderate to severe epigastric pain and sometimes he vomits and has heartburn. Today, he went to the pharmacy to buy medications and the pharmacist advised him to consult the facility as he suspects Mr. MM to have peptic ulcer disease.

Using library textbooks and/internet respond to the following questions:

1. What are the risk factors for peptic ulcer diseases?
2. If you were assigned to treat that patient, suggest 4 main classes of drugs to use in peptic ulcers with a short description of mechanism of action for each.

CONTENT SUMMARY

An ulcer is an erosion of the gastrointestinal mucosa. It is always associated with inflammation of the affected part. Although ulcers may occur in any portion of the alimentary canal, the duodenum is the most common site. The term peptic ulcer is specific to the lesion located in either the stomach that is named gastric ulcer or small intestine which is the duodenal ulcer.

The **risk factors** for developing peptic ulcers (PUD) are many and include close family history of PUD, blood group (persons with blood group O were found at higher risk), smoking tobacco because it leads to an increase of gastric acid secretion, consuming the beverages and food that contain caffeine and or other irritant like spices. Consuming some drugs expose to peptic ulcer diseases. Those drugs are corticosteroids, nonsteroidal anti-inflammatory drugs ibuprofen for example that causes direct cellular damage to GI mucosal cells and a reduced secretion of protective mucus and bicarbonate ion, platelet inhibitors such as aspirin also increase risk to PUD. In addition to that, excessive psychological stress, as well as infection with Helicobacter pylori are the risk factors to peptic ulcer diseases.

The primary cause of PUD is infection by the gram-negative bacterium Helicobacter pylori. Different clinical studies and research have revealed that, approximately 50% of the population has H. pylori present in their stomach and proximal small intestine. The NSAIDs and H. pylori infection act synergistically to promote ulcers. Their combination poses a 3.5 times greater risk of ulcers than either factor alone.

The characteristic symptoms of duodenal ulcer are an aggravating or burning upper abdominal pain that occurs 1 to 3 hours after a meal. The pain is worse when the stomach is empty and often disappears on ingestion of food. Night-time pain, nausea, and vomiting are uncommon. If the erosion progresses deeper into the mucosa, bleeding occurs, which may be evident as either bright red blood in vomit or black, tarry stools. In general, most of duodenal ulcers heal spontaneously even though they frequently recur after months of remission.

Gastric ulcers are less common than the duodenal type and have different symptoms. Although relieved by food, pain may continue even after a meal. Loss of appetite, weight loss and vomiting are more common. Remissions may be uncommon or absent. Medical follow-up of gastric ulcers should continue for several years, because a small percentage of the erosions become cancerous. The most severe ulcers may penetrate the wall of the stomach and cause death. Whereas duodenal ulcers occur most frequently in males in the 30- to 50-year age group, gastric ulcers are more common in women over age 60. The nonsteroidal anti-inflammatory drugs related ulcers are more likely to produce gastric ulcers, whereas H. pylori associated ulcers are more likely to be duodenal. Ulceration in the distal small intestine is known as Crohn's disease, and erosions in the large intestine are called ulcerative colitis. These diseases, together categorized as inflammatory bowel disease.

Pharmacotherapy is not the first option in treating peptic ulcers and gastritis unless the patient has helicobacter pylori infection. Before initiating drugs, the patients are usually advised to change lifestyle factors contributing to the severity of PUD. It is necessary to quit smoking, avoid alcohol consumption, stress reduction or completely avoid it, avoid or limit some foods then all these measures will allow healing of ulcer enhance it to go to. For patients who are taking NSAIDs, the initial approach to PUD is to switch the patient to an alternative medication, such as acetaminophen or a selective COX-2 inhibitor. This is not always possible, because NSAIDs are drugs of choice for treating chronic arthritis and other disorders associated with pain and inflammation. If discontinuation of the NSAID is not possible, or if symptoms persist after the NSAID has been withdrawn, antiulcer medications are indicated.

For patients with PUD who are infected with H. pylori, elimination of the bacteria using anti-infective therapy is the primary goal of pharmacotherapy. If the treatment includes only antiulcer drugs without eradicating H. pylori, a very high recurrence rate of PUD is observed. It has also been found that eradicating H. pylori infection prophylactically decreases the incidence of peptic ulcers in patients who subsequently take NSAIDs.

The goals of drug therapy for PUD pharmacotherapy are to provide immediate relief from symptoms, promote healing of the ulcer, and prevent future recurrence of the disease. Drugs for PUD are available both as on prescription and OTC drugs are available.

The primary classes of drugs used to treat peptic ulcer diseases are:

- **Proton pump inhibitors.**
- **H2-receptor antagonists.**
- **Antacids.**
- **Miscellaneous drugs.**
- **Antibiotics**.

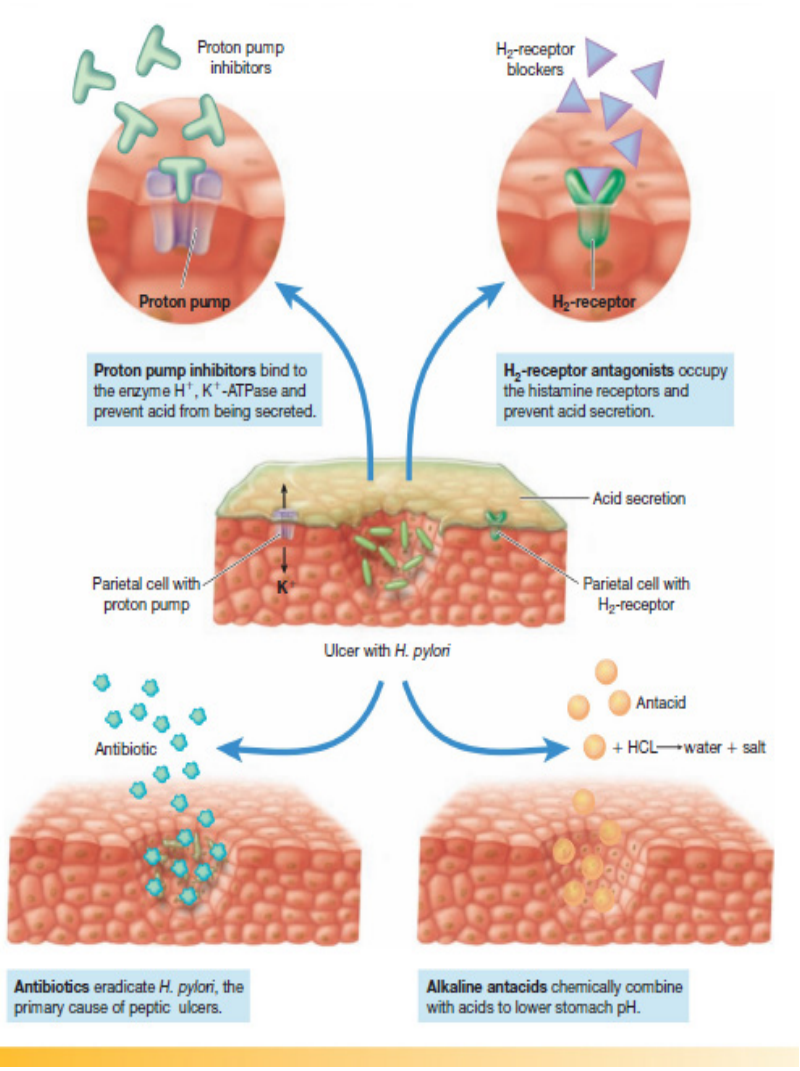


Figure: Brief description on mechanism of action for main drugs for gastritis and peptic ulcer disease.

Self assessment 2.2

An adult male patient consults the health facility where you are carrying out the clinical attachment complaining of epigastric pain and vomiting up blood. In the history taking, he tells you that he has been diagnosed with a gastric ulcer at a referral hospital. He also complains of chronic arthritis that is managed with over-the-counter pain medications.

1. Which of the following classes of drugs would you advise the client to take with caution in order to prevent worsening the peptic ulcer disease?
    A. Proton pump inhibitors
    B. Antacid medications
    C. NSAIDs such as diclofenac
    D. H2-receptor antagonists.
2. Which of the following classes of drugs used in Peptic ulcer disease management eradicate the Helicobacter pylori?
    A. Proton pump inhibitors
    B. Antibiotic medications
    C. Antacid medications
    D. H2-receptor antagonists.
3. Using antiulcer drugs alone suffices to cure peptic ulcer disease induced by Helicobacter pylori. TRUE or FALSE

2.3. Proton pump inhibitors and H2-receptor antagonists

Learning Activity 2.3

The patient consulted the health facility after the symptoms of epigastric pain. In history taking, the patient told you that he received cimetidine which did not help. The investigations done at a teaching hospital confirmed excessive secretion of gastric acid, and the specialist confirmed the peptic ulcer disease. The specialist took a decision to switch to omeprazole which finally improved the client's state.

Using library textbooks or internet, respond to the following questions

1. In which class of antiulcer drugs does cimetidine belong?
2. In which class of antiulcer drugs does omeprazole belong?
3. What are the indications of cimetidine?
4. Identify the side effects of omeprazole?

CONTENT SUMMARY

The proton pump inhibitors (PPIs) are the commonly drugs used to treat peptic ulcer diseases. They act by blocking the enzyme responsible for secreting hydrochloric acid in the stomach. They are drugs of choice for the short-term therapy of PUD. Proton pump inhibitors (PPIs) reduce acid secretion in the stomach by binding irreversibly to H+, ATPase, the enzyme that acts as a pump to release acid (also called H+, or protons) onto the surface of the GI mucosa. The PPIs reduce acid secretion to a greater extent than the H2-receptor antagonists and have a longer duration of action. PPIs heal more than 90% of duodenal ulcers within 4 weeks and about 90% of gastric ulcers in 6 to 8 weeks.

Several days of PPI therapy may be needed before patients gain relief from ulcer pain. Beneficial effects continue for 3 to 5 days after the drugs have been stopped. These drugs are used only for the short-term control of peptic ulcers. The typical length of therapy is 4 weeks.

Among them we have Omeprazole and lansoprazole that are used concurrently with antibiotics to eradicate *H. pylori.* Esomeprazole (Nexium) and pantoprazole (protonix) offer the convenience of once-a-day dosing.

Omeprazole is a widely used proton pump inhibitor. It was the first PPI to be approved for PUD and it is available for both prescription and OTC forms. It reduces acid secretion in the stomach by binding irreversibly to the enzyme H+, K+-ATPase. Although this drug can take 2 hours to reach therapeutic levels, its effects last up to 72 hours.

Omeprazole is used for the short-term, 4- to 8-week therapy of active peptic ulcers. Most patients are symptom free after 2 weeks of therapy. It is used for longer periods in patients who have chronic hypersecretion of gastric acid, a condition known as Zollinger–Ellison syndrome. It is the most effective drug for this syndrome. Omeprazole is available only in oral form whereas in combination with antacid bicarbonates, it is called Zegerid. If possible, it is better to administer it before breakfast on an empty stomach. It may be administered with antacids. It is available as capsules or tablets should not be chewed, divided, or crushed.

It is pregnancy **category C drug**.

Adverse effects of omeprazole are generally minor and include headache, nausea, diarrhea, rash, and abdominal pain. Although rare, blood disorders may occur, causing unusual fatigue and weakness. Therapy is generally limited to 2 months. Atrophic gastritis and hypomagnesaemia have been reported rarely with prolonged treatment with PPIs.

Omeprazole interacts with other drugs, affect laboratory investigations' results. When administered concurrently with diazepam, phenytoin, and central nervous system (CNS) depressants may cause increased blood levels of these drugs. Concurrent use with warfarin may increase the likelihood of bleeding; alcohol can aggravate the stomach mucosa and decrease the effectiveness of omeprazole. Omeprazole may increase values for ALT, AST, and serum alkaline phosphatase. There is no specific treatment for overdose for omeprazole

Tables 2.3.1: Proton pump inhibitors drugs

	Esomeprazole (Nexium)
Route and dose	20–40 mg/day Per os
Contraindications	Hypersensitivity to esomeprazole or its Components
Adverse effects	Agitation, aggression, depression, dizziness, headache, hallucinations, hepatic encephalopathy ,dry mouth, mucosal discoloration, sinusitis, stomatitis, taste disturbance jaundice, nausea, pancreatitis, etc

	Lansoprazole (Prevacid
Route and dose	15–60 mg/day Per os
Contraindications	Hypersensitivity to esomeprazole or its Components
Adverse effects	Dizziness, headache, abdominal pain, anorexia, diarrhea, elevated liver enzymes, hepatotoxicity, increased appetite, nausea, pancreatitis, pseudomembranous colitis, vomiting, urine retention, aplastic anemia, decreased haemoglobin, haemolytic anemia, leukopenia, neutropenia, pancytopenia, thrombocytopenia, arthralgia, myositis, upper respiratory tract infection, Erythema multiform, pruritus, rash, Stevens-Johnson syndrome, toxic, anaphylaxis, hyperkalemia, injection site reaction

	Omeprazole (Prilosec)
Route and dose	20–60 mg one to two times/day Per os
Contraindications	Hypersensitivity to or its Components
Adverse effects	To treat duodenal or gastric ulcer associated with Helicobacter pylori To treat gastroesophageal reflux disease (GERD) without oesophageal lesions, to prevent erosive esophagitis

	Pantoprazole (Protonix)
Route and dose	40 mg/day Per os
Contraindications	Hypersensitivity to pantoprazole, substitute or their components
Adverse effects	Anxiety, asthenia, confusion, dizziness, headache, hypertonia, hyperkinesia, insomnia, malaise, migraine, increased salivation, pharyngitis, rhinitis, sinusitis, tinnitus, hyperglycaemia abdominal pain, constipation, diarrhea, elevated liver function tests results, flatulence, gastroenteritis, hepatotoxicity, indigestion, nausea, vomiting elevated serum creatinine level, interstitial nephritis, back or neck pain, dyspnoea, increased cough, upper respiratory tract infection, elevated creatine kinase flulike symptoms

H2-RECEPTOR ANTAGONISTS: The discovery of the H2-receptor antagonists in the 1970s marked a major breakthrough in the treatment of PUD. Since their discovery, they are available as OTC and are widely used in the treatment of hyperacidity disorders of the GI tract. Histamine has two types of receptors, H1 and H2. Activation of H1 receptors produces the classic symptoms of inflammation and allergy, whereas the H2 receptors are responsible for increasing acid secretion in the stomach. The H2-receptorantagonists are effective at suppressing the volume and acidity of parietal cell secretions. Duodenal ulcers usually heal in 6 to 8 weeks,

and gastric ulcers may require up to 12 weeks of therapy. All of the H2-receptor antagonists are available the outer of the counter for the short-term 2 weeks treatment of gastro esophageal reflux (GERD).

All H2-receptor antagonists have similar safety profiles: Adverse effects are minor and rarely cause discontinuation of therapy. Patients, who are taking high doses, or those with renal or hepatic disease, may experience confusion, restlessness, hallucinations, or depression.

Cimetidine (Tagamet) is used less frequently than other H2-receptor antagonists because of numerous drug–drug interactions that commonly lead to inhibition of hepatic drug-metabolizing enzymes and because it must be taken up to four times a day. Antacids should not be taken at the same time because the absorption of the H2-receptor antagonist will be diminished. All H2-receptor antagonists have similar safety profiles.

Cimetidine is indicated for the treatment and prevention of recurrence of duodenal ulcer, the treatment of active and benign gastric ulcer. It is also used to manage gastroesophageal reflux disease, to treat pathological hypersecretory conditions, such as Zollinger-Ellison syndrome and to prevent stress-related upper GI bleeding during hospitalization

Adverse effects are minor and rarely cause discontinuation of therapy. Patients who are taking **high doses**, or those with renal or hepatic disease, may experience confusion, restlessness, hallucinations, or depression.

Ranitidine or zantac is a commonly used H2-Receptor antagonist. Ranitidine acts by blocking H2 receptors in the stomach to decrease acid production. It has a higher potency than cimetidine, which allows it to be administered once daily, usually at bedtime. Adequate healing of the ulcer takes approximately 4 to 8 weeks, although those at high risk for PUD may continue on drug maintenance for prolonged periods to prevent recurrence. Gastric ulcers require longer therapy for healing to occur. Intravenous (IV) and intramuscular (IM) forms are available for the treatment of acute, stress-induced bleeding ulcers. Tritec is a combination drug with ranitidine and bismuth citrate. Ranitidine is available in a dissolving tablet form (EFFER dose) for treating GERD in children and infants older than 1 month of age. Administer after meals and monitor liver and renal function.

Ranitidine does not cross the blood–brain barrier to any appreciable extent, so it does not cause the confusion and CNS depression observed with cimetidine. Although rare, severe reductions in the number of red and white blood cells and platelets are possible; thus, periodic blood counts may be performed. High doses may result in impotence or loss of libido in men. It is a pregnancy **category B drug**.

Contraindications include hypersensitivity to H2-receptor antagonists, acute porphyria, and OTC administration in children less than 12 years of age.

Drug–Drug Interactions: Ranitidine has fewer drug–drug interactions than cimetidine. Ranitidine may reduce the absorption of cefpodoxime, ketoconazole, and itraconazole. Antacids should not be given within 1 hour of H2-receptor antagonists because the effectiveness may be decreased due to reduced absorption.

Smoking decreases the effectiveness of ranitidine. For the laboratory tests, ranitidine may increase the values of serum creatinine, AST, ALT, LDH, alkaline phosphatase and bilirubin. It may produce false positives for urine protein. With herbal and food absorption of vitamin B12 depends on an acidic environment; thus, deficiency may occur. Iron is also better absorbed in an acidic environment.

Cimetidine forms:

Tables 2.3.2: H2-Receptor Antagonists

	Famotidine (Pepcid)
Route and dose	PO (Active ulcers); 20 mg bid or 40 mg at bedtime for 4–8 week PO (GERD); PO: 20 mg bid for 6 week
Contraindications	Hypersensitivity to famotidine, other H2-receptor antagonists, or their components
Adverse effects	Palpitations, dry mouth, laryngeal edema, taste alteration, tinnitus, abdominal pain, anorexia, jaundice, constipation, diarrhea, elevated liver enzymes, hepatitis, nausea, vomiting Decreased libido, muscle cramps dyspnea, interstitial pneumonia, wheezing, acne, alopecia, dry skin.

	Famotidine (Pepcid)
Route and dose	PO (Active ulcers); 20 mg bid or 40 mg at bedtime for 4–8 week, PO (GERD); PO: 20 mg bid for 6 week
Contraindications	Hypersensitivity to famotidine, other H2-receptor antagonists, or their components
Adverse effects	Palpitations, dry mouth, laryngeal edema, taste alteration, tinnitus, abdominal pain, anorexia, jaundice, constipation, diarrhea, elevated liver enzymes, hepatitis, nausea, vomiting, decreased libido, muscle cramps, dyspnea, interstitial, pneumonia, wheezing, acne, alopecia, dry skin.

	Nizatidine (Axid)
Route and dose	PO; 150–300 mg at bedtime
Contraindications	Hypersensitivity to Nizatidine or other H2- receptor antagonists
Adverse effects	Agitation, anxiety, confusion, depression,dizziness, fatigue, fever, hallucinations, headache, insomnia, somnolence, chest pain, vasculitis, dry mouth, laryngeal , edema, pharyngitis, rhinitis, sinusitis , Abdominal pain, constipation, diarrhea, hepatitis, nausea, vomiting , Decreased libido, Anemia, aplastic anemia, hemolytic anemia, Back pain, myalgia Bronchospasm, cough diaphoresis, dermatitis, jaundice,pruritus, skin rashes.

	Ranitidine (Zantac)
Route and dose	PO; 100–150 mg bid or 300 mg at bedtime IV/IM; 50 mg every 6-8 h
Contraindications	Hypersensitivity to H2-receptor antagonists, acute porphyria, children less than 12 years of age
Adverse effects	Musculoskeletal pain, tachycardia, blood dyscrasia, blurred vision

Self assessment 2.3

1. Ranitidine is one of the drugs used in the management of peptic ulcer diseases, and it belongs to the class of H2-receptor antagonists. TRUE or FALSE
2. The proton pump inhibitors reduce acid secretion to a lesser extent than the H2-receptor antagonists and have a shorter duration of action. TRUE or FALSE
3. What is an ideal duration for using omeprazole in short-term management of active peptic ulcers?
   A. Two to three weeks
   B. Four to eight weeks
   C. One to three weeks
   D. Three to eight weeks
4. What are the adverse effects of cimetidine when taken at high doses?

2.4. Antacid drugs

Learning Activity 2.4

An associate nurse student in the clinical attachment approaches the nurse seeking for advice on how to manage a patient who is complaining of mild epigastric pain and heartburn for 3 days. The nurse instructs the student to give an antacid drug (Aluminium hydroxide). In addition, the nurse instructs the student to educate the patient to take the prescribed drug at least 2 hours before or after other drugs he/she is taking.

1. What is the rationale for this interval in taking other drugs with antacid?
2. Due to their acidic properties, the antacids neutralize acid in the stomach. TRUE or FALSE
3. Combining aluminium compounds with magnesium increases their effectiveness and reduces the potential for constipation. TRUE or FALSE

CONTENT SUMMARY

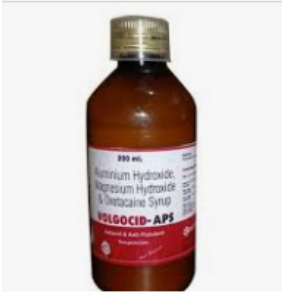
Antacids are alkaline substances that are used to neutralize stomach acid. They provide temporary relief from heartburn or indigestion and for this they are sometimes also called anti-heartburn drugs, but they do not promote healing of the ulcer, nor do they help to eradicate H. pylori. The anti-acid drugs are alkaline,

inorganic compounds of aluminum, magnesium, sodium, or calcium. Combinations of aluminum hydroxide and magnesium hydroxide, the most common type, are capable of rapidly neutralizing stomach acid. Chewable tablets and liquid formulations are available.

A few products combine antacids and H2-receptor blockers into a single tablet; for example, Pepcid Complete contains calcium carbonate, magnesium hydroxide, and famotidine. Simethicone is sometimes added to antacid preparations, because it reduces gas bubbles that cause bloating and discomfort. For example, Mylanta contains simethicone, aluminum hydroxide, and magnesium hydroxide. Simethicone is classified as an antiflatulent, because it reduces gas. It also is available by itself in OTC products such as Gas-X and Mylanta Gas.

Aluminium hydroxide is an inorganic agent used alone or in combination with other antacids. Combining aluminium compounds with magnesium (Gaviscon, Maalox, and Mylanta) increases their effectiveness and reduces the potential for constipation. Unlike calcium-based antacids that can be absorbed and cause systemic effects, aluminium compounds are minimally absorbed. Their primary action is to neutralize stomach acid by raising the pH of the stomach contents. Unlike H2-receptor antagonists and PPIs, aluminium antacids do not reduce the volume of acid secretion. They are most effectively used in combination with other antiulcer drugs for the symptomatic relief of heartburn due to PUD or GERD. A second aluminium salt, aluminium carbonate (Basaljel), is also available to treat heartburn.

The available forms are:



Aluminium compounds should not be taken at the same time as other medications, because they may interfere with absorption. Use with sodium polystyrene sulfonate may cause systemic alkalosis. When this drug is administered some lab tests may vary. For example, the values for serum gastrin and urinary pH may increase. Serum phosphate values may decrease. About food and herbal interaction, aluminium antacids may inhibit the absorption of dietary iron. There is no specific treatment for overdose for hydroxide aluminium.

When taken regularly or in high doses, aluminium antacids cause constipation. At high doses, aluminium products bind with phosphate in the GI tract and long-term use can result in phosphate depletion. Those at risk include those who are malnourished, alcoholics, and those with renal disease.

This drug is not indicated for patients with suspected bowel obstruction. Precaution should be taken while administering antacid. Administer aluminium antacids at least 2 hours before or after other drugs because absorption could be affected. They are pregnancy category C.

Tables 2.4.1: Antacid drugs

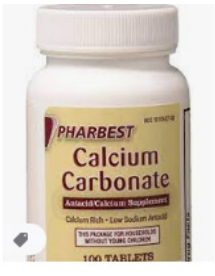
	Aluminium hydroxide (AlternaGEL, others)
Route and dose	600 mg tid–qid Per os
Contraindications	Hypersensitivity to aluminium Encephalopathy
Adverse effects	Constipation, intestinal obstruction, white-speckled stool, osteoporosis, electrolyte imbalances.

	Calcium carbonate (Titralac, Tums) Calcium carbonate with magnesium hydroxide(Mylanta, Rolaids)
Route and dose	1–2 g bid–tid Per os 2–4 capsules or tablets prn (max: 12 tablets/day) per os
Contraindications	Hypercalcemia, hypersensitivity to calcium salts or their components, hypophosphatemia,renal calculi
Adverse effects	Constipation, flatulence fecal impaction,metabolic alkalosis, hypercalcemia, renal calculi

	Magnesium hydroxide (Milk of Magnesia)
Route and dose	5–15 mL or 2–4 tablets as needed up to four times daily Per os
Contraindications	Hypersensitivity to magnesium salts or any component of magnesium-containing preparations or vomiting), diverticulitis, fecal impaction, intestinal obstruction or perforation, or ileostomy, severe renal impairment, ulcerative colitis
Adverse effects	Confusion, decreased reflexes, dizziness, Syncope, arrhythmias, hypotension, flatulence, vomiting, muscle cramps, dyspnea, respiratory depression or paralysis, diaphoresis, allergic reactions, hypermagnesemia

	Sodium bicarbonate (Alka-Seltzer, baking soda)
Route and dose	325 mg–2 g one to four times/day Per os
Contraindications	Hypocalcemia in which alkalosis may lead to tetany;Hypochloremic alkalosis Pre-existing metabolic or respiratory Alkalosis
Adverse effects	Asthenia, dizziness, fatigue, fever, headache,hypertonia, nervousness, paresthesia syncope, Chest pain, generalized edema, hypertension, hypotension, tachycardia, dry mouth, abdominal pain, diarrhea, nausea, vomiting, haemorrhage, back pain, leg cramps

ANTACIDS FORMS:



Self assessment 2.4

1. Antacids are alkaline substances that are effective in eradication of Helicobacter pylori. TRUE or FALSE
2. All the following statements best describes the effects of antacids, **EXCEPT:**
    C. They are used to neutralize stomach acid
    D. They provide relief from indigestion
    E. They provide relief from heartburn
    F. They promote healing of the peptic ulcer
3. Which of the following is the primary action of Aluminium hydroxide?
    A. To neutralize stomach acid by raising the pH of the stomach contents.
    B. To neutralize stomach acid by decreasing the pH of the stomach contents.
    C. To neutralize stomach acid by decreasing reducing the volume of acid secretion.
    D. To neutralize stomach acid by increasing reducing the volume of acid

2.5. Other drugs used to manage gastritis and peptic ulcer disease (Miscellaneous drugs and antibiotics)

Learning Activity 2.5

A university student in management who has been treated for peptic ulcer disease curiously wanted to discuss with a nurse about her treatment. She said that she had used antiulcer drugs specifically proton pump inhibitors, H2-receptors antagonist, antacids drugs. She added that, currently her friend told her that she can even use misoprostol and different antibiotics but when she did a Google search, she found that misoprostol is for inducing uterine contractions, and the antibiotics have other numerous indications. Bringing her laboratory results, the nurse found that the student was tested positive for helicobacter pylori. Now, she is worried about the treatment she will receive today after all investigations.

Using Library textbooks/internet explain the following

1. What is the mechanism of action of misoprostol in the treatment of peptic ulcer diseases?
2. Give one example of antibiotic used in the management of peptic ulcer disease.
3. Which properties does bismuth have to exert effect against helicobacter pylori when administered?

CONTENT SUMMARY

MISCELLANEOUS DRUGS FOR PUD

Prostaglandin Analogues

Misoprostol is a synthetic analogue of prostaglandin E1 which inhibits gastric acid secretion, causes vasodilatation in the submucosa and stimulates the production of protective mucus.

Indications

Even though it is used some times to terminate the pregnancy, misoprostol (Cytotec) inhibits gastric acid secretion and stimulates the production of protective mucus. Its primary use is for the prevention of peptic ulcers in patients who are taking high doses of NSAIDS or corticosteroids.

The purpose of its use is to enhance the healing of duodenal ulcer and gastric ulcer, including those induced by NSAIDs and as prophylaxis of gastric and duodenal ulceration in patients on NSAID therapy.

Side effects

The side effects of cytotec are diarrhea, abdominal pain, nausea and vomiting, dyspepsia, flatulence, abnormal vaginal bleeding, rashes and dizziness. It is a pregnancy X drug. Misoprostol is available in tablet forms

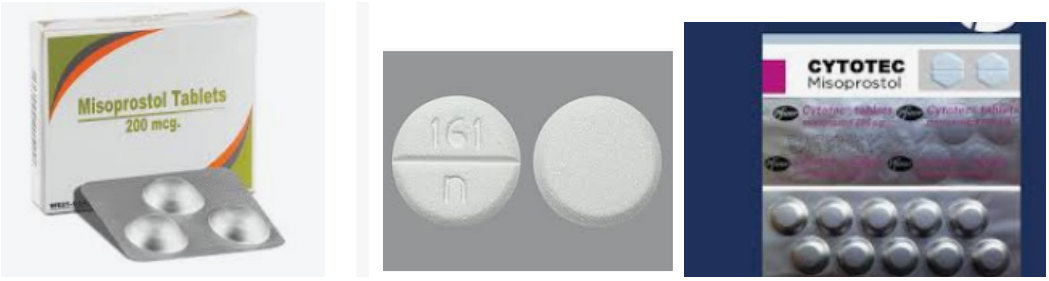


Figure 2.5.1 Misoprostol tablet forms

Bismuth Chelate

Mechanism of action

Bismuth chelate is a colloidal tripotassium dicitratobismuthate that precipitates at acid PH to form a layer over the mucosal surface and ulcer base, where it combines with the proteins of the ulcer exudate. This coat is protective against acid and pepsin digestion. It also stimulates mucus production and may chelate with pepsin, thus speeding ulcer healing. Several studies have shown it to be as active as **cimetidine** in the healing o duodenal and gastric ulcers after four to eight weeks of treatment. It has a direct toxic effect on H. pylori.

Indications

It is used as part of triple therapy in the treatment of peptic ulcer diseases associated with helicobacter pylori.

Bismuth chelate elixir is given diluted with water 30 minutes before meals and two hours after the last meal of the day. This liquid has an ammoniacal, metallic taste and odour which is unacceptable to some patients and chewable tablets can be used instead. Antacids or milk should not be taken concurrently. Ranitidine bismuth citrate tablets are also available for the treatment of peptic ulcers and for use in H. pylori eradication regimes.

Adverse effects

The adverse effects include blackening of the tongue, teeth and stools causing potential confusion with melaena and nausea. Bismuth is potentially **neurotoxic.** Urine bismuth levels rise with increasing oral dosage, indicating some intestinal absorption. Although with normal doses the blood concentration remains well below the toxic threshold.

Contraindication: It should not be used in renal failure

Figure 2.5.2 Forms of Bismuth

Antibiotics Used to Treat PUD

Peptic ulcer diseases have many risk factors and cause. **Helicobacter pylori**; a gram-negative bacterium is associate with duodenal ulcer in 80% of patient and 70% of patients with gastric ulcer. If not well eradicated, it is strongly associated with gastric cancer. This explains the magnitude of several antibiotic use's inpatient with peptic ulcer diseases. This bacterium has adapted well as human pathogen by creating ways to neutralize the high acidity of its surrounding by making adhesion which is a substance that allows the bacterium to stick tightly to the mucosa of the GI. The infecting bacterium can remain active for life if not treated appropriately. Elimination of this organism allows ulcers to heal more rapidly and remain in remission longer. Because acid-reducing drugs have little or no effect of H. pylori, antibiotics must be used to eliminate the bacterium

A combination of antibiotics is used concurrently to eradicate H. pylori. Once eliminated from the stomach, reinfection with H. pylori is uncommon. Those with peptic ulcers who are not infected with H. pylori should not receive antibiotics because it has been shown that these patients have a worse outcome if they receive H. pylori treatment. Thus, patients should be tested for H. pylori before initiating treatment for infection.

Two or more antibiotics are given concurrently to increase the effectiveness of therapy and to lower the potential for bacterial resistance. The antibiotics are also combined with a PPI or an H2-receptor antagonist. Bismuth compounds (Pepto-Bismol, Tritec) are sometimes added to the antibiotic regimen. Although technically not antibiotics, bismuth compounds inhibit bacterial growth and prevent H. pylori from adhering to the gastric mucosa. Antibiotic therapy generally continues for 7 to 14 days.

Drugs used to eradicate helicobacter pylori

The presence of the **bacterium helicobacter pylori** is a major causative factor in the aetiology of peptic ulcer disease. The incidence of H. pylori infection in patients with gastric ulcer approaches 100%. The strongest evidence of a causal relationship between H. pylori and peptic ulcer disease is the marked reduction in ulcer recurrence and complications following successful eradication of the organism. It has been shown that the speed of ulcer healing obtained with acid-suppressing agents is accelerated if H. pylori eradication is achieved concomitantly. Eradication of H. pylori infection prior to the commencement of NSAIDs therapy reduces the occurrence of gastro- duodenal ulcers in patients who have not had previous exposure to NSAIDs. H. pylori appears to be associated with increased risk of gastric cancer of the corpus. For these reasons, it is very important to eradicate that pathogen.

In eradication of that pathogen, **Amoxicillin, clarithromycin** are the commons antibiotics used in combination for tritherapy or Quadritherapy. A combination of **3 drugs called tritherapy** or **4 drugs** known as **Quadritherapy** is necessary. The Following are possible combination:

First line: Tri-therapy

PPI+ clarithromycin+ metronidazole

PPI+ amoxicillin+ Tinidazole

Anti H2+ Clarithromycin +amoxicillin

Anti H2+ Amoxicillin+ metronidazole

Examples:

1. Bismuth + metronidazole+ amoxicillin for two weeks. This combination has a success rate of 70-80%.
2. Omeprazole 20mg bid (on empty stomach) + metronidazole 500mg at the end of the meal+ clarithromycin 500mg for one week. This combination has a success rate of 95-100%.

Second line: Quadritherapy

Tritherapy + misoprostol (cytotec) or add bismuth to tritherapy

Note: For persons with penicillin intolerance, tetracycline should be used in place of tetracycline.

Non pharmacological management

In addition to pharmacological management, it is important to educate the patient about hygienodietetic measures of ulcer prevention and enhancement for healing.

It is recommended to consume milk as it contains calcium and avoid some food like cabbages, sombe, and spicy foods as well as quit smoking and avoid alcohol consumption.

Self assessment 2.5

1. One of the following antibiotics is included in tritherapy for eradication of helicobacter pylori.
   A. Cotrimoxazole
   B. Doxycycline
   C. Amoxicillin
   D. Ampicillin
2. Which of the following is a side effect of bismuth chelate?
   A. Neurotoxicity
   B. Dyspepsia
   C. Flatulence
   D. Vaginal bleeding
3. Which statement is true about misoprostol?
   A. Is diluted with water and taken 30 minutes before meals
   B. Inhibits gastric acid secretion
   C. It is a pregnancy B category drug
   D. It should be part of quadritherapy for H. pylori eradication
4. List 4 drugs used in the quadritherapy for Helicobacter pylori eradication.

2.6. Antiemetic drugs

Learning Activity 2.6

In this morning you receive a patient in the health clinic where you are in the clinical attachment. The patient complains of vomiting after each meal for the last 3 days.

1. How can define an antiemetic drug?
2. Using library and internet, identify 2 drugs that should be given to the patient to reduce or stop vomiting.
3. What are the classes of antiemetic drugs?

CONTENT SUMMARY

Antiemetic are drugs for treating or preventing nausea and vomiting. Their mechanism of action is of inhibiting dopamine or serotonin receptors in the brain. **Nausea** is an unpleasant, subjective sensation that is accompanied by weakness, diaphoresis, and hyperproduction of saliva. It is sometimes accompanied by dizziness. Intense nausea often leads to vomiting, or emesis. **Vomiting** is a defense mechanism used by the body to clear itself of toxic substances. Vomiting is a reflex primarily controlled by the vomiting center of the medulla of the brain, which receives sensory signals from the digestive tract, the inner ear, and the chemoreceptor trigger zone (CTZ) in the cerebral cortex.

The various classes of antiemetics target different pro-emetic pathways to alleviate nausea and vomiting. Some target more than one pathway. The classes of antiemetics include **antagonists of dopamine, serotonin, neurokinin, histamine** and **acetylcholine**, as summarized in table 1 below:

Table 2.6.1: Antiemetic drugs

CLASS	MECHANISMS OF ACTION
Dopamine antagonists – Metoclopramide – Domperidone – Prochlorperazine – Chlorpromazine – Butyrophenones – Droperidol – Haloperidol	Block dopamine type 2 (D2) receptors centrally in the chemoreceptor trigger zone and peripherally in the gastrointestinal tract. Domperidone blocks peripheral D2 receptors only. At higher doses, effects on other receptors are seen. These include blockade of serotonin, histamine, adrenergic and muscarinic receptors.
Serotonin Antagonists – Ondansetron – Granisetron – Palonosetron – Tropisetron	**Block 5-HT3 receptors in the chemoreceptor trigger zone and gastrointestinal tract.**

Antihistamines – Doxylamine – Cyclizine – Pheniramine – Promethazine	**Block H1 receptors:** Cyclizine, doxylamine, promethazine and pheniramine all block muscarinic receptors. Promethazine also blocks dopamine D2 receptors.

Tables 2.6.2: Summary of Serotonin (5-HT3) blockers

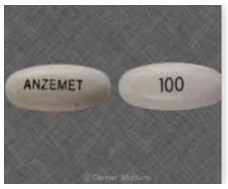
	Dolasetron (*Anzemet*)
Dosage and route	**Adult:** 100 mg PO within 1 h of procedure, 12.5 mg IV for postoperative vomiting, **Pediatric (2–16 y):** 1.8 mg/kg PO 1 h ; 1.8 mg/kg IV 30 min 1.2 mg/kg IV for postoperative vomiting
Indications:	Treatment of nausea and vomiting associated with emetogenic chemotherapy, prevention of postoperative nausea and vomiting
Contraindications	Hypersensitivity to dolasetron or components
Adverse effects	Abnormal gait, agitation, anxiey, asthenia, depression, dizziness, dream disturbances, fatigue, fever, headache, hostility, insomnia, nervousness, seizures, somnolence, syncope, t bradycardia, chest pain, edema, heart failure, hypertension OR hypotension Hyperglycaemia Abdominal pain, anorexia, constipation, diarrhea, dyspepsia, gastroenteritis, fecal incontinence, nausea, vomiting , urinary frequency or incontinence, anemia.

	Granisetron (*Kytril*)
Dosage and route	**Adult and pediatric (>2 y):** 10 mcg/kg IV over 5 min *or* 1 mg PO b.i.d.
Indications:	Treatment of nausea and vomiting associated with emetogenic chemotherapy
Contraindications	Hypersensitivity to granisetron or its components

Adverse effects	Asthenia, chills, CNS stimulation, drowsiness, fever, headache, insomnia, somnolence, hypertension, taste perversion, abdominal pain, anorexia, constipation, diarrhea, elevated liver function test results, nausea, vomiting, anemia, leukopenia, thrombocytopenia

	Ondansetron (*Zofran*)
Dosage and route	Adult: 8 mg PO t.i.d. or 24 mg PO , 0.15-mg/kg doses IV over Pediatric (4–12 y): 4 mg PO t.i.d.
Indications:	Treatment of severe nausea and vomiting associated with emetogenic chemotherapy, radiation therapy, postoperativesituations
Contraindications	Hypersensitivity to ondansetron or its components
Adverse effects	Agitation, anxiety, ataxia, dizziness, drowsiness, fever, headache,hypotension, restlessness, seizures, syncope, somnolence, weakness chest pain, hypotension, pulmonary embolism, shock, tachycardia,Accommodation disturbances, altered taste, blurred vision, dry mouth,

	Palonosetron (*Aloxi*)
Dosage and route	0.25 mg IV as a single dose over 30 s given 30 min before the start of chemotherapy, do not repeat dose for 7 days
Indications:	Treatment of acute and delayed vomiting associated with highly emetogenic chemotherapy
Contraindications	Hypersensitivity to palonosetron or its components
Adverse effects	Anxiety, dizziness, drowsiness, fatigue, headache, insomnia, weakness, bradycardia, hypotension, tachycardia, Abdominal pain, constipation, diarrhea **d**ermatitis, pruritus, rash, hyperkalemia, hypersensitivity reaction, injection site reaction (burning, induration, discomfort, pain)



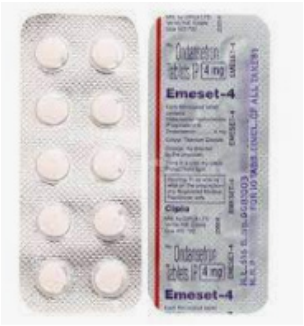


Figure 2.6.1 Serotonin (5-HT3) blockers forms

Tables 2.6.3: Summary of Dopamine antagonists

	Chlorpromazine (*Thorazine*):
Dosage and route	**Adult**: 10–25 mg PO q4–6h *or* 50–100 mg PR or 25 mg IM. **Pediatric**: 0.5 mg/kg PO q4–6h, 1.1 mg/kg PR q6–8h, or 0.5 mg/kg IM q6–8h.
Indications:	Treatment of nausea and vomiting, including that specifically associated with anaesthesia; severe vomiting; intractable hiccoughs.
Contraindications	Comatose states; hypersensitivity to chlorpromazine, phenothiazines, or their components.
Adverse effects	Drowsiness, seizures orthostatic hypotension; tachycardia, Blurred vision, dry mouth, nasal congestion, ocular changes (fine particle, deposits in lens and cornea) with long-term therapy or hyperglycemia, or hypoglycaemia, lactation, moderate breast engorgement constipation, ileus, nausea, amenorrhea, ejaculation disorders, impotence, priapism, urine retention , agranulocytosis, aplastic anemia, hemolytic anemia, leukopenia, pancytopenia, dermatitis, jaundice, photosensitivity, tissue necrosis

	Prochlorperazine (*Compazine*)
Dosage and route	**Adult**: 5–10 mg PO t.i.d. to q.i.d.; 25mg PR b.i.d.; 5–10 mg IM q3–4h, up to 40mg/d; 5–10 mg IM 1–2 h before, during, or after anesthesia, may repeat in 30 min. **Pediatric**: 9.1–13.2 kg: 2.5 mg PO or PR daily to b.i.d., do not exceed 7.5 mg/d 13.6–17.7 kg: 2.5 mg PO or PR b.i.d. to t.i.d., do not exceed 10 mg/d 18.2–38.6 kg: 2.5 mg PO or PR t.i.d. to 5 mg b.i.d., do not exceed 15 mg/d, *or* 0.132 mg/ kg IM as a single dose.
Indications:	Treatment of severe nausea and vomiting, including that specifically associated with anaesthesia.
Contraindications	Age less than 2 years, bone marrow depression, coma, coronary artery disease, hepatic dysfunction,hypersensitivity to phenothiazines, pediatric surgery, severe CNS depression, severehypertension or hypotension, use of large quantities of CNS depressants, weight less than 9 kg.
Adverse effects	Altered temperature regulation, dizziness, drowsiness, extrapyramidal reactions, hypotension, orthostatic hypotension,tachycardia, blurred vision, dry mouth, nasal congestion, ocular changes, pigmentary retinopathy, galactorrhea, gynecomastilc , Constipation, epigastric pain, nausea, Vomiting, dysuria, ejaculation disorders, menstrual irregularities, urine retention, decreased sweating, photosensitivity, pruritus, rash, weight gain.

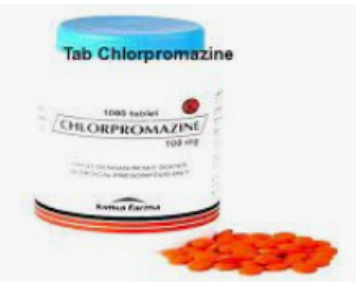


Figure 2.6.1: Dopamine **antagonists**

Table 2.7: Anticholinergics/antihistamine antiemetics

	Buclizine (Bucladin)
Dosage and route	50 mg PO, up to 150 mg/d The dose may be repeated every four to six hours if needed (q4–8h)
Indications:	Treatment of nausea and vomiting associated with motion sickness in adults
Contraindications	**Hypersensitivity to Buclizine or any of its components, Neonates**, Glaucoma, gastrointestinal obstruction
Adverse effects	Hypersensitivity reaction, sedation, tremors, seizures, hallucinations, paradoxical excitation especially in children, hypotension

	Cyclizine (Marezine)
Dosage and route	**Adult**: 50 mg PO **Pediatric**: (6–12 y): 25 mg PO up to three times per day
Indications:	Treatment of nausea and vomiting associated with motion sickness
Contraindications	Hypotension, prostatic hypertrophy, urinary retention, glaucoma, pyloroduodenal obstruction, hepatic disease, and epilepsy. Children and the elderly are more susceptible to side effects

Adverse effects	Drowsiness, dry mouth, blurred vision

	Meclizine (Antivert)
Dosage and route	25–50 mg PO 1h before travel, may repeat q24h during trip
Indications:	Treatment of nausea and vomiting associated with motion sickness in patients >12 y
Contraindications	closed angle glaucoma, liver problems, enlarged prostate. chronic idiopathic constipation
Adverse effects	Hypersensitivity reaction, sedation, tremors, seizures, hallucinations, paradoxical excitation

	Promethazine
Dosage and route	**Adult**: 25 mg PO or PR, repeat doses of 12.5–25 mg q4–6h as needed; 12.5 25 mg IM or IV q4–6h **Pediatric**: 1 mg/kg PO q4–6h as needed
Indications:	Prevention and control of nausea and vomiting associated with anesthesia and surgery
Contraindications	In comatose states, and in individuals known to be hypersensitive or to have had an idiosyncratic reaction to promethazine or to other phenothiazines.

Adverse effects	Confusion, dizziness, drowsiness, dystonia, euphoria, excitation, fatigue, hallucinations, hysteria, incoordination, insomnia, irritability, nervousness, neuroleptic malignant syndrome, paradoxical stimulation, pseudo parkinsonism, restlessness, sedation, seizures, syncope, tardive dyskinesia, tremor tadycardia, hypertension, or hypotension, tachycardia, Blurred vision; diplopia; dry mouth, nose, and throat; nasal congestion; tinnitus; vision changes, hyperglycaemia , Anorexia, cholestatic jaundice, ileus, nausea, rectal burning or stinging (suppository form), vomiting, Dysuria, leukopenia, thrombocytopenia, thrombocytopenic purpura, apnea , respiratory depression, tenacious, bronchial secretions, Dermatitis, diaphoresis, jaundice, photosensitivity, rash,

Self assessment 2.6

1. Which of the following antiemetic drugs is classified in antihistamine antiemetics?
   A. Promethazine
   B. Chlorpromazine
   C. Ondansetron
   D. Metoclopramide
2. Which of the following antiemetic drugs is classified in serotonin (5-HT3) blockers?
   A. Promethazine
   B. Chlorpromazine
   C. Ondansetron
   D. Metoclopramide
3. State the contraindications of chlorpromazine.

2.7. Laxative drugs

Learning Activity 2.7

As an associate nurse student in the clinical attachment, you receive a patient complaining of difficulty passing stool. In your assessment, you realize that the patient usually has a sedentary life and drinks fluids less frequently. You diagnose the condition to be constipation, and you wish to administer drugs that increase bowel movements.

1. How do we call a broad class of medications that increase bowel movements such as in case of constipation?
2. List the categories of drugs used to treat constipation, and give one example for reach category.

CONTENT SUMMARY

Laxatives are drugs that promote bowel movements. Laxatives promote the evacuation of the bowel, or defecation, and are widely used to prevent and treat constipation. Indications for laxative include either the prophylaxis of constipation or treatment of chronic constipation. Prophylactic laxative pharmacotherapy is appropriate following abdominal surgeries. Such treatment reduces straining or bearing down during defecation a situation that has the potential to precipitate increased intra-abdominal, intraocular, or blood pressure. Prophylactic laxative therapy may be initiated in pregnant women, patients and iron supplements are just some of the medications that promote constipation. Foods that can cause constipation include alcoholic beverages, products with a high content of refined white flour, dairy products, and chocolate.

In addition, certain diseases such as hypothyroidism, diabetes, and irritable bowel syndrome (IBS) can cause constipation. The normal frequency of bowel movements varies widely among individuals, from two to three per day, to as few as one per week. Constipation occurs more frequently in older adults, because faecal transit time through the colon slows with aging; this population also exercises less and has a higher frequency of chronic disorders that cause constipation.

All patients should understand that variations in frequency are normal, and that a daily bowel movement is not a requirement for good health. Occasional constipation is self-limiting and does not require drug therapy. Lifestyle modifications that incorporate increased dietary fibers, fluid intake, and physical activity should be considered before drugs are used for constipation.

Chronic, infrequent, and painful bowel movements, accompanied by severe straining, may justify initiation of treatment. In its most severe form, constipation

can lead to a fecal impaction and complete obstruction of the bowel for people who are unable to exercise, or patients who are taking drugs that are known to cause constipation.

The most common use for laxatives is to treat simple, chronic constipation. Occasionally, laxatives are administered to accelerate the movement of ingested toxins following poisoning or to remove dead parasites in the intestinal tract following anthelminthic therapy. In addition, laxatives are often given to cleanse the bowel prior to diagnostic or surgical procedures of the colon or genitourinary tract. The main classes are **chemical stimulants, bulk stimulants and lubricants.**

CHEMICAL STIMULANT LAXATIVES

These are a group of medications that stimulate the normal gastrointestinal reflexes by chemically irritating the lining of the gastrointestinal wall, leading to increasing of its activity. The drugs found in this group are **bisacodyl (Dulcolax), cascara (generic), castor oil (Neoloid), and senna (Senokot**). Castor oil is used when a thorough evacuation of the intestine is desirable. All of these agents begin working at the beginning of the small intestine and increase motility throughout the rest of the GI tract by irritating the nerve plexus. Because castor oil blocks absorption of fats (including fat-soluble vitamins) and may lead to constipation from GI tract exhaustion when there is no stimulus to movement, its frequent use is not desirable. Bisacodyl acts in a similar manner but is somewhat milder in effect; it can also be given in a water enema to stimulate the activity in the lower GI tract. Cascara is somewhat milder than castor oil and is often used when effects are needed overnight. Senna is available orally in tablet and syrup form and as a rectal suppository.

Most of these agents are only minimally absorbed and exert their therapeutic effect directly in the GI tract. Changes in absorption, water balance, and electrolytes resulting from GI changes can have adverse effects on patients with underlying medical conditions that are affected by volume and electrolyte changes. Castor oil has an onset of action in 2 to 6 hours; the remaining chemical stimulants have an onset of action of 6 to 8 hours, making them preferable if one wants the drug to work overnight and see effects in the morning.

Laxatives are contraindicated with allergy to any component of the drug to prevent hypersensitivity reactions and in acute abdominal disorders, including appendicitis, diverticulitis, and ulcerative colitis, when increased motility could lead to rupture or further exacerbation of the inflammation. Laxatives should be used with caution in heart block, coronary artery disease (CAD), or debilitation, which could be affected by the decrease in absorption and changes in electrolyte levels that can occur and with great caution during pregnancy and lactation because, in some cases, stimulation of the GI tract can precipitate labor and many of these agents cross the placenta and are excreted in breast milk.

The adverse effects most commonly associated with laxatives are GI effects such as diarrhea, abdominal cramping, and nausea. Central nervous system (CNS) effects, including dizziness, headache, and weakness, are not uncommon and may relate to loss of fluid and electrolyte imbalances that may accompany laxative use. Sweating, palpitations, flushing, and even fainting have been reported after laxative use. These effects may be related to a sympathetic stress reaction to intense neurostimulation of the GI tract or to the loss of fluid and electrolyte imbalance.

A very common adverse effect that is seen with frequent laxative use or laxative abuse is cathartic dependence. This reaction occurs when patients use laxatives over a long period of time and the GI tract becomes dependent on the vigorous stimulation of the laxative. Without this stimulation, the GI tract does not move for a period of time which could lead to constipation and drying of the stool and ultimately to impaction. Specifically related to chemical stimulants, cascara, although a reliable agent, may have a slow, steady effect or may cause severe cramping and rapid evacuation of the contents of the large intestine. Castor oil blocks absorption of fats (including fat-soluble vitamins) and may lead to constipation from GI tract exhaustion when there is no stimulus to movement.

Interactions: because laxatives increase the motility of the GI tract and some interfere with the timing or process of absorption, it is advisable not to take laxatives with other prescribed medications. The administration of laxatives and other medications should be separated by at least 30 minutes.

Tables 2.7.1: Chemical stimulant laxatives

	Bisacodyl (*Dulcolax*)
Dosage and route	10–15 mg PO or 2.5 g in water via enema
Indications:	Emptying of the gastrointestinal (GI) tract before some surgeries or diagnostic tests (e.g., barium enema); prevention of constipation and straining after GI surgery, myocardial infarction (MI), obstetrical delivery; short-term treatment of constipation
Contraindications	Ileus, intestinal obstruction, acute abdominal conditions including appendicitis, acute inflammatory bowel diseases, and severe abdominal pain associated with nausea and vomiting which may be indicative of the aforementioned severe conditions.
Adverse effects	Nausea, diarrhoea, stomach pain or cramps.

	Castor oil (*Neoloid*)
Dosage and route	15–30 mL PO
Indications:	Emptying of the GI tract for diagnostic testing, short-term treatment of constipation **Special considerations**: Avoid frequent use to prevent constipation from GI tract exhaustion when there is no stimulus to movement
Contraindications	Appendicitis, hiatal hernia, blockage of the stomach or intestine, difficulty swallowing, weakened patient, bedridden patient or one unable to move around freely, pregnancy, problems of emptying stomach contents
Adverse effects	Dizziness, abdominal cramps. Diarrhea, nausea. Electrolyte disturbance, low blood pressure, pelvic congestion

	Senna (*Senokot*)
Dosage and route	One to eight tablets per day at bedtime or 10–25 mL of syrup
Indications:	Short-term treatment of constipation, treatment of encopresis, found in many over-the-counter (OTC) preparations
Contraindications	Hypersensitivity.Gastrointestinal (GI) obstruction or perforation.Ulcerative colitis.Symptoms of appendicitis or acute surgical abdomen.Acute intestinal inflammation (Crohn's disease), Fecal impaction and GI or rectal bleeding.
Adverse effects	Stomach cramps and diarrhoea

Figure 2.7. 1: Forms of chemical stimulant laxative

BULK STIMULANT LAXATIVES

Bulk stimulant laxatives increase the bulk by osmotic pull of fluid into the feces. That increase the increased bulk stretches the gastro-intestinal wall, leading to the stimulation and increased GI movement. The bulk stimulants are also called mechanical stimulants. The commonly used bulk stimulants include magnesium sulfate (Epsom salts), magnesium citrate (Citrate of Magnesia), magnesium hydroxide (Milk of Magnesia), lactulose (Chronulac), polycarbophil (FiberCon), psyllium (Metamucil), and polyethylene glycol-electrolyte solution (GoLYTELY, MiraLAX).

Therapeutic action

Lactulose is a saltless osmotic laxative that pulls fluid out of the venous system and into the lumen of the small intestine. Magnesium citrate is a milder and slower-acting laxative. It works by a saline pull, bringing fluids into the lumen of the GI tract.

Magnesium hydroxide is a milder and slower-acting laxative. It also works by a saline pull, bringing fluids into the lumen of the GI tract. Magnesium sulfate acts by exerting a hypertonic pull against the mucosal wall, drawing fluid into the intestinal contents.

Polycarbophil is a natural substance that forms a gelatin-like bulk out of the intestinal contents. This agent stimulates local activity. It is considered milder and less irritating than many other bulk stimulants. Patients must use caution and take polycarbophil with plenty of water. Polyethylene glycol-electrolyte solution is a hypertonic fluid containing many electrolytes that pulls fluid out of the intestinal wall to increase the bulk of the intestinal contents.

Psyllium, another gelatin-like bulk stimulant, is similar to polycarbophil in action and effect.

These drugs are all taken orally. They are directly effective within the GI tract and are not generally absorbed systemically. They are rapidly acting, causing effects as they pass through the GI tract.

Bulk laxatives are contraindicated with allergy to any component of the drug to prevent hypersensitivity reactions and in acute abdominal disorders, like appendicitis, diverticulitis, and ulcerative colitis, when increased motility could lead to rupture or further exacerbation of the inflammation.

Laxatives should be used with caution in heart block, CAD and debilitation, which could be affected by the decrease in absorption and changes in electrolyte levels that can occur.

They are used with great caution during pregnancy and lactation because, in some cases, stimulation of the GI tract can precipitate labor and many of these agents cross the placenta and are excreted in breast milk.

Polyethylene glycol electrolyte solution should be used with caution in any patient with a history of seizures because of the risk of electrolyte absorption causing neuronal instability and precipitating seizures.

The most common adverse effects most commonly associated with bulk laxatives are GI effects such as diarrhea, abdominal cramping, and nausea CNS effects, including dizziness, headache, and weakness, are not uncommon and may relate to loss of fluid and electrolyte imbalances that may accompany laxative use, palpitations, flushing, and even fainting

Figure 2.7.2 Forms of bulk laxatives

Table 2.7.2: Bulk laxatives drugs

	Lactulose (Chronulac)
Dosage and route	15–30 mL PO
Indications:	Short-term treatment of constipation, alternative choice for patients with cardiovascular disorders
Contraindications	Prior to surgery, especially if the procedure requires electrocautery during proctoscopy or colonoscopy.
Adverse effects	Diarrhoea, bloating and wind

	Magnesium citrate (Citrate of Magnesia
Dosage and route	One glassful, 1/2 glass for pediatric patient
Indications:	Stimulates bowel evacuation before GI diagnostic tests and examinations.
Contraindications	Decreased kidney function, diarrhoea, high amount of magnesium in the blood, low amount of sodium in the blood, dehydration, appendicitis, blockage of the stomach or intestine, seizures.
Adverse effects	Pain with bowel movements, rectal bleeding; watery diarrhea, nausea, vomiting, severe stomach pain; painful or difficult urination; flushing, warmth, redness, or tingly feeling

	Magnesium hydroxide (Milk of Magnesia)
Dosage and route	15–30 mL PO
Indications:	Short-term treatment of constipation, prevention of straining after GI surgery, obstetrical delivery, MI
Contraindications	Renal failure, existing electrolyte imbalance, appendicitis symptoms or acute surgical abdomen, myocardial damage or heart block, fecal impaction or rectal fissures, intestinal obstruction or perforation, undiagnosed abdominal pain.
Adverse effects	Severe nausea, vomiting, or diarrhea; no bowel movement after using the medicine as a laxative;rectal bleeding; or. worsening symptoms

	Magnesium sulfate (Epsom salts)
Dosage and route	10–25 mg PO
Indications:	Very potent laxative used for total, rapid evacuation of the GI tract (e.g., for treatment of GI poisoning)
Contraindications	severe stomach pain;nausea or vomiting; a perforated bowel; a bowel obstruction or severe constipation; colitis or toxic megacolon or. a sudden change in bowel habits lasting 2 weeks or longer
Adverse effects	Difficult breathing; swelling of your face, lips, tongue, or throat. Common side effects may include diarrhea or upset stomach.

LUBRICANT DRUGS

For some persons, there may be a need to make defecation easier without using drugs designed to stimulate the gastrointestinal tract, in this case they benefit from lubricants usage. Patients with hemorrhoids and those who have recently had rectal surgery may need lubrication of the stool. Some patients who could be harmed by straining might also benefit from this type of laxative. The type of laxative recommended depends on the condition of the patient, the speed of relief needed,

and the possible implication of various adverse effects. Lubricating laxatives include docusate (Colace), glycerin (Sani-Supp), and mineral oil (Agoral Plain).

Therapeutic actions

Docusate has a detergent action on the surface of the intestinal bolus, increasing the admixture of fat and water and making a softer stool. **Glycerin** is a hyperosmolar laxative that is used in suppository form to gently evacuate the rectum without systemic effects higher in the GI tract.

Mineral oil is the oldest of these laxatives. It is not absorbed and forms a slippery coat on the contents of the intestinal tract. When the intestinal bolus is coated with mineral oil, less water is absorbed out of the bolus, and the bolus is less likely to become hard or impacted. These drugs are not absorbed systemically and are excreted in the feces. Docusate and mineral oil are given orally. Glycerin is available as a rectal suppository or as a liquid for rectal retention.

These laxatives are **contraindicated** with allergy to any component of the drug to prevent hypersensitivity reactions and in acute abdominal disorders, including appendicitis, diverticulitis, and ulcerative colitis, when increased motility could lead to rupture or further exacerbation of the inflammation.

The adverse effects most commonly associated with lubricant laxatives are GI effects such as diarrhea, abdominal cramping, and nausea. In addition, leakage and staining may be a problem when mineral oil is used and the stool cannot be retained by the external sphincter. CNS effects, including dizziness, headache, and weakness, are not uncommon and may relate to loss of fluid and electrolyte imbalances that may accompany laxative use. Sweating, palpitations, flushing, and even fainting have been reported after laxative use. These effects are less likely to happen with the lubricant laxatives than with the chemical or mechanical stimulants. Frequent use of mineral oil can **interfere** with absorption of the fat-soluble vitamins A, D, E, and K.

Tables 2.7.3: Lubricant laxatives

	Docusate (Colace)
Dosage and route	50–240 mg PO
Indications:	Prophylaxis for patients who should not strain (such as after surgery, MI, or obstetrical delivery)
Contraindications	Hypersensitivity reaction to any of the docusate ingredients. Avoid concomitant use of mineral oil. Increased absorption of the oil may result

Adverse effects	Abdominal cramping, Stomach pain, Diarrhea. Excessive bowel activity. Intestinal obstruction. Throat irritation. Rash.Low electrolyte levels, Headaches, dizziness, nausea, vomiting and excessive thirst

	Glycerin (Sani-Supp)
Dosage and route	4 mL of liquid suppository
Indications:	Short-term treatment of constipation
Contraindications	Abdominal pain, nausea, or vomiting present) Rectal bleeding or failure to have bowel movement requires physician care
Adverse effects	Headaches, dizziness, nausea, vomiting and excessive thirst

	Mineral oil (Agoral Plain)
Dosage and route	5–45 mL PO
Indications:	Short-term treatment of constipation
Contraindications	Appendicitis, hiatal hernia, blockage of the stomach or intestine, difficulty swallowing.Weakened patient, bedridden patient or one unable to move around freely, problem emptying stomach contents.
Adverse effects	Fecal incontinence, intestinal malabsorption, impaired absorption of fat-soluble vitamins, rectal discharge of mineral oil, anal itching and irritation, abdominal cramps, nausea.

Figure 2.7.2 Forms of lubricant laxatives

Self assessment 2.7

1. All of the following drugs are bulk laxatives, **EXCEPT:**
   A. Polycarbophil
   B. Glycerin
   C. Lactulose
   D. Magnesium hydroxide
2. Which of the following drugs is a lubricant laxative?
   A. Bisacodyl
   B. Lactulose
   C. Mineral oil
   D. Magnesium hydroxide
3. All of the following conditions are indications of laxatives, **EXCEPT**:
   A. To treat simple, chronic constipation.
   B. To accelerate the movement of ingested
   C. Before diagnostic procedures of the colon
   D. To treat mild to moderate diarrhea
4. Explain the mechanism of action of bulk laxatives.
5. Explain the mechanism of action of chemical stimulant laxatives.

2.8. Oral Rehydration Salts (ORS) and home-made rehydration solution

Learning Activity 2.8

A nurse receives a 23years old female patient in health centre who is complaining of diarrhea. When a patient is asked about frequency, she responded that she is passing 3 watery stool every 12hrs and this started 2days ago. The nurse decided to give oral rehydration salts to that patient for rehydration.

Using internet, work on the following topics and make notes

1. Discuss the composition of oral rehydration salt
2. What are the indications of oral rehydration salts?
3. Discuss how you can prepare homemade rehydration solutions

CONTENT SUMMARY

The oral rehydration solution (ORS) is an oral powder that contains mixture of glucose, sodium chloride, potassium chloride, and sodium citrate. It is dissolvable in water and after being dissolved in the requisite volume of water they are intended to be used for the prevention and treatment of dehydration due to diarrhea. It is always combined with zinc are recommended by the WHO and UNICEF to be used collectively to ensure the effective treatment of diarrhea. ORS replaces the essential fluids and salts lost through diarrhea. Zinc decreases the duration and severity of an episode and reduces the risk of recurrence in the immediate short term. ORS and zinc are highly effective and affordable products for treatment of childhood diarrhea that could prevent deaths in up to 93% of diarrhea cases.

ORS is a powder for dilution in 200ml, 500ml and 1L and they are hermetically sealed, laminated sachets made of multiply laminations with aluminium foil or polyethylene foil. They are two types of ORS; ***high osmolality rehydration salt*** that has the osmolality of 311molm/L, ***low osmolality oral rehydration solution*** that has 245molm/L. The latter,being very effective, it is recommended by WHO for use due to its great pharmacological and therapeutic effect. It is available as low osmolarity 20.5g/1L and low osmolarity 10.2g/0.5L

Table 2.8.1: Compositions of oral rehydration salution

COMPONENT	CHEMICAL FORMULA	CONCENTRATION g/l
Sodium chloride	Na cl	2.6
Glucose anhydrous	$C_6H_{12}O_6$	13.5
Potassium chloride	KCL	1.5
Trisodium citrate dehydrate	C6H5NA3O7,2HO2	2.9
After dissolution in drinking water		
Component	Concentration	Total
Sodium	75mmol/L	245mosm/L
Chloride	65mmol/L	
Glucose, anhydrous	75mmol/L	
Potassium	20mmol/L	
Citrate	10mmol/L	

ORS has contributed to life saving due to the pharmacokinetics and therapeutic values of its components.

Glucose facilitates the absorption of sodium and hence water in small intestine. **Sodium** and potassium are important in replacement of losses of the essential ions during diarrhea and vomiting. **Citrate** corrects the acidosis that occurs as a result of diarrhea and dehydration.

Figure 2.8.1 ORS FORMS

In clinical practice, ORS is indicated for the treatment of fluid losses especially in case of diarrhea in infants, children and adults with mild to moderate dehydration.

The amount to be given is determined on basis of weight and the amount of solution require depend largely on child status. For child with marked signs of dehydration or who combines to pass frequently watery stools will require more solution than those with less marked signs or who are not passing frequent stools.

The approximate amount of ORS solution to give in the first 4 hours:

Below 4 months / less than 5 kg: 200–400 mL

4–11 months / 5–7.9 kg: 400–600 mL

12–23 months / 8–10.9 kg: 600–800 mL

To 4 years / 11–15.9 kg: 800–1,200 mL

To 14 years / 16–29.9 kg: 1,200–2,200 mL

15 years or older / 30 kg or more: 2,200–4,000 mL

If a child wants more than the estimated amount of ORS solution, and there are no signs of overhydration, give more.

In case the child's weight is unknown, use patient's age and if the weight is known the amount of ORS is estimated by multiplying the child's weight in kg times 75ml. During the initial stages of therapy, while still dehydrated, adults can consume up to 750 mL per hour, if necessary, and children up to 20 mL/kg body weight per hour. Normal feeding can continue after the initial fluid deficit has been corrected. Breastfeeding should continue between administrations of ORS.

Edematous (puffy) eyelids are a sign of overhydration. If this occurs, stop giving ORS solution, but give breast milk or plain water, and food. Do not give a diuretic. When the edema has gone, resume giving ORS solution or home fluids according to Treatment Plan A. After 4 hours, reassess the child fully. Then decide what treatment to give next: If signs of severe dehydration have appeared, IV therapy should be started following WHO Treatment Plan C

If the patient still has signs indicating some dehydration, continue oral rehydration therapy by repeating the treatment described above. At the same time, start to offer food, milk and other fluids, as described in WHO Treatment Plan A. If there are no signs of dehydration, the patient should be considered fully rehydrated.

ORS should not be taken when a patient has cirrhosis of liver, congestive heart cardiac failure, nephrotic syndrome acute and renal failure, ischemic heart diseases, adrenocortical insufficiency, hyperkalemic periodic paralysis, hyperkalemia, hypoventilatory states, chloride depletion due to continuous gastric fluid loss,

metabolic or respiratory alkalosis, hypocalcaemia, hyperosmolar states in anuria or oliguria, edematous sodium retaining conditions, hypertension, peripheral or pulmonary edema or toxaemia of pregnancy, severe vomiting, diarrhea and dehydration requiring fluid therapy, dextrose malabsorption, diabetes mellitus, thiamine deficiency, severe under nutrition as another specific solution ''**ReSoMal"** is appropriate, hemodilution, hypophosphatemia, sepsis, and trauma.

ORS is also contraindicated for use in patients undergoing treatment with the following: sodium-retaining drugs such as corticosteroids, NSAIDs, carbenoxolone, or diuretics known to produce hypochloremic alkalosis.

It is very important to note that, ORS is administered with care in cases of acute dehydration, heat cramps, extensive tissue destruction, or if patients are receiving potassium-sparing diuretics. Concurrent use with other potassium-containing drugs may precipitate hyperkalemia.

It is very important to dissolve ORS in water of the correct volume. A weak solution will not contain optimum glucose and electrolyte concentration and a strong solution may give rise to electrolyte imbalance. Diarrhea can have very serious consequences in children under 3 years old. Immediate medical advice should be sought. In other age groups, if symptoms persist for more than 24–48 hours, consult a doctor.

If nausea and vomiting are present with the diarrhea, small and frequent amounts of ORS should be drunk first. In infants, immediate medical assistance should be obtained. Use within 1 hour of reconstitution, or within 24 hours if stored in a refrigerator.

ORS interact with other medicinal products.t increases excretion of lithium, resulting in a reduced plasma-lithium concentration.

Potassium chloride ACE inhibitors (hyperkalemia), cyclosporine leads to increased risk of hyperkalemia, potassium-sparing diuretics where hyperkalemia may result. No known interactions to other actives. For more details, see also under "Contraindications" section.

Undesirable effects

Adverse effects are not very common but in case of excessive amount, hypernatremia, edema, nausea, vomiting, diarrhea, abdominal cramps, thirst, reduced salivation, lachrymation, sweating, fever, tachycardia, renal failure, respiratory arrest, headache, dizziness, restlessness, irritability, weakness, muscular twitching, coma, convulsions, hyperkalemia, gastrointestinal ulceration, metabolic alkalosis, muscle hypertonicity, flatulence, dehydration, and raised blood pressure may arise.

In case of overdose, sodium, potassium restriction, and water intake plus measures to increase renal sodium, potassium and water output by using loop diuretics for example are recommended.

HOME-MADE ORAL REHYDRATION SALT

Homemade oral rehydration solution is a rehydration solution prepared at home using sugar, salt and water locally available at home. It less expensive most effective but require attention in preparation as in case of error in preparation it may worsen diarrhoea or cause imbalances.

Table 2.8.2: Components of homemade oral rehydration salts and dosage

Ingredients	**Amount**
Purified water	1l
Salt	2.5ml=1.2 teaspoon
Sugar	30ml=6teaspoons
Dosage	
Age	**Amount**
Under 2years	50-100ml or ¼ to ½ cup after each stool max 0.5l or 2 cups per day
2-9YEARS	100-200ml or ½ to 1 cup after each stool max1L OR 41/4 cups each day
10years and above	As much as s/he wants approx. 2l or 81.2 cups per day

PREPARATION OF HOME-MADE ORS

Materials

Teaspoon

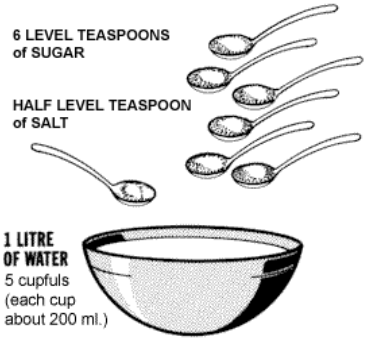
Salt

Sugar

Clean or boiled water

Container 1 L OR above

Step1



Step 2

Step 3

Step 4

Step 5 (container colour to be changed)

Self assessment 2.9

Respond by True or false

1. High osmolality oral rehydration solutions are more effective than low osmolality solutions.
2. Oral rehydration salt is indicated in case of diarrhea with mild dehydration.
3. You have to avoid oral rehydration salt for a patient with severe acute malnutrition.
4. When treating a child with mild diarrhea, there is no need to go to the health facility as you can offer homemade oral rehydration solution.

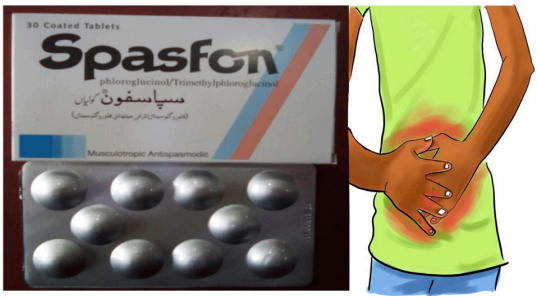
Chose the correct answer

1. The components of oral rehydration salt include the following **Except**
   A. Sodium
   B. Magnesium
   C. Sugar
   D. Citrate
2. What is the amount of ORS to be given to a patient weighing 30Kg in the first 4hours?
   A. 2,200–4,000 mL
   B. 3000-5000ml
   C. 1000-2100ml
   D. 500ml-1500ml
3. For a child with diarrhea, which advice will you give to the caregiver about moment of ORS administration
   A. When child wake up
   B. When the child asks
   C. After each stool
   D. B and C
4. The ingredients for homemade oral rehydration solution are
   A. Salt, beans, sugar and water
   B. Rice, sugar and beans
   C. Sugar, salt and water
   D. Sugar, salt and rice

5. Which action should be taken for a patient when there is no improvement and the dehydration worsened, after 4hrs of ORS administration?

   A. Increase the amount
   B. Start IV fluids
   C. Administer antibiotics
   D. Continuation of monitoring

2.9. Anti-spasmodic drugs



Learning Activity 2.9

1. What is an antispasmodic drug?
2. Give 4 indications of antispasmodic drugs?

CONTENT SUMMARY

Gastrointestinal antispasmodics are medications used to treat spasms of the gastrointestinal tract muscles, which can occur in diseases like irritable bowel syndrome, or IBS for short, biliary colic, and pancreatitis it relieves some of the symptoms of Irritable Bowel Syndrome (IBS) , prevents, or lowers the incidence of muscle spasms(colic), bloating and tummy (abdominal) pain, especially those of smooth muscle such as in the bowel wall, and it reduce the movement (motility) of the gut (intestines).

Antispasmodics are also used in some other conditions such as:

- Diverticular disease.
- Prevention of nausea, vomiting, and dizziness associated with motion sickness.

- Adjunctive therapy for treatment of GI ulcers
- Decrease secretions before anesthesia or intubation
- Maintenance treatment of bronchospasm associated with COPD.
- Treatment of irritable or hyperactive bowel in adults.

The most common antispasmodic contain anticholinergic properties, which is helpful in relieving symptoms, such as abdominal pain. They are classified into two main types: smooth muscle relaxant such as alveline and mebeverine, and anticholinergics such as hyoscin. However not everybody with IBS finds that antispasmodics work well, but they are worth trying, as they work well in a good number of cases.

There are two main types antispasmodic drugs**: Antimuscarinics drugs and Smooth muscle relaxants:**

Smooth muscle relaxants work directly on the smooth muscle in the wall of the gut. Here they help to relax the muscle and relieve the pain associated with a contraction of the gut.

A. Antimuscarinic drugs

Antimuscarinic medications are a group of anticholinergic agents, specifically known for blocking the activity of muscarinic receptors. These receptors play an important role in mediating the functions of the parasympathetic nervous system, which controls many involuntary functions to conserve energy, including the contraction of smooth muscle, dilation of blood vessels, increased bodily secretions, gastrointestinal activity, and heart rate. Because muscarinic receptors are also found in other parts of the body, taking an antimuscarinic can have other effects. For example, muscarinic receptors also help to control the production of saliva in the mouth.

Therefore, antimuscarinics work by inhibiting the functions of the parasympathetic nervous system. The two most commonly prescribed antimuscarinics are atropine and scopolamine(Hyoscine), derived from the Atroppa belladonna plant.

1. Hyoscine (Buscopan 10 mg Tablets)

Hyoscine butylbromide are indicated for the relief of spasm, by helps dismiss lower tummy (abdominal) muscle cramp and pain, it one of antispasmodic medicine which is indicated to treat cramps in the stomach, the genito-urinary tract or gastro-intestinal tract and for the symptomatic relief of Irritable Bowel Syndrome or bladder. In gastro- intestinal tract, specificaly it helps to ease bloating and the spasm-type pain that can be associated with irritable bowel syndrome and diverticular disease. It works by relaxing some of the muscles in your gastrointestinal and urinary systems. Each tablet contains hyoscine butylbromide 10 mg.

Posology and method of administration

Buscopan 10 mg tablets are for oral administration only.

Buscopan 10 mg tablets should be swallowed whole with adequate water.

Adults: 2 tablets four times daily. For the symptomatic relief of Irritable Bowel Syndrome, the recommended starting dose is 1 tablet three times daily, this can be increased up to 2 tablets four times daily if necessary.

Children: 6 - 12 years: 1 tablet three times daily.

Contraindications

Buscopan 10 mg Tablets are contraindicated in: patients who have demonstrated prior hypersensitivity to hyoscine butylbromide or any other component of the product, myasthenia gravis, mechanical stenosis in the gastrointestinal tract, paralytic or obstructive ileus, megacolon, narrow angle glaucoma.

Special Precautions: Buscopan 10 mg Tablets should not be taken on a continuous daily basis or for extended periods without investigating the cause of abdominal pain. In case severe, unexplained abdominal pain persists or worsens, or occurs together with symptoms like fever, nausea, vomiting, changes in bowel movements, abdominal tenderness, decreased blood pressure, fainting, or blood in stool, medical advice should immediately be sought.

Interaction with other medicinal products and other forms of interaction

The anticholinergic effect of drugs such as tri- and tetracyclic antidepressants, antihistamines, quinidine, amantadine, antipsychotics (e.g. butyrophenones, phenothiazines), disopyramide and other anticholinergics (e.g. tiotropium, ipratropium, atropine-like compounds) may be intensified by Buscopan. Concomitant treatment with dopamine antagonists such as metoclopramide may result in diminution of the effects of both drugs on the gastrointestinal tract. The tachycardic effects of beta-adrenergic agents may be enhanced by Buscopan.

Adverse Reactions:

Many of the listed undesirable effects can be assigned to the anticholinergic properties of buscopan

- Immune system disorders: anaphylactic shock, anaphylactic reactions, dyspnoea, other hypersensitivity
- Cardiac disorders: tachycardia
- Gastrointestinal disorders: dry mouth
- Skin and subcutaneous tissue disorders: skin reactions (e.g. urticaria, pruritus), abnormal sweating
- Renal and urinary disorders urinary retention (Rare)

Overdose

Serious signs of poisoning following acute overdosage have not been observed in man. In the case of overdosage, anticholinergic effects such as urinary retention, dry mouth, reddening of the skin, tachycardia, inhibition of gastrointestinal motility and transient visual disturbances may occur, and Cheynes-Stokes respiration has been reported.

Pharmacokinetics

Absorption

As a quaternary ammonium compound, hyoscine butylbromide is highly polar and hence only partially absorbed following oral (8%) or rectal (3%) administration. After oral administration of single doses of hyoscine butylbromide in the range of 20 to 400 mg, mean peak plasma concentrations between 0.11 ng/mL and 2.04 ng/mL were found at approximately 2 hours.

Distribution

Because of its high affinity for muscarinic receptors and nicotinic receptors, hyoscine butylbromide is mainly distributed on muscle cells of the abdominal and pelvic area as well as in the intramural ganglia of the abdominal organs. Plasma protein binding (albumin) of hyoscine butylbromide is approximately 4.4%. Animal studies demonstrate that hyoscine butylbromide does not pass the blood-brain barrier, but no clinical data to this effect is available.

Metabolism and elimination

Following oral administration of single doses in the range of 100 to 400 mg, the terminal elimination half-lives ranged from 6.2 to 10.6 hours. The main metabolic pathway is the hydrolytic cleavage of the ester bond. Orally administered hyoscine butylbromide is excreted in the faeces and in the urine. Studies in man show that 2 to 5% of radioactive doses is eliminated renally after oral, and 0.7 to 1.6% after rectal administration. Approximately 90% of recovered radioactivity can be found in the faeces after oral administration. The urinary excretion of hyoscine butylbromide is less than 0.1% of the dose. The mean apparent oral clearances after oral doses of 100 to 400 mg range from 881 to 1420 L/min, whereas the corresponding volumes of distribution for the same range vary from 6.13 to 11.3 x 105 L, probably due to very low systemic availability. The metabolites excreted via the renal route bind poorly to the muscarinic receptors and are therefore not considered to contribute to the effect of the hyoscine butylbromide.

2. Atropine

Atropine is a type of medicine called an antimuscarinic (or sometimes called an anticholinergic). It works by relaxing the involuntary muscle that is found in the

walls of the stomach and intestines (gastrointestinal tract). Cholinergic antagonism with atropine reduces proximal gastric emptying, reduces atrial contractility and notably slows gastric emptying. Atropine is also used in case of hypersalvation, bronchial secretions, or bradycardia. This drug can be used also before anesthesia to prevent the mucus secretion.

Indication

Relieving stomach cramps or colicky-type abdominal pain, for example associated with conditions such as irritable bowel syndrome (IBS).

Therapeutic action

Atropine is a type of medicine called an antimuscarinic (or sometimes called an anticholinergic). It works by relaxing the involuntary muscle that is found in the walls of the stomach and intestines (gastrointestinal tract). Atropine works by blocking receptors called muscarinic (sometimes called cholinergic) receptors that are found on the surface of the muscle cells in the walls of the gut. This prevents a natural body chemical called acetylcholine from acting on these receptors. Normally when acetylcholine acts on these receptors it causes the muscle in the gut to contract. By preventing this, atropine helps the muscle in the gut to relax. This reduces involuntary contractions and spasms of the muscle. Spasms in the muscle of the gut wall can cause colicky abdominal pain, cramps, bloating, wind and discomfort. Atropine relieves these symptoms by relaxing the muscle.

Administration

Atropine tablets should be swallowed whole with a glass of water. They can be taken either with or without food. The usual dose is one or two tablets to be taken at night. Follow the instructions given by your doctor or pharmacist.

Use with caution in Elderly people, Children, People with Down's syndrome. Gastro-esophageal reflux disease (GORD). Inflammation of the bowel and back passage (ulcerative colitis), Diarrhea, People with a high temperature (fever). People with disorders of the involuntary nervous system that controls body functions such as blood pressure, heart rate, sweating, bowel and bladder emptying, and digestion (autonomic neuropathy), People with an overactive thyroid gland (hyperthyroidism), High blood pressure (hypertension), Heart attack (myocardial infarction) and Glaucoma.

Atropine should not be used in people with a condition called myasthenia gravis, where there is abnormal muscle weakness, people with inactivity of the muscle in the gut that is causing a blockage or obstruction of the gut (paralytic ileus), people who have narrowing of the outlet of the stomach, making it difficult for food to pass into the intestines (pyloric stenosis), Men with an enlarged prostate gland (prostatic hypertrophy) and people with allergic of its ingredients. If you feel you

have experienced an allergic reaction, stop using this medicine and inform your doctor or pharmacist immediately.

Pregnancy and breastfeeding

This medicine should be used with caution during pregnancy, and only if the expected benefit to the mother is greater than any possible risk to the developing baby, it passes into breast milk in small amounts. It should be used with caution by breastfeeding mothers, and only if the expected benefit to the mother is greater than any possible risk to the nursing infant.

Side effects

Medicines and their possible side effects can affect individual people in different ways. The following are some of the side effects that are known to be associated with Atropine. Just because a side effect is stated here, it does not mean that all people using this medicine will experience that or any side effect.

Constipation, dry mouth, flushing and dryness of the skin, increased body temperature, blurred vision, **dilated pupils** and dislike of bright light, faster than normal heartbeat (tachycardia), awareness of your heartbeat (palpitations), irregular heartbeats (arrhythmias), difficulty passing urine (urinary retention), confusion (especially in elderly people), feeling or being sick, closed angle glaucoma.

Interaction

It is important to tell your doctor or pharmacist what medicines you are already taking, including those bought without a prescription and herbal medicines, before you start treatment with this medicine. Similarly, check with your doctor or pharmacist before taking any new medicines while using this one, to make sure that the combination is safe. There may be an increased risk of antimuscarinic side effects, such as dry mouth, blurred vision, constipation, difficulty passing urine and confusion in elderly people, if this medicine is taken with other medicines that have antimuscarinic effects, for example the following:

- Amantadine: antihistamines, e.g. brompheniramine, chlorphenamine
- Antimuscarinic medicines for Parkinson's symptoms, eg procyclidine, orphenadrine, trihexyphenidyl
- Certain antipsychotic medicines, e.g. haloperidol, chlorpromazine, clozapine
- Other antispasmodic medicines, e.g. hyoscine
- Antidepressants, e.g. phenelzine, tranylcypromine
- Tricyclic antidepressants, e.g. amitriptyline, clomipramine.

Drug interactions

This medicine may reduce the effects of the following medicines: Cisapride, domperidone, ketoconazole, metoclopramide. If you experience a dry mouth as

a side effect of this medicine you may find that medicines that are designed to dissolve and be absorbed from under the tongue, e.g. sublingual glyceryl trinitrate (GTN) tablets, become less effective. This is because the tablets do not dissolve properly in a dry mouth. To resolve this, drink a mouthful of water before taking sublingual tablets.

B. Smooth muscle relaxants

Smooth muscle relaxants work directly on the smooth muscle in the wall of the gut. Here they help to relax the muscle and relieve the pain associated with a contraction of the gut. A muscle relaxant is a drug that affects skeletal muscle function and decreases the muscle tone. It may be used to alleviate symptoms such as muscle spasms, pain, and hyperreflexia. The term "muscle relaxant" is used to refer to two major therapeutic groups: neuromuscular blockers and spasmolytic. Neuromuscular blockers act by interfering with transmission at the neuromuscular end plate and have no central nervous system (CNS) activity. They are often used during surgical procedures and in intensive care and emergency medicine to cause temporary paralysis. Spasmolytics, also known as "centrally acting" muscle relaxant, are used to alleviate musculoskeletal pain and spasms and to reduce spasticity in a variety of neurological conditions. While both neuromuscular blockers and spasmolytics are often grouped together as muscle relaxant, the term is commonly used to refer to spasmolytics only. The most common **Smooth muscle relaxant prototype are alverine, mebeverine, peppermint oil (colpermin) and papaverine**

Self assessment 2.9

1. The antimuscarinics are used:
   A. To accelerate the parasympathetic system
   B. To block the parasympathetic system
   C. As the drugs of choice for treating ulcers
   D. To stimulate gastrointestinal activity
2. Atropine belongs to the class of antimuscarinics. True or False.
3. All of the following antispasmodic drugs belongs to the class of smooth muscle relaxants, **EXCEPT:**
   A. Atropine
   B. Papaverine
   C. Alverine
   D. Peppermint oil

End unit assessment 2

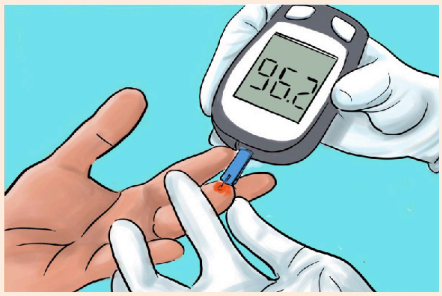
1. Which of the following is **NOT** a risk for peptic ulcer diseases?
   B. Smoking
   C. NSAIDs use
   D. Skin color
   E. Stress
2. Which of the following groups of drugs is used to treat peptic ulcer diseases?
   A. Antifungals
   B. Antivirals
   C. Analgesics
   D. Antacids.
3. Which statement is **true** about the mechanism of action of H2 receptor antagonists?
   A. The occupy the histamine receptors and prevent acid secretion
   B. They bind to enzyme H-,K-ATPase and increase histamine release
   C. They block prostaglandin secretion and decrease histamine release
   D. They neutralize the secreted acid directly in the stomach lining
4. Which of the following is among the side effects of metoclopramide?
   A. Constipation
   B. Drowsiness
   C. Fever
   D. Headache
5. Which of the following laxatives acts without causing the systemic effect?
   A. Bisacodyl
   B. Lactulose
   C. Glycerin
   D. Magnesium citrate
6. Which one among the following conditions reflects a contraindication of antispasmodic drugs?
   A. Irritable bowel syndrome
   B. Biliary colic
   C. Pancreatitis
   D. Gastrointestinal obstruction

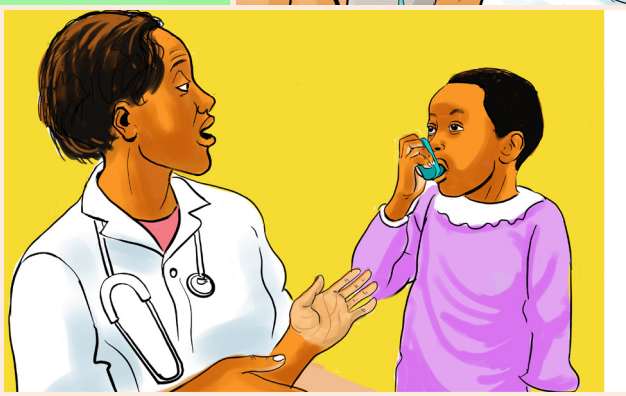
MEDICATIONS USED FOR NON-COMMUNICABLE DISEASES

Key Unit Competence

At the end of this unit, the learner will be able to provide appropriate medications for hypertension, diabetes mellitus and asthma.

Introductory activity 3.0





1) What do you observe on these images?
2) In which medical conditions are the materials in these images used?
3) What types of medications are the patients taking?

Learning Activity 3.1

As an associate Nurse Student doing a clinical placement in the hospital, you received a 66-year-old male patient in consultation room. His vitals were: the blood pressure was 150/100 mmHg, temperature 36.5^{0}C, heart rate 17 movements per minute, SPO2: 99%, and pulse of 65 beats per minute. The physician concluded that the patient had hypertension.

a) What is hypertension?

b) Identify the classes of hypertension considering their grade.

c) Enumerate at least 3 classes of hypertensive drugs.

3.1. Introduction to antihypertensive drugs

CONTENT SUMMARY

The cardiovascular system is a closed system of blood vessels that is responsible for delivering oxygenated blood to the tissues and removing waste products from the tissues. Blood pressure is the force exerted by circulating blood against the walls of the body's arteries, the major blood vessels in the body.

A Blood pressure is written as two numbers. The first (systolic) number represents the pressure in blood vessels when the heart contracts or beats. The second (diastolic) number represents the pressure in the vessels when the heart rests between beats.

The body uses this responsiveness to regulate blood pressure on a constant basis, to ensure that there is enough pressure in the system to deliver sufficient blood to the brain.

Hypertension is defined as a high blood pressure. It is diagnosed if, when it is measured on two different days, the systolic blood pressure readings on both days is ≥140 mmHg and/or the diastolic blood pressure readings on both days is ≥90 mmHg.

As blood pressure increases, it is more difficult to control it at the target level through lifestyle modifications alone, and treatment with antihypertensive drugs becomes necessary. The occurrence of cardiovascular disease can be prevented by reducing the blood pressure with antihypertensive drugs.

Table 3.1.1: Classification of hypertension

Classification	Systolic B.P(mmhg)	Diastolic B.P(mmhg)
Optimal	<120	<80
Normal	<130	<85
High normal	130-139	85-89
HYPERTENSION		
Grade 1: Mild	140-159	90-99
Grade2:Moderate	160-179	100-109
Grade 3 :Severe	180	≥110
Isolated diastolic/systolic		
Grade 1	140-159	≥90
Grade 2	≥160	≥ 100

Antihypertensive drugs

Anti-hypertensive drugs are a class of drugs that are used to treat hypertension. Antihypertensive therapy seeks to prevent the complications of high blood pressure, such as stroke and myocardial infarction. Appropriate antihypertensive drugs should be selected considering compelling indications, contraindications and conditions that require the careful use of drugs and the presence or absence of complications. Antihypertensive drugs are administered once a day, in principle, but as it is more important to control the blood pressure over 24 h splitting the dose into twice a day is desirable in some situations.

A gradual reduction in blood pressure is desirable in hypertensive patients in general, but the target control level should be achieved within several weeks in high-risk patients, such as those with grade III hypertension and multiple risk factors. The use of two or three drugs in combination is often necessary to achieve the target of blood pressure control Simplification of the prescription using fixed-combination drugs is useful for improving adherence and controlling blood pressure.

The major classes of antihypertensive drugs are:

- Diuretics
- Calcium channel blockers
- Angiotensin converting enzyme inhibitors
- Angiotensin II receptor antagonists/blockers,

- Adrenergic blockers, centrally and peripherally acting blockers (sympatholytics),
- Peripheral vasodilators

Self-assessment 3.1

You are working in a health centre and today you receive a client in the consultation room. When you take the blood pressure you find that the patient has a B.P of 160/100mmHg, then you tell your client that he has hypertension. The latter asks you what about the grade of his B.P.

1. What would be the response to the client?

2. Which one among the following classes of drugs is an antihypertensive?

   a) Diuretics

   b) Analgesics

   c) Antibiotics

   d) Antihistamines

3.2.Diuretic drugs

Learning Activity 3.2

As associate Nurse Student in the clinical placement in hospital, you receive a 50-year-old male patient in the consultation room. His vital signs are: the blood pressure is150/100 mmHg, temperature 36.5^{0}C, respiration rate 17 movements per minute, SPO2: 99%, and pulse of 65 beats per minute. The patient complains of frequent urination, and the nurse informs the patient that the drugs the patient is taking are associated with an frequent urination. When the student wants more explanation, the nurse replies that the drugs fall to the class of diuretics.

Using library textbooks, read and take note while responding to the following questions.

1) What is diuretic drug?

2) Identify the categories of diuretic drugs and give an example for each.

CONTENT SUMMARY

Diuretics are drugs that increase sodium excretion and lower blood volume, consequently lower the blood pressure. Diuretics are divided into four categories according to their action: thiazide diuretics, loop diuretics, potassium-sparing diuretics, and osmotic diuretics. The type of diuretic used is determined by the condition being treated. They are used to treat mild hypertension and often first agents used, often used in combination with other agents

Thiazide diuretics

Thiazide agents are the most commonly used type of diuretic, increasing excretion of water, sodium, chloride, and potassium. Their site of action is proximal part of the distal convoluted tubule, and all of them have antihypertensive effect.

They are contraindicated in case of diabetes, severe renal failure, impaired liver function, and a history of gout.

Tables 3.2.1: Thiazide diuretics

	Chlorothiazide (*Diuril*)
Dose	**Adult**: 0.5– 2 g/d PO for hypertension **Paediatric (<6 mo)**: up to 33 mg/kg/d PO **Paediatric (>6 mo)**: 22 mg/kg/d PO in two divided doses
Indications	Adjunctive treatment of Hypertension
Adverse effects	Dizziness, light-headedness, headache, blurred vision, loss of appetite, stomach upset, diarrhea, or constipation

	Hydrochlorothiazide (*HydroDIURIL*)
Dose	**Adult**: 25–100 mg/d PO for hypertension **Paediatric (<6 mo)**: up to 3.3 mg/kg/d PO in two divided doses **Paediatric (6 mo–2 y)**: 12.5–37.5 mg/d PO in two divided doses **Paediatric (2–12 y):** 37.6–100 mg/d PO in two divided doses

Indications	Monotherapy or as adjunctive treatment of hypertension
Adverse effects	Low B.P, dizziness. Headache, weakness, erectile dysfunction, tingling in your hands, legs, and feet.

Figure 3.2.1: Thiazide diuretics

Loop diuretics

Loop diuretics are drugs that act on the Loop of Henle not prescribed routinely for hypertension, but are used when diuresis is required. Loop diuretics are used in the treatment of oedema associated with impaired renal kidney function or liver disease. They are also commonly prescribed for the treatment of congestive heart failure, pulmonary oedema, and ascites caused by malignancy or cirrhosis.

If thiazides are ineffective in the treatment of hypertension, loop diuretics sometimes are used in combination with other antihypertensive(s).

The most commonly used loop diuretic is furosemide (Lasix). Its usual dose is 20–80 mg/d but up to 600mg/d may be given.

For Intravenous or intramuscular20–40 mg IM or IV given slowly; 40 mg IV over 1–2 min for acute pulmonary oedema, increase to 80 mg after 1 h if response is not adequate; 40 mg PO b.i.d. for hypertension.

Pediatric: 2 mg/kg/d PO for hypertension, not to exceed 6 mg/kg/d; 1 mg/kg IV or IM for edema, increased by 1 mg/kg as needed; not to exceed 6 mg/kg Treatment of acute HF; acute pulmonary edema; hypertension; and edema of HF, renal disease, or liver disease

Loop diuretics are contraindicated in dehydrated patients, those with anuria and in case of hypersensitivity to the drug or its components.

Figure 3.2.2: Dosage forms of furosemide

Potassium-Sparing Diuretics

The potassium-sparing agents are used in the management of edema associated with congestive heart failure, hepatic cirrhosis with ascites, the nephrotic syndrome, and idiopathic edema and used in combination with other drugs in the management of hypertension. Their site of action is Distal tubule and collecting duct. They are aldosterone antagonist. Potassium-sparing drugs are contraindicated for patients with anuria, acute renal insufficiency, impaired renal function, or hyperkalemia

Tables 3.2.2: Potassium sparing diuretics:

	Amiloride (Midamor)
Dose	**Adult** 15–20 mg/d PO with monitoring of electrolytes
Indications	Adjunctive treatment of edema caused by HF, liver disease, or renal disease; hypertension; hyperkalemia and hyperaldosteronism
Adverse effects	Abdominal pain. difficulty with breathing. irregular heartbeat. nausea or vomiting. numbness or tingling in the hands, feet, or lips. Shortness of breath. weakness or heaviness of the legs.

	Spironolactonem (Aldactone)
Dose	**Adult** 50–100 mg/d PO **Pediatric**: 3.3 mg/kg/d PO
Indications	Adjunctive treatment of edema caused by HF, liver disease, or renal disease; hypertension; hyperkalemia; andhyperaldosteronism
Adverse effects	Drowsiness,dizziness, light-headedness, stomach upset, diarrhea, nausea, vomiting, or headache

Figure3.2.3: Dosage forms of Thiazide diuretics

NURSING CONSIDERATIONS FOR PATIENT RECEIVING DIURETICS

- Assess for contraindication or cautions including any allergy or hypersensitivity
- Perform a physical assessment to establish baseline data before beginning therapy, to determine the effectiveness of therapy, and to evaluate for occurrence of any adverse effects associated with drug therapy.
- Obtain an accurate body weight to provide a baseline to monitor fluid balance.
- Monitor intake and output and assess voiding patterns to evaluate fluid balance and renal function.
- Administer oral drug with food or milk to buffer the drug effect on the stomach lining if GI upset is a problem.
- Administer intravenous diuretics slowly to prevent severe changes in fluid and electrolytes.
- Administer oral form early in the day so that increased urination will not interfere with sleep.
- Monitor the dose carefully and reduce the dose of one or both drugs if given with antihypertensive agents; loss of fluid volume can precipitate hypotension.
- Monitor the patient response to the drug (e.g., blood pressure, urinary output, weight, serum electrolytes, hydration, periodic blood glucose monitoring) to
- evaluate the effectiveness of the drug and monitor for adverse effects.
- Assess weight daily to evaluate fluid balance.
- Check skin turgor to evaluate for possible fluid volume deficit, and assess edematous areas for changes, including a decrease in amount or degree of pitting.
- Provide comfort measures, including skin care and nutrition consultation, to increase compliance with drug therapy and decrease the severity of adverse effects; provide safety measures if dizziness and weakness are a problem to prevent injury.

Note: Spironolactone can be used in children but with careful monitoring of electrolytes. **Amiloride** is indicated for use in children.

Self-assessment 3.2

1. The thiazide diuretics work at the proximal part of the convoluted tubule. TRUE or FALSE
2. Which drug among the following is a potassium sparing diuretic?

a) Furosemide

b) Captopril

c) Aldactone

d) Diuril

3. Which of the following is a side effect of hydrochlorothiazide?

a) High blood pressure

b) Decreased urination

c) Excessive dysphagia

d) Erectile dysfunction

4. Enumerate the contraindications of Lasix.

3.3. Calcium channel blockers drugs

Learning Activity 3.3

A patient was given medications and he tells you that he wants to know much about the regimen he was given to control his hypertension. When you read, you found that among them there is one called nifedipine. Remembering that he had only covered diuretic drugs among hypertensive drugs, you want to give him full information about the class where nifedipine belongs.

Using library texbooks and internet, read and take note about the following:

1) In which class does nifedipine belong?
2) What are the other drugs found in this class?
3) What is the mechanism of action of the drugs from this class?

CONTENT SUMMARY

Calcium channel blockers are a type of drug that block the entry of calcium into smooth muscle cells as well as myocytes. They produce arterial vasodilation and thereby reduce arterial blood pressure. Calcium channel blockers relax and open

up narrowed blood vessels, reduce heart rate and lower blood pressure. They lower blood pressure by reducing myocardial contractility.

Tables 3.3.1: Commonly used calcium channel blockers:

	Amlodipine (Norvasc)
Dose and route	5-10mg/d p.o with reduction in hepatic and geriatric clients
Indications	Used alone or in combination with other agents for treatment of hypertension and angina in adult
Adverse effects	Headache, swelling of hands, feet, ankles or lower legs, stomach upset, nausea, dizziness, drowsiness, excessive tiredness

	Diltiazem (Cardizem,dilacor CR
Dose and route	60-120mg PO b.id
Indications	Extended release preparation used to treat hypertension in adults or other preparations are used for angina
Adverse effects	Swollen hands ,ankles or feet , headache, feeling dizzy, tired and lightheaded, weakness, redness of the skin,

	Nifedipine (Procardia XL,adalat)
Dose and route	30-60mg/d PO
Indications	Extended-release preparations only for the treatment of hypertension in adults
Adverse effects	Dizziness, flushing, weakness, swelling, ankles/feet, constipation, headache

	Verapamil (Calan SR, Covera-HS, isoptin, Verelan)
Dose and route	120-240mg/d PO, reduce dose in morning, extended release capsules 100-300mg.d at bedtime

Indications	Extended-release formulations for the treatment of essential hypertension,other preparations are used for angina and treating various arrhythmias in adults
Adverse effects	Blue lips and fingernails, chest pain, coughing difficult breathing, wheezing, dizziness and faintness

Figure 3.3.1: Forms of calcium channel blockers

Nursing considerations

- Assess for contraindications or cautions : known Allergies, impaired liver or kidney function, heart block, and current status of pregnancy or lactation.
- Perform a physical assessment to establish baseline status before beginning therapy and during therapy to determine the effectiveness and evaluate for any potential adverse effects.
- Inspect skin for color and integrity to identify possible adverse skin reactions.
- Assess cardiopulmonary status closely, including pulse rate, blood pressure, heart rate, and rhythm, to determine the effects of therapy and identify any adverse effects.
- Monitor vital signs and auscultate lungs to evaluate changes in cardiac output.
- Monitor laboratory test results, including liver and renal function tests, to determine the need for possible dose adjustment.
- Provide comfort measures to help the patient tolerate drug effects.
- Offer support and encouragement to help the patient deal with the diagnosis and the drug regimen.
- Provide thorough patient teaching.
- Monitor patient response to the drug.
- Monitor for adverse effects.

- Monitor the effectiveness of comfort measures and compliance with the regimen.
- Evaluate the effectiveness of the teaching plan.

Self-assessment 3.3

1) Which among the following drugs is a calcium channel blocker?
   a) Atenolol
   b) Aldactone
   c) Adalat
   d) Furosemide
2) You are assigned to take care of a patient who is on verapamil. Give at least five elements you must monitor while you are caring for that patient.
3) Enumerate the side effects of amlodipine.

3.4. Angiotensin converting enzyme inhibitors and angiotensin II receptor blockers

Learning Activity 3.4

In a class of pharmacology, the teacher asked her students about antihypertensive drugs and wanted to know if they know the drugs that interfere with the activity of angiotensin in human body.

Using library textbooks, read and take note on the following points:

a) Identify 2 categories of drugs that interfere with the activity of angiotensin.
b) Give one example for each category.

CONTENT SUMMARY

Angiotensin-converting enzyme (ACE) inhibitors slow the formation of angiotensin II, which reduces vascular resistance, blood volume, and blood pressure. ACE inhibitors are becoming the drugs of choice in the first-line treatment of essential hypertension. ACE inhibitors are contraindicated in patients with hypersensitivity to these agents, kidney damage, heart failure, hepatic impairment, and diabetes mellitus. ACE inhibitors are avoided during pregnancy (category D). Safety during lactation or in children is not established. Although ACE inhibitors as a group are relatively free of side effects or toxicities in most patients, they do occur, and some can be life-threatening.

The adverse effects of ACE inhibitors may include: dizziness, angioedema, loss of taste, photosensitivity, severe hypotension, dry cough, hyperkalemia, blood dyscrasias, and renal impairment.

ACE inhibitors should be used cautiously in patients with renal impairment or hypovolemia, or who are receiving diuretics or undergoing dialysis. These drugs are used with caution in patients with congestive heart failure, hepatic impairment, and diabetes mellitus.

Table 3.4.1: commonly used ACE inhibitors

Drug	Dose and route
Captopril (capoten)	P.O 6.25-25mg t.i.d may be increase to 50mg
Enalapril (vasotec)	5-40mg OD or bid

Figures 3.4.1: ACE inhibitors

Nursing considerations

- Assess for the cautions or contraindications to use of the drug like known allergies to these drugs to prevent hypersensitivity reactions; impaired kidney function, pregnancy or lactation.
- Physical assessment to determine the baseline status before beginning therapy to determine any potential adverse effects.
- Encourage patient to implement lifestyle changes, including weight loss, smoking cessation, decreased alcohol and salt in the diet, and increased exercise, to increase the effectiveness of antihypertensive therapy.

- Administer on an empty stomach 1 hour before or 2 hours after meals to ensure proper absorption of the drug.
- Consult with the prescriber to reduce the dose in patients with renal failure.
- Monitor the patient carefully in any situation that might lead to a drop in fluid volume (e.g., excessive sweating, vomiting, diarrhea, dehydration) to detect and treat excessive hypotension that may occur.
- Provide comfort measures to help the patient tolerate drug effects. These include small, frequent meals; access to bathroom facilities; bowel program as needed; environmental controls; safety precautions; and appropriate skin care as needed.
- Provide thorough patient teaching, including the name of the drug, dosage prescribed, measures to avoid adverse effects, warning signs of problems, and the need for periodic monitoring and evaluation, to enhance patient knowledge about drug therapy and to promote compliance.
- Offer support and encouragement to help the patient deal with the diagnosis and the drug regimen.

Angiotensin II receptor antagonists/blockers :

Angiotensin II receptor antagonist drugs work by blocking the binding of angiotensin II to the angiotensin I receptors. By blocking the receptor site, these agents inhibit the vasoconstrictor effects of angiotensin II as well as preventing the release of aldosterone due to angiotensin II from the adrenal glands. This class of drugs has been one of the most rapidly growing groups of drugs for the treatment of hypertension.

All of the ACE inhibitors are administered orally. Angiotensin II receptor antagonists are contraindicated in patients with a known hypersensitivity to these agents. These drugs are also contraindicated in pregnancy (category C, first trimester; category D, second and third trimesters) and lactation.

Angiotensin II receptor antagonists are used cautiously in patients with concurrent administration of high-dose diuretics, potassium-sparing diuretics, or potassium salt substitutes, and in diabetes or lactation.

Angiotensin II receptor antagonists should be used with caution in patients with hepatic or renal impairment, or in elderly patients.

Table 3.4.2: Commonly used Angiotensin receptor blockers

Drug Name	Route and dosage
Losartan potassium(Cozaar)	25-50mg/day
Valsartan (Diovan)	80-160mg/day

Figure3.4.2: Angiotensin receptor blockers

Nursing considerations

- Assess for the contraindications and cautions before administration. These include allergies, impaired kidney or liver functions, pregnancy and lactation, hypovolemia.
- Assess the baseline status before beginning therapy to determine any potential adverse effects.
- Encourage patient to implement lifestyle changes, to increase the effectiveness of antihypertensive therapy.
- Administer without regard to meals; give with food to decrease GI distress.
- Ensure that the female patient is not pregnant before beginning therapy, and suggest the use of barrier contraceptives while she is taking these drugs.
- Monitor the patient carefully in any situation that might lead to a drop in fluid volume like excessive sweating, vomiting, diarrhea, dehydration, to detect and treat excessive hypotension that may occur.
- Provide comfort measures to help the patient tolerate drug effects, including small, frequent meals; access to bathroom facilities; safety precautions if central nervous system effects occur; environmental controls; appropriate skin care as needed; and analgesics as needed.
- Provide thorough patient teaching, including the name of the drug, dosage prescribed, measures to avoid adverse effects, warning signs of problems, and the need for periodic monitoring and evaluation, to enhance patient knowledge about drug therapy and to promote compliance.
- Offer support and encouragement to help the patient deal with the diagnosis and the drug regimen.
- Monitor patient response to the drug (maintenance of blood pressure within normal limits).
- Monitor for adverse effects.
- Evaluate the effectiveness of the teaching plan (patient can name drug, dosage, adverse effects to watch for, measures to avoid them, and the importance of continued follow-up).
- Monitor the effectiveness of comfort measures and compliance with the regimen.

Self-assessment 3.4

1) Which of the following drugs is an ACE inhibitor?
   a) Captopril
   b) Lasix
   c) Cozaar
   d) Diovan
2) Which of the following drugs is an ARB drug?
   a) Captopril
   b) Lasix
   c) Cozaar
   d) Enalapril
3) Enumerate at least two contraindications of ARBs.
4) What are the side effects of ACE inhibitors?

3.5. Vasodilators and Sympathetic Nervous System Blockers

Learning Activity 3.5

You are a Senior six associate nurse student in clinical practicum at the emergency department and they receive a 39 years old female with history of hypertension. Her blood pressure was found to be 280/150mmHg. After notifying the physician, the latter ordered an IV drug which is a vasodilator in attempt to manage this hypertension. You want to know more about how the vasodilators may help in controlling the blood pressure, and you are assigned to read more about these drugs and present in the morning staff meeting the next day. In addition, you have been requested to read on other drugs that decrease the blood pressure by working on the sympathetic nervous system.

1) How do vasodilators work to reduce the blood pressure? Give at least two examples of vasodilator drugs.
2) Give at least two classes of drugs that work on the sympathetic nervous system to reduce the blood pressure.

Guidance: Use library textbooks and internet.

CONTENT SUMMARY

Vasodilators are used to relax or dilate vessels throughout the body. They block the movement of calcium into the smooth muscle of the blood vessels to cause relaxation of the smooth muscle, and dilation of the resistance vessels.

Some work on either veins or arteries; others work on both. Vasodilators are prescribed as second-line agents to initial therapy in patients taking diuretics, beta-blockers, ACE inhibitors, calcium-channel blockers, alpha adrenergic blocker, or alpha/betaadrenergic blockers.

Vasodilator agents are reducers of hypertension. A peripheral vasodilator is frequently used in the treatment of moderate to severe hypertension.

Common adverse effects of vasodilator drugs include headache, dizziness, tachycardia, palpitations, anxiety, nausea, vomiting, disorientation, depression, edema, impotence, and allergic reactions.

They are contraindicated in patients with coronary artery disease, mitral valvular rheumatic heart disease, atriovenous shunt, and myocardial infarction. Safe use of vasodilators during pregnancy (category C) or lactation is not established.

Table 3.5.1: Commonly used vasodilators

Drug name	Dose and route	Indications
Hydralazine (aprosoline)	Adult: 20-40mg IM or IV repeated as necessary	Severe hypertension
Nitroprusside (nitropress)	Adult and pediatric: 3mcg/kg/min do not exceed 10mcg/kg/min	Treatment of hypertensive crisis, also used to maintain controlled hypotension during surgery

SYMPATHETIC NERVOUS SYSTEM BLOCKERS

Drugs that block the effects of the sympathetic nervous system are useful in blocking many of the compensatory effects of the sympathetic nervous system. They include beta-blockers, alpha blockers, alpha and beta blockers and alpha-adrenergic blockers.

Beta-blockers act by blocking vasoconstriction, decrease heart rate, decrease cardiac muscle contraction, and tend to increase blood flow to the kidneys, leading to a decrease in the release of renin. These drugs have many adverse effects and are not recommended for all people. They are often used as monotherapy in step 2 treatment, and in some patients, they control blood pressure adequately. The commonly used beta blockers are acebutolol, atenolol (Tenormin) and propranolol.

Their common contraindications are diabetes mellitus, chronic obstructive pulmonary disease (COPD) and asthma.

Table 3.5.2: Commonly used beta blockers

	Acebutolol hydrochloride (Sectral)
Dose and route	P.O 200-800mg/day in 2 div. doses
Indication	Treatment of hypertension and premature ventricular contraction in adults

	Atenolol (Tenormin)
Dose and route	P.O 25-100mg once/day
indications	Most widely used than the other drugs of this class for hypertension

	Propranolol hydrochloride (Inderal)
Dose and route	P.O 40-60mg b.i.d usually requires 160-480mg/day
indications	Hypertension, angina pectoris

Self-assessment 3.5

1) Among the antihypertensive drugs, which one is a vasodilator used in case of hypertensive crisis?

   a) Atenolol

   b) Acebutelol

   c) Carvedilol

   d) Nitroprusside

2) Which of the following classes of antihypertensive drugs acts on sympathetic nervous system?

   a) Diuretics

   b) Beta-blockers

   c) Calcium channel blockers

   d) ACE inhibitors

3.6. Treatment guidelines of hypertension

Learning Activity 3.6

A 40-year-old female patient consults a health facility where you are placed in the clinical placement. It is a known case of prehypertension who was on lifestyle measures and on her arrival, her blood pressure is 150/90 mmHg. She is then screened for diabetes, and the glycaemia shows that the patient meets the criteria to be diagnosed as a diabetic patient. The fellow associate nurse student in the clinical placement wants you to advice on the class of first line antihypertensive medications.

1) What class of antihypertensive medications can you advise to prescribe for this patient according the national guidelines?

2) Apart from glycemia, what other laboratory investigations may be requested before starting the antihypertensive drugs according to the national guidelines?

Table 3.6.1: Treatment of hypertensive emergency

Medication	Dosing	Special note
Captopril	25mg orally	Contraindicated in pregnancy and renal (Cr ≥ µmol/L)
Nifedipine (immediate release)	10mg orally	
Hydralazine	25mg orally or 20mg iv	
Furosemide	40mg orally or 20mg iv	If evidence of pulmonary congestion

Treatment of essential hypertension

STAGE 1 (BP 140/90 – 159/99 mmhg) WITHOUT RISK FACTORS

1) Encourage lifestyle modifications
2) If unable to achieve a blood pressure < 140/90 mmhg in 12 months, start one antihypertensive
3) Monitor every 3 months

STAGE 1 (BP 140/90 – 159/99 mmhg) WITH RISK FACTORS:

1) Encourage lifestyle modifications
2) If unable to achieve a blood pressure <140/90 mmhg in 3 months, start one antihypertensive
3) Monitor every 3 months

STAGE 2 (BP 160/100 – 179/109 mmhg):

1) Start two hypertensive medications
2) Encourage lifestyle modifications
3) Follow-up in 1 month
4) Lifestyle Modifications:

STAGE 3 (BP > 180/110 mmhg) without danger signs:

1) Start two anti-hypertensive drugs immediately.
2) Encourage lifestyle modifications.
3) Follow-up in 2 weeks

Table 3.6.2: Treatment of essential hypertension

Treatment line	Medication	Titration Dose	Maximum Dose	Notes
1st Line (Thiazide diuretics)	HCTZ	12.5mg oral 1x/day	25mg oral 1x/day	Can cause dehydration and hypokalemia. Contraindicated in pregnancy!
2 nd Line (Calcium channel Blockers)	Amlodipine	5mg oral 1x/day	10mg oral 1x/day	Can cause lower extremity edema and worsen antihypertensive+ volume overload. Can cause dizziness/ lightheadedness. Safe in pregnancy.
	Nifedipine (Sustained Release)	20mg oral 2x/day	60mg oral 2x/day	
3 rd Line (ACE Inhibitors)	Lisinopril	10mg oral 1x/day	40mg oral 1x/day	Can cause acute kidney injury, hyperkalemia, angioedema, cough Contraindicated in pregnancy!
	Captopril	12.5-25mg oral 3x/day	50mg oral 3x/day	
4 th Line (Betablockers)	Atenolol	12.5-25mg oral 1x/day	100mg oral 1x/day	Contraindicated if HR < 60 bpm Atenolol should not be used in pregnancy. Carvedilol is safe in pregnancy.
	Carvedilol	6.2512.5mg oral 2x/day	25mg oral 2x/day	
5 th Line	Hydralazine	25mg oral 3x/day	100mg oral 3x/day	Headaches are common. Safe in pregnancy.

Treatment of Hypertension with complications

Diabetes: ACE-Inhibitors are first line.

Proteinuria: ACE-Inhibitors are first line.

Cardiomyopathy: Ace-Inhibitors, Beta-blockers, Spironolactone are preferred.

Chronic Renal Failure:

1st Line: Furosemide, Amlodipine or Nifedipine

2nd Line: Beta-blockers and hydralazine

Table 3.6.3: Treatment of Hypertension with complications

	Stage 1HTN	Stage 2 or 3 HTN
Medication change	Return in 4-6 weeks	Return in 2-4 weeks
Ace-inhibitor change	Check creatinine and potassium in 2-4 weeks	Check creatinine and potassium in 1-2 weeks
No medication change	Return in 3-4months	Return in 2-4weeks

Self-assessment 3.6

Read carefully the scenario below:

1) Two patients A and B presented to the outpatient department of the hospital where you work as an associate nurse. The first has a high B.P of 144/95mmHg and the second one has a BP of 198/150mmHg. Both of them have no other risk factors.

i. All of the following are the options for patient A management, EXCEPT:
   a) Encourage lifestyle modifications
   b) If BP >140/90 in 12 months, start one antihypertensive
   c) Monitor every 3 months
   d) Administer hydralazine

ii. All of the following are the options for patient B management:
   a) Encourage lifestyle modifications
   b) If BP >140/90 in 12 months, start one antihypertensive
   c) Administer hydralazine IV if available
   d) Monitor every 3 months

2) Which of the following antihypertensive drugs is classified in the third line of anti-hypertensive drugs based on national guidelines?
   a) Captopril
   b) Atenolol
   c) Amlodipine
   d) Hydralazine

3.7. Oral antidiabetic medications

Learning Activity 3.7

The patient has been followed up after episode of hyperglycemia but the advice given on a diet and exercise do not impact on his blood glucose level. Today, the health care providers would like to prescribe oral antidiabetic drugs.

Using library textbooks and internet respond to the following questions:

1) When are oral anti diabetic agents indicated?
2) What are the contraindication of Metformin anti diabetic drug

CONTENT SUMMARY

Diabetes Mellitus (DM), is a group of metabolic diseases that occur with increased levels of glucose (hyperglycemia) in the blood. It is non-communicable disease resulting from defects in insulin secretion, insulin action or both. It is associated with acute complications

Insulin is a hormone that allows the body to efficiently use glucose as fuel. Diabetes has major classifications that include type 1 diabetes, type 2 diabetes, gestational diabetes, and diabetes mellitus associated with other conditions.

Table 3.7.1: Classification of diabetes based on etiology.

Type 1 diabetes	Results from destruction most commonly autoimmune, of the pancreatic beta cells. Insulin is required for survival.
Type 2 diabetes	Characterized by insulin resistance and/or abnormal insulin secretion, either of which may predominate, but both of which are usually present. It is the most common type of diabetes.
Other specific types of Diabetes	These are less common and include genetic disorders, infections, and diseases of the exocrine pancreas, endocrinopathies or as a result of drugs.
Gestational diabetes	Appearing or recognized for the first time in pregnancy.

Table 3.7.2: Diagnosis of diabetes mellitus based on glycaemia

Result	Fasting Plasma Glucose (FPG)
Normal	Less done 100mg/dl
Prediabetes	100mg/dl to 125mg/dl
Diabetes	126mg/dl or higher

To convert mmol/l into mg/dl, multiply mmol/l by 18

Diabetes is a serious chronic disease that has no cure. However, it can be controlled but its complications are inevitable. Their prevention is the cornerstone of therapy and include non-pharmacological management measures like nutrition, exercise, monitoring and education (what foods to eat, how much and how often to eat, how to exercise and its precautions) and pharmacological management (how and when to take medications) including oral antidiabetic medications and parenteral antidiabetic medications. The goal is to keep the blood sugar level as close to normal as possible to delay or prevent complications. Generally, the goal is to keep daytime blood sugar levels before meals between 80 and 130 mg/dL (4.44 to 7.2 mmol/L) and after-meal numbers no higher than 180 mg/dL (10 mmol/L) two hours after eating.

ORAL ANTIDIABETIC MEDICATIONS

Oral hypoglycaemic agents stimulate the pancreas to secrete more insulin and increase the sensitivity of insulin receptors in target tissues. Oral hypoglycaemic agents are indicated for the treatment of uncomplicated type II diabetes in patients whose diabetes cannot be controlled by diet or exercise only.

They are grouped in five classes: Sulfonylureas, alphaglucosidase inhibitors, biguanides, meglitinides, and thiazolidinediones. Their common adverse effects are nausea, vomiting, headache, blurred vision, sedation, confusion, anxiety, nightmares, and tachycardia.

Oral hypoglycemic agents are contraindicated in patients who are receiving sulfonamide or thiazide-type diuretics, who are hypersensitive to the agents, and who have acidosis, severe burns, or severe diarrhea. These agents should be used cautiously in patients with high fevers, severe infections, hyperthyroidism, or kidney function impairment.

Commonly used oral hypoglycemic agents:

1) METFORMIN

Metformin hydrochloride (glucophage®):

Metformin belongs to the class of biguanides. It lowers blood glucose by helping the body to make better use of insulin. It is an adjunct to diet to lower blood glucose in type 2 diabetics.

Indications: Type 2 diabetes mellitus, prediabetes, Type 1 diabetes mellitus (T1DM) Metformin is sometimes used in T1DM to limit insulin dose requirement.

Contraindications: Hypersensitivity, chronic heart failure, metabolic acidosis with or without coma, diabetic ketoacidosis (DKA), severe renal disease, abnormal creatinine clearance resulting from shock, septicaemia, or myocardial infarction and lactation.

The commonly reported side effects of metformin include: **lactic acidosis, diarrhea, nausea, vomiting** and **flatulence. Other side effects include asthenia, and decreased vitamin b12 serum concentrate.**

Dose: Adults: 500–850 mg/d PO in divided doses; reduce dose in geriatric and renal-impaired patients; maximum dose: 2,550 mg/d.

Children: 10–16 y: 500 mg/d PO with a maximum dose of 2,000 mg/d; do not use extended release form.

Figure 3.7.1: Forms of metformin

2) GLIBENCLAMIDE

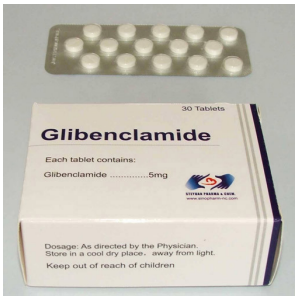
Glibenclamide (GBC) or glyburide is an oral hypoglycemic drug that stimulates the pancreatic beta cells to secrete insulin and is used to treat type 2 diabetes, including diabetes during pregnancy.

It belongs to a group of medicines called sulfonylureas. Glibenclamide lowers blood glucose by increasing the amount of insulin produced by your pancreas. It is recommended that it be taken together with diet and exercise. It may be used with other antidiabetic medication and t is not recommended for use by itself in type 1 diabetes.

Dose: Initially 2.5-5mg daily, adjusted in increments of 2.5mg at weekly intervals, based on patient's response. Maximum: 20mg daily.

Dose 10mg may be given in 2 divided doses

In elderly *>70 years contraindicated*.



Forms of Glibenclamide

3) VILDAGLIP TIN

Vildagliptin (Galvus) is an oral anti-hyperglycaemic agent of the dipeptidyl peptidase-4 inhibitor class of drugs.

Dose: 50 mg once or twice daily. The maximum daily dose of Galvus is 100 mg. For monotherapy, and for combination with metformin, with a TZD or with insulin (with or without metformin), the recommended dose of Galvus is 50 mg or 100 mg daily.

Figure 3.7.2: Forms of vildagliptin

Self-assessment 3.7

1) Among the following drugs, which one is an oral antidiabetic drug?
   a) Insulin
   b) Lasix
   c) Daonil
   d) Diovan

2) For a patient who is taking oral antidiabetic agents, which complain a nurse will expect from them?

a) Hypertension
b) Nightmares
c) Fever
d) Chills

3) Which of the following drug is a sulfonylurea?

a) Vildagliptin
b) Glucophage
c) Glibenclamide
d) All of them

3.8. Parenteral antidiabetic drugs

Learning Activity 3.8

In clinical session students were shown different oral antidiabetic medications used to treat diabetic patients. After a long discussion, students wanted to know if apart from oral medications, there are no other forms of antidiabetic medications available. A senior nurse replied that there are injectable antidiabetic medications that were kept in the fridge in another room and requested them to take this as an assignment that they will present the following week. You are among the class members, respond the following questions to prepare that presentation.

1) Which antidiabetic drug is administered parenterally?
2) When is that drug indicated?
3) What are different types of that drug?

CONTENT SUMMARY

Insulin is the only parenteral antidiabetic available for use in treatment of diabetes. Normally, insulin is used for the treatment of type I diabetics if the pancreas does not produce enough insulin but some patients with type 2 diabetes already on maximum oral therapy may also require insulin injections or in case of DKA or glucose >400mg/dL, pregnancy, renal (>150mmol/L) and Children < 18 years old.

Insulin preparations are available from three different species, including cows, pigs, and humans. Human insulin now is produced by chemical conversion from porcine insulin and by Escherichia coli, into which the human genes for insulin have been

inserted. The recombinant product has the same physiological properties as insulin from beef or pork but is much less likely to cause allergic reactions.

Adverse Effects

The most dangerous adverse effect of insulin therapy is hypoglycemia. The other adverse effects include tachycardia, sweating, drowsiness, and confusion. If severe hypoglycemia is not immediately treated with glucose, convulsions, coma, and death may occur.

Indications for insulin: Insulin is used to control hyperglycemia in the diabetic patient, and for the emergency treatment of acute ketoacidosis. It may be administered intravenously or subcutaneously.

Contraindications and Precautions

Insulin is contraindicated in patients with hypersensitivity to insulin animal protein. It is also contraindicated during episodes of hypoglycemia. Insulin should be used with caution in patients with insulin-resistant hyperthyroidism or hypothyroidism, during lactation, in older adults, during pregnancy (category B), and in those with renal or hepatic impairment.

Drug Interactions

Alcohol, anabolic steroids, MAOIs, and salicylates may potentiate hypoglycemic effects. Dextrothyroxine, corticosteroids, and epinephrine may antagonize hypoglycemic effects. Herbals such as garlic and ginseng may potentiate the hypoglycemic effects of insulin.

- Type 1 or malnutrition type diabetes
- DKA or glucose >400mg/dL
- Type 2 DM patients already on maximum oral therapy
- Pregnancy
- Renal (>150mmol/L)
- Children < 18 years old

Types of insulin

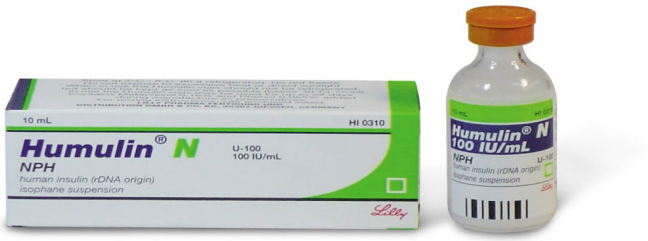
Insulins are classified based on their time of pharmacological action as rapid acting insulin, short-acting, intermediate-acting, and long-acting and mixed.

1. Rapid-acting insulin: Rapid-acting insulin starts working somewhere between 2.5 to 20 minutes after injection. Its action is at its greatest between one and 3 hours after injection and can last up to 5 hours. This type of insulin acts more quickly after a meal, similar to the body's natural insulin, reducing the risk of a low blood glucose (blood glucose below 4 mmol/L). When use this type of insulin, patient must eat

immediately or soon after injection. Eg are: insulin glulisine (Apidra), insulin lispro (Humalog) and insulin aspart (Novolog).

2. Short-acting insulin(regular) include:. Short-acting insulin takes longer to start working than the rapid-acting insulins. Short-acting insulin begins to lower blood glucose levels within 30 minutes, so you need to have your injection 30 minutes before eating. It has its maximum effect 2 to 5 hours after injection and lasts for 6 to 8 hours. Examples: Actrapid®, Humulin R and Novolin R

3. Intermediate-acting insulins include: Intermediate-acting and long-acting insulins are often termed background or basal insulins. The intermediate-acting insulins are cloudy in nature and need to be mixed well. These insulins begin to work about 60 to 90 minutes after injection, peak between 4 to 12 hours and last for between 16 to 24 hours. Example: Humulin® NPH (a human isophane insulin), insulin NPH (Novolin N, Humulin N), Protaphane® (a human isophane insulin).

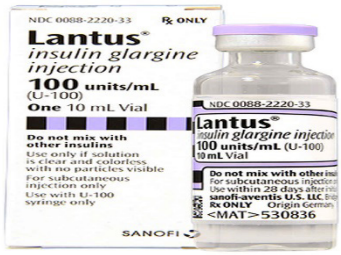


4. Mixed insulin: Mixed insulin contains a pre-mixed combination of either very rapid-acting or short-acting insulin, together with intermediate-acting insulin

The mixed insulins currently available are:

- **Rapid-acting and intermediate-acting insulin:** NovoMix® 30 (30% rapid, 70% intermediate Protaphane), Humalog® Mix 25 (25% rapid, 75% intermediate Humulin NPH), Humalog®, Mix 50 (50% rapid, 50% intermediate Humulin NPH)
- **Rapid-acting and long-acting inslulin ;**Ryzodeg 70:30 (70% long acting Degludec, 30% rapid Aspart)
- **Short-acting and intermediate-acting insulin:** Mixtard® 30/70 (30% short, 70% intermediate Protaphane), Mixtard® 50/50 (50% short, 50% intermediate Protaphane), Humulin® 30/70 (30% short, 70% intermediate Humulin NP

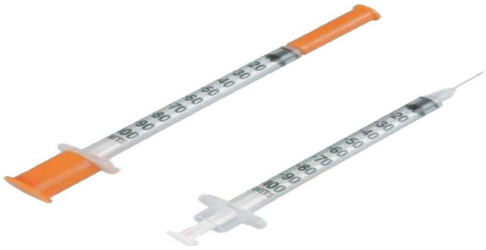
5. Long-acting insulin: Lantus® (glargine insulin) – slow, steady release of insulin with no apparent peak action. One injection can last up to 24 hours. It is usually injected once a day but can be taken twice daily, (glargine insulin) – this insulin has a strength of 300 units per ml so is 3 times the concentration of another insulin. It is given once a day and lasts for at least 24 hours. It should not be confused with regular Lantus which has a strength of 100 units per ml.



Insulin delivery devices

Different insulin devices are available. Many people who take insulin use a syringe, but there are other options as well like insulin pens and insulin pumps.

Insulin syringes: Syringes are manufactured in 30-unit (0.3 ml), 50-unit (0.5 ml) and 100-unit (1.0 ml) measures. The size of the syringe needed will depend on the insulin dose. The needles on the syringes are available in lengths ranging from 6 to 8 mm. For example, it is easier to measure a 10-unit dose in a 30-unit syringe and 55 units in a 100 unit syringe.



Insulin pens: Insulin companies have designed insulin pens (disposable or reusable) to be used with their own brand of insulin.

Disposable insulin pens already have the insulin cartridge in the pen. They are discarded when they are empty, when they have been out of the fridge for one month, or when the use-by date is reached.

Reusable insulin pens require insertion of a 3 ml insulin catridge. The insulin strength per ml is 100 units. When finished, a new cartridge or penfill is inserted. Reusable insulin pens are designed by the insulin companies to fit their particular brand of insulin cartridge/penfill.

Pen cartridges also need to be discarded one month after commencing if insulin still remains in the cartridge.

They are available in different lengths, ranging from 4 to 12.7 mm. However, research recommends that size 4 to 5 mm pen needles are used. The thickness of the needle (gauge) also varies – the higher the gauge, the finer the needle. It is important that a new pen needle is used with each injection. Your diabetes nurse educator can advise you on the appropriate needle length and show you correct injection technique

Insulin pumps: An insulin pump is a small programmable device that holds a reservoir of insulin and is worn outside the body. The insulin pump is programmed to deliver insulin into the fatty tissue of the body (usually the abdomen) through thin plastic tubing known as an infusion set or giving set. Only rapid-acting insulin is used in the pump.

The infusion set has a fine needle or flexible cannula that is inserted just below the skin. This is changed every 2 to 3 days.

The pump is pre-programmed by the user and their health professional to automatically deliver small continual amounts of insulin to keep blood glucose levels stable between meals. Individuals can instruct the pump to deliver a burst of insulin each time food is eaten, similar to the way the pancreas does in people without diabetes.

Insulin injection sites

Insulin is injected through the skin into the fatty tissue known as the subcutaneous layer. It shouldn't go into muscle or directly into the blood, as this changes how quickly the insulin is absorbed and works. Absorption of insulin varies depending on where in the body it is injected.

- The abdomen absorbs insulin the fastest and is used by most people.
- The upper arms, buttocks and thighs have a slower absorption rate and can also be used.
- The proper technics is to Pinch the skin up and use a 90-degree angle. The best angle for a thin person is 90 degrees with the skin pinched up.
- The area is not massaged and it is not necessary to warm it.
- Injections are made into the subcutaneous tissue. Most individuals are able to lightly grasp a fold of skin, release the pinch, then inject at a 90° angle.

Factors affecting insulin absorption

Variation in insulin absorption can cause changes in blood glucose levels. Insulin absorption is increased by:

- Injecting into an exercised area such as the thighs or arms, and the abdomen is used for a more consistent absorption
- High temperatures due to a hot shower, bath, hot water bottle, spa or sauna
- Massaging the area around the injection site
- Injecting into muscle – this causes the insulin to be absorbed more quickly and could cause blood glucose levels to drop too low.

Insulin absorption can be delayed by:

- Over-use of the same injection site, which causes the area under the skin to become lumpy or scarred (known as lipohypertrophy)
- Insulin that is cold (for example, if insulin is injected immediately after taking it from the fridge)
- Cigarette smoking.

Insulin storage

Insulin needs to be stored correctly. This includes:

- Store unopened insulin on its side in a fridge.
- Keep the fridge temperature between 2 and 8 °C.
- Make sure that insulin does not freeze.
- Once opened, keep it at room temperature (less than 25 °C) for not more than one month and then dispose of it safely.
- Avoid keeping insulin in direct sunlight.

Extreme (hot or cold) temperatures can damage insulin so it doesn't work properly. It must not be left where temperatures are over 30 °C. In summer your car can get this hot (above 30 °C) so don't leave your insulin there.

Insulin safety

All insulin should be checked for expiration date and clearness. Insulin should not be given if it appears cloudy, Vials should not be shaken but rotated in between the hands to mix contents, the vial in use can be stored at room temperature. Vials should not be put in glove. compartments, suitcases, or trunks. If regular insulin is to be mixed with NPH or Lente insulin, the regular insulin should be drawn into the syringe first. Record of blood glucose levels and insulin doses it is important and keeping a record of blood glucose levels helps the patient and your healthcare professional to know when the insulin dosage needs adjustment.

When the patient is using insulin, the nurse has responsibility to educate and support the patient about the following:

- The type and action of your insulin
- How, where and when to inject insulin
- How to rotate injection sites
- Where to get your insulin and how to store it safely
- How to manage low blood glucose
- How to keep a record of your blood glucose levels and insulin dose

Other medication used in case of diabetes

Additional medications also may be prescribed for people with diabetes milletu , such as:

High blood pressure medications: Angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs) for patients with diabetes who have blood pressures above 140/90 millimetres of mercury (mm Hg).

Aspirin: junior or regular aspirin daily to protect the heart when there is an increased risk for a cardiovascular event, but if there is no the potential risk of bleeding.

Cholesterol-lowering drugs as patients with diabetes have a higher risk of increase in cholesterol and elevated risk of heart disease.

Self-assessment 3.8

1) When is insulin indicated?
   a) For treating hypoglycemia
   b) Patient with diabetes ketoacidosis
   c) Patient with high blood pressure
   d) For a patient with high cholesterol
2) What is the most common route of administration of insulin?
   a) Oral
   b) Intra-rectal
   c) Subcutaneous
   d) Intradermal
3) Nurse A. is given a report of a patient who is going to start insulin therapy. She is wondering the appropriate site where she will inject the prescribed insulin. The correct answer will be:
   a) On abdomen subcutaneously
   b) Abdomen intramuscularly
   c) On the back intramuscularly
   d) On the back subcutaneously

3.9. Nursing considerations during diabetes mellitus drug therapy

Learning Activity 3.9

1) Patient X, a 18-year-old female, a hard working chef accountant who stays long time in the office presents to the health centre with complaints of polydipsia, polyphagia, and fatigue for the past month, while she takes antidiabetic medication regularly. The patient reveals that she has had diabetes for the past 2 years, and likes to take often carbohydrates on every serving of food. Which of the following nursing considerations should the associate student nurse in the clinical placement take into account while assessing this patient?

   a) Do not focus on the nutritional intake as it usually has no effect on the anticipated response to insulin therapy.

   b) Monitor the patient's food intake and ensure that the patient eats when using insulin to ensure therapeutic effect and avoid hypoglycemia.

   c) Monitor the patient's food intake and ensure that the patient avoids any kind of eating when using insulin as it can limit its effectiveness.

   d) Focus on the nutritional intake and encourage the patient to keep taking a lot of carbohydrates to increase the effectiveness of insulin.

2) Which the following discharge notes should the nurse include in the client teaching for a type 1 patient who uses insulin?

   a) Self-inject insulin at home by the subcutaneous route only, and rotate injection sites regularly

   b) Self-inject insulin at home by the intramuscular route only, and rotate injection sites regularly

   c) Self-inject insulin at home by the intramuscular route only, and never rotate injection sites

   d) Self-inject insulin at home by the subcutaneous route only, and never rotate injection sites

CONTENT SUMMARY

During care of patient with diabetes under medication, nurses should provide accurate and up-to-date information about the patient's condition so that the health-care team can come up with appropriate interventions and management.

A nurse will assess the following:

- Assess for contraindications or cautions: any known allergy to any insulin and current status of pregnancy or lactation so that appropriate monitoring and dose adjustments can be completed, including possible need to use animal-source insulin. Perform a physical assessment to establish a baseline before beginning therapy, and during therapy to evaluate the effectiveness of therapy and for any potential adverse effects. Assess for presence of any skin lesions; orientation and reflexes; baseline pulse and blood pressure; respiration or adventitious breath sounds, which could indicate response to high or low glucose levels and potential risk factors in giving insulin.
- Assess body systems for changes suggesting possible complications associated with poor blood glucose control. Investigate nutritional intake, noting any problems with intake and adherence to prescribed diet that could alter the anticipated response to insulin therapy.
- Assess activity level, including amount and degree of exercise, which could alter anticipated response to insulin therapy.
- Inspect skin areas that will be used for injection of insulin; note any areas that are bruised, thickened, or scarred, which could interfere with insulin absorption and alter anticipated response to insulin therapy. Obtain blood glucose levels as ordered to monitor response to insulin and need to adjust dose as needed. Monitor the results of laboratory tests, including urinalysis, for evidence of glycosuria.

The nurse will also:

- Ensure that the patient is following a dietary and exercise regimen and using good hygiene practices to improve the effectiveness of the insulin and decrease adverse effects of the disease. Gently rotate the vial containing the agent and avoid vigorous shaking to ensure uniform suspension of insulin.
- Select a site that is free of bruising and scarring to ensure good absorption of the insulin.
- Give maintenance doses by the subcutaneous route only, and rotate injection sites regularly to avoid damage to muscles and to prevent subcutaneous atrophy. Give regular insulin intramuscularly or intravenously in emergency situations.
- Monitor response carefully to avoid adverse effects; blood glucose monitoring is the most effective way to evaluate insulin dose.
- Monitor the patient for signs and symptoms of hypoglycemia, especially during peak insulin times, when these signs and symptoms would be most likely to appear, to assess the response to insulin and the need for dose adjustment or medical intervention.

- Always verify the name of the insulin being given because each insulin has a different peak and duration, and the names can be confused.
- Use caution when mixing types of insulin; administer mixtures of regular and NPH insulins within 15 minutes after combining them to ensure appropriate suspension and therapeutic effect.
- Store insulin in a cool place away from direct sunlight to ensure effectiveness. Predrawn syringes are stable for 1 week if refrigerated; they offer a good way to ensure the proper dose for patients who have limited vision.
- Monitor the patient during times of trauma or severe stress for potential dose adjustment needs.
- Monitor the patient's food intake; ensure that the patient eats when using insulin to ensure therapeutic effect and avoid hypoglycemia.
- Monitor the patient's exercise and activities; ensure that the patient considers the effects of exercise in relationship to eating and insulin dose to ensure therapeutic effect and avoid hypoglycemia
- Protect the patient from infection, including good skin care and foot care, to prevent the development of serious infections and changes in therapeutic insulin doses.
- Monitor the patient's sensory losses to incorporate his or her needs into safety issues, as well as potential problems in drawing up and administering insulin.
- Help the patient to deal with necessary lifestyle changes, including diet and exercise needs, sensory loss, and the impact of a drug regimen that includes giving injections, to help encourage compliance with the treatment regimen.
- Instruct patients who are also receiving beta-blockers about ways to monitor glucose levels and signs and symptoms of glucose abnormalities to prevent hypoglycemic and hyperglycemic episodes when SNS and warning signs are blocked.
- Provide thorough patient teaching, including diet and exercise needs; measures to avoid adverse effects, including proper food care and screening for injuries; warning signs of problems, including signs and symptoms of hypoglycemia and hyperglycemia; the importance of increased screening when ill or unable to eat properly; proper administration techniques and proper disposal of needles and syringes; and the need to monitor disease status, to enhance patient knowledge about drug therapy and promote compliance.

The nurse will evaluate the following

- Monitor patient response to the drug (stabilization of blood glucose levels).
- Monitor for adverse effects (hypoglycemia, ketoacidosis, and injection-site irritation).

- Evaluate the effectiveness of the teaching plan (patient can name drug, dosage, adverse effects to watch for, specific measures to avoid them, and proper administration technique).
- Monitor the effectiveness of comfort measures and compliance with the regimen.

Self-assessment 3.9

A nurse R is assigned to manage a patient for whom antidiabetic medications are going to be initiated.

1) Which statement is correct about the nursing assessment before initiation of antidiabetic administration?
   a) Assess for contraindications or cautions
   b) Assess the drug effect
   c) Assess for the side effects
   d) Monitor sensory losses
2) Which statement is NOT CORRECT about the nursing evaluation after antidiabetic administration?
   a) Evaluate the drug's effectiveness
   b) Evaluate for the side effects
   c) Evaluate contraindications
   d) Evaluate the blood glucose levels

3.10. National treatment guidelines for diabetes mellitus

Learning Activity 3.10

The patient diagnosed of type 2 diabetes mellitus, and was admitted in Medical unit in the hospital where most of health care providers were new and studied outside of the country. The nurse had heard that the patient was shifted to the third line of antidiabetic drugs but doesn't know about the national guideline. The latter wants the guidance from the matron.

1) Which information do you expect to be delivered by the matron?

Guidance: Use the national guideline for NCDs book in Rwanda 2016

CONTENT SUMMARY

Management of type 1 Diabetes

Anyone who has type 1 diabetes needs lifelong insulin therapy. Treatment for type 1 diabetes includes: Taking insulin; carbohydrate, fat and protein counting; eating healthy foods; frequent blood sugar monitoring; exercising regularly and maintaining a healthy weight.

Management of type 2 Diabetes (Oral Therapy)

Management of type 2 Diabetes is based on Lifestyle and observe measures: Healthy diet, physical activity, avoid /decrease alcohol, weight control. In addition to lifestyle modification, the patients are started on oral antidiabetic drugs.

Table 3.10.1: First Line

STEP	METFORMIN		GLIBENCLAMIDE	
	7AM	7PM	7AM	7PM
	500mg	-	5mg	-
	500mg	500mg	5mg	5mg
	1000mg	500mg	10mg	5mg
	1000mg	1000mg	10mg	10mg
	Add GLIBENCLAMIDE		Add Metformin	

Glimepiride is alternative of Glibenclamide when there is frequent hypoglycemia with Glibenclamide,1 or 2 mg given orally once daily with breakfast or the first major meal of the day.

Indication for starting with either Metformine or Glibenclamide BMI >25kg/m^2: Metformin 500mg PO BMI <25kg/m^2: Glibenclamide 5mg PO

The dose may be increased by 1-2 mg in 1-2 weeks' interval up to 4 mg maximum based on blood sugar response and is given once daily.

Second Line

If despite adequate titration of doses of medication blood glucose targets are not being attained after 6 months at the most (HbA1C should fall at least by 1% or persistent hyperglycemia of more than 180mg/dl in the past 3 months). Check the patient's adherence (understanding of medical and self-management, reinforcement of lifestyle factors influencing health and fitness targets). Exclude other conditions that can disturb glycaemic control (e.g., steroids).

In addition to lifestyle measures, adherence to medication and dose Optimization add

Vildagliptin (50mg) + Metformin (850 or 1000mg) Twice/day.

Third line

On third line in addition to lifestyle measures, adherence to medication and dose optimization. Give in preference Metformin (if tolerated) + Basal (long acting) Insulin. Add Prandial (short acting) with time if required.

Self-assessment 3.10

1) According to the national guide line for NCDs, which drug is given as first line to treat a patient with diabetes type 2?
   a) Glibenclamide
   b) Insulin
   c) Amoxicillin
   d) Vildagliptin
2) According to the national guide line for NCDs, which drug is given as second line to treat a patient with diabetes type 2?
   a) Insulin+ metformin
   b) Vildagliptin + Metformin
   c) Glibenclamide+ Glucophage
   d) Insulin+ Glibenclamide

3.11. Anti-inflammatory drugs in asthma management

Learning Activity 3.11

Read the scenario below and answer the related questions.

During your clinical practice you receive a client in consultation room. The client reports that he is taking anti-asthmatic drugs. Visit the library or use internet and come with:

1) List classes of anti-asthmatic drugs
2) List four types of inhalation devices use when administering anti-asthmatic drug by inhalation
3) Give two examples of drugs fall into Anti-inflammatory anti-asthmatic class.

CONTENT SUMMARY

Asthma is a common chronic inflammatory disorder characterized by breathlessness and tightness in the chest, together with wheezing, dyspnea, and cough. The underlying cause is immune-mediated airway inflammation.

Anti-asthmatic drugs fall into two main pharmacologic classes: Anti-inflammatory agents mainly the glucocorticoids, and bronchodilators mainly ,beta2 agonists . For chronic asthma, glucocorticoids are administered on a fixed schedule, almost always by inhalation. Beta2 agonists may be administered on a fixed schedule (for long-term control) or PRN (to manage an acute attack). Like the glucocorticoids, beta2 agonists are usually inhaled.

Most anti-asthma drugs can be administered by inhalation. This route has three advantages:

1) Therapeutic effects are enhanced by delivering drugs directly to their site of action,
2) Systemic effects are minimized, and
3) Relief of acute attacks is rapid.

Inhalation Devices

Four types of inhalation devices are employed: metered-dose inhalers, Respimats, dry-powder inhalers, and nebulizers.

Metered-Dose Inhalers (MDIs): are small, hand-held, pressurized devices that deliver a measured dose of drug with each actuation. Dosing is usually accomplished with one or two inhalations.

Dry-Powder Inhalers (DPIs) are used to deliver drugs in the form of a dry, micronized powder directly to the lungs.

A nebulizer: is a small machine used to convert a drug solution into a mist. The droplets in the mist are much finer than those produced by inhalers, resulting in less drug deposit on the oropharynx and increased delivery to the lung. Inhalation of the nebulized mist can be done through a face mask or through a mouthpiece held between the teeth.

Steroidal Anti-Inflammatory Drugs

The anti-inflammatory drugs, especially inhaled glucocorticoids are the foundation of asthma treatment. These drugs are taken daily for long-term control.

The drugs used to affect inflammation are the inhaled steroids, the leukotriene receptors, and a mast cell stabilizer, which can affect both bronchodilator and inflammation.

1. INHALED STEROIDS

Inhaled steroids have been found to be a very effective treatment for bronchospasm. Agents approved for this use include beclomethasone (Beclovent and others), budesonide (Pulmicort), ciclesonide (Alvesco), fluticasone (Flovent), and triamcinolone (Azmacort and others). The drug of choice depends on the individual patient's response; a patient may have little response to one agent and do very well on another. It is usually useful to try another preparation if one is not effective within 2 to 3 weeks.

Therapeutic Actions and Indications: Inhaled steroids are used to decrease the inflammatory response in the airway. They have two main effects: Decreased swelling associated with inflammation and promotion of beta-adrenergic receptor activity, which may promote smooth muscle relaxation and inhibit bronchoconstriction.

Pharmacokinetics: These drugs are rapidly absorbed from the respiratory tract, but they take from 2 to 3 weeks to reach effective levels, and so patients must be encouraged to take them to reach and then maintain the effective levels. They are metabolized by natural systems, mostly within the liver, and are excreted in urine. The glucocorticoids are known to cross the placenta and to enter breast milk.

Contraindications and Cautions: Inhaled steroids are not for emergency use and not for use during an acute asthma attack or status asthmaticus. They should not be used during pregnancy or lactation.

Adverse Effects: Adverse effects are limited because of the route of administration. Sore throat, hoarseness, coughing, dry mouth, and pharyngeal and laryngeal fungal infections are the most common side effects encountered. If a patient does not administer the drug appropriately or develops lesions that allow absorption of the drug, the systemic side effects associated with steroids may occur.

Table 3.11.1: Inhaled steroids

Drug Name	Usual Dosage	Usual Indications
Beclomethasone (Beclovent)	**Adult**: 84–168 mcg t.i.d. to q.i.d. (two inhalations) **Pediatric (6–12 y)**: one to two inhalations t.i.d. to q.i.d., do not exceed 10 inhalations per day	Prevention and treatment of asthma; treatment of chronic steroid-dependent bronchial asthma; used as adjunctive therapy for asthma patients who do not respond to traditional bronchodilators
Budesonide (Pulmicort)	**Adult and pediatric (>6 y):** 200–400 mcg b.i.d. (two inhalations), maximum dose 800 mcg b.i.d. **Pediatric (>6 y):** 200 mcg b.i.d.	Prevention and treatment of asthma; treatment of chronic steroid-dependent bronchial asthma; used as adjunctive therapy for asthma patients who do not respond to traditional bronchodilators

2. Leukotriene Receptor Antagonists

This is a newer class of drugs, the leukotriene receptor antagonists, was developed to act more specifically at the site of the problem associated with asthma. Because this class is relatively new, long-term effects and the benefits of one drug over another have not yet been determined.

Examples: Zafirlukast (Accolate) ,Montelukast (Singulair) and zileuton (Zyflo)

Therapeutic Actions and Indications: Leukotriene receptor antagonists selectively and competitively block (zafirlukast, montelukast) or antagonize (zileuton) receptors for the production of leukotrienes. As a result, these drugs block many of the signs and symptoms of asthma, such as neutrophil and eosinophil migration, neutrophil and monocyte aggregation, leukocyte adhesion, increased capillary permeability, and smooth muscle contraction. These factors contribute to the inflammation, edema, mucus secretion, and bronchoconstriction seen in patients with asthma.

Pharmacokinetics: These drugs are given orally. They are rapidly absorbed from the GI tract. Zafirlukast and montelukast are extensively metabolized in the liver by the cytochrome P450 system and are primarily excreted in feces. Zileuton is metabolized and cleared through the liver. These drugs cross the placenta and enter breast milk (see Contraindications and Cautions).

Contraindications and Cautions: These drugs should be used cautiously in patients with hepatic or renal impairment , these drugs should be used during pregnancy only if the benefit to the mother clearly outweighs the potential risks to the fetus. No adequate studies have been done on the effects on the baby if these drugs are used during lactation; caution should be used. These drugs are not indicated for the treatment of acute asthmatic attacks, because they do not provide any immediate effects on the airways. Patients need to be cautioned that they should not rely on these drugs for relief from an acute asthmatic attack

Adverse Effects: Adverse effects associated with leukotriene receptor antagonists include headache, dizziness, nausea, diarrhea, abdominal pain, elevated liver enzyme concentrations, vomiting, generalized pain, fever, and myalgia. Because these drugs are relatively new, there is little information about their long-term effects. Patients should be advised to monitor their use of these drugs and to report any increase of acute episodes or lack of response to the drug, which could indicate a worsening problem or decreased responsiveness to drug therapy

Clinically Important Drug–Drug Interactions

Use caution if propranolol, theophylline, terfenadine, or warfarin is taken with these drugs because increased toxicity can occur. Toxicity may also occur if these drugs are combined with calcium channel blockers, cyclosporine, or aspirin; decreased dose of either drug may be necessary.

Table 3.11.2: Leukotriene Receptor Antagonists

Drug Name	Usual dosage	Indications
Zafirlukast (Accolate)	**Adult and pediatric (>12 y):** 20 mg PO b.i.d. **Pediatric (5–11 y)**: 10 mg PO b.i.d.	Prophylaxis and treatment of chronic bronchial asthma in adults and in children 5 y and older
Zileuton (Zyflo)	**Adult and pediatric (≥12 y):** 600 mg PO q.i.d. for a total of 2,400 mg/d	Prophylaxis and treatment of chronic bronchial asthma in patients ≥12 y of age

3. Mast Cell Stabilizer

A mast cell stabilizer prevents the release of inflammatory and bronchoconstricting substances when the mast cells are stimulated to release these substances because of irritation or the presence of an antigen. Cromolyn (Nasacort) is the only drug still available in this class, only available in an over-the-counter form, and it is no longer considered part of the treatment standards because of the availability of more specific and safer drugs.

CROMOLYN

Cromolyn is an inhalational agent that suppresses bronchial inflammation. The drug is used for prophylaxis—not quick relief in patients with mild to moderate asthma. Anti-inflammatory effects are less than with glucocorticoids; therefore, cromolyn is not a preferred drug for asthma therapy. When glucocorticoids create problems, however, cromolyn may be prescribed as alternative therapy.

Mechanism of Action: Cromolyn suppresses inflammation; it does not cause bronchodilation. The drug acts in part by stabilizing the cytoplasmic membrane of mast cells, preventing release of histamine and other mediators. In addition, cromolyn inhibits eosinophils, macrophages, and other inflammatory cells.

Pharmacokinetics: Cromolyn is administered by nebulizer. The fraction absorbed from the lungs is small and rarely produces significant systemic effects. Absorbed cromolyn is excreted unchanged in the urine.

Therapeutic Uses

Chronic asthma: Cromolyn is an alternative to inhaled glucocorticoids for prophylactic therapy of asthma. When administered on a fixed schedule, cromolyn reduces both the frequency and intensity of asthma attacks. Maximal effects may take several weeks to develop. No tolerance to effects is seen with long-term use. Cromolyn is especially effective for prophylaxis of seasonal allergic attacks and for acute allergy prophylaxis immediately before allergen exposure (e.g., before mowing the lawn).

Adverse Effects: Cromolyn is the safest of all antiasthma medications. Significant adverse effects occur in fewer than 1 of every 10,000 patients. Occasionally, cough or bronchospasm occurs in response to cromolyn inhalation.

Preparations, Dosage, and Administration

Cromolyn is administered using a power-driven nebulizer. The initial dosage for adults and children is 20 mg 4 times a day. For maintenance therapy, the lowest effective dosage should be established.

NURSING CONSIDERATIONS FOR PATIENTS RECEIVING *STEROIDAL ANTI-INFLAMMATORY DRUGS*

Before, during and after administration of steroidal anti-inflammatory drugs, a nurse the following are nurse's considerations:

Assessment

- Assess for possible contraindications or cautions
- Perform a physical examination to establish baseline.
- Assess vital signs and parameters
- Examine the nares to evaluate for any lesions that might lead to systemic absorption of the drug
- Evaluate liver and renal function tests to assess for impairments that could interfere with metabolism or excretion of the drugs.
- Perform an abdominal evaluation to monitor gastrointestinal (GI) effects of the drug

Also the nurse will implement the following:

- Taper systemic steroids carefully during the transfer to inhaled steroids; deaths have occurred from adrenal insufficiency with sudden withdrawal.
- Do not administer inhaled steroid to treat an acute asthma attack or status asthmaticus because these drugs are not intended for treatment of acute attack and will not provide the immediate relief that is needed.
- Have the patient use decongestant drops before using the inhaled steroid to facilitate penetration of the drug if nasal congestion is a problem.
- Have the patient rinse the mouth after using the inhaler because this will help to decrease systemic absorption and decrease gastrointestinal (GI) upset and nausea.
- Monitor the patient for any sign of respiratory infection; continued use of steroids during an acute infection can lead to serious complications related to the depression of the inflammatory and immune responses.

- Provide thorough patient teaching, including the drug name and prescribed dosage, measures to help avoid adverse effects, warning signs that may indicate problems, and the need for periodic monitoring and evaluation, to enhance patient knowledge about drug therapy and to promote compliance
- Instruct the patient to continue to take the drug to reach and then maintain effective levels (drug takes 2 to 3 weeks to reach effective levels).
- Offer support and encouragement to help the patient cope with the disease and the drug regimen. Administer drug on an empty stomach, 1 hour before or 2 hours after meals; the bioavailability of these drugs is decreased markedly by the presence of food.
- Caution the patient that these drugs are not to be used during an acute asthmatic attack or bronchospasm; instead, regular emergency measures will be needed.
- Caution the patient to take the drug continuously and not to stop the medication during symptom free periods to ensure that therapeutic levels are maintained.
- Provide appropriate safety measures if dizziness occurs to prevent patient injury.
- Urge the patient to avoid over-the-counter preparations containing aspirin, which might interfere with the effectiveness of these drugs.
- Provide thorough patient teaching, including the drug name and prescribed dosage, measures to help avoid adverse effects, warning signs that may indicate problems, and the need for periodic monitoring and evaluation, to enhance patient knowledge about drug therapy and to promote compliance.
- Offer support and encouragement to help the patient cope with the disease and the drug regimen.

The nurse monitors the following:

- Monitor patient response to the drug (improved breathing).
- Monitor for adverse effects (nasal irritation, fever, GI upset).
- Evaluate the effectiveness of the teaching plan (patient can name drug, dosage, adverse effects to watch for, specific measures to avoid them, and measures to take to increase the effectiveness of the drug).
- Monitor the effectiveness of other measures to ease breathing
- Monitor patient response to the drug (improved breathing).
- Monitor for adverse effects (drowsiness, headache, abdominal pain, myalgia).
- Evaluate the effectiveness of the teaching plan (patient can name drug, dosage, adverse effects to watch for, specific measures to avoid them, and measures to take to increase the effectiveness of the drug).
- Monitor the effectiveness of other measures to ease breathing

Self-assessment 3.11

1) Most anti-asthma drugs can be administered by inhalation. List three advantages of administering anti-asthmatic drugs by inhalation.
2) The main anti-inflammatory drugs used in treatment of asthma are ……
3) Patient was consulted at health post for asthma crises arriving at the health post. The Patient met with associate nurse student G who was in clinical placement mentored by senior nurse in the service. When the senior nurse requested the student G to provide treatment to the patient, the student should reflect on different classes of anti-asthmatic drugs available to treat the asthma and she found at the health post were only anti-inflammation drugs .

What should be the nursing evaluation during the use of this anti-inflammatory drugs ?

3.12. Bronchodilator antiasthmatics

Learning Activity 3.12

During your clinical practice, you receive a client with signs and symptoms of asthma.

You hear senior nurse saying that he patient will be administered an anti-asthmatic drug that belongs to bronchodilators classes.

Using pharmacology book or internet

1) How do anti-asthmatic bronchodilators facilitate respiration to treat asthma
2) Give three groups of bronchodilator anti-asthmatic drugs

CONTENT SUMMARY

Bronchodilator anti-asthmatics are medications used to facilitate respirations by dilating the airways. They are helpful in symptomatic relief or prevention of bronchial asthma and for bronchospasm associated with COPD.

Bronchodilators include xanthines, sympathomimetics, and anticholinergics.

1) XANTHINES

The xanthines have a direct effect on the smooth muscles of the respiratory tract, both in the bronchi and in the blood vessels. They include aminophylline (Truphylline), caffeine (Caffedrine and others), dyphylline (Dilor and others), and

theophylline (Slo-Bid, Theo-Dur). They have a relatively narrow margin of safety and interact with many other drugs, they are no longer considered the first-choice bronchodilators.

Therapeutic Actions and Indications: Xanthines work by directly affecting the mobilization of calcium within the cell. They do this by stimulating two prostaglandins, resulting in smooth muscle relaxation, which increases the vital capacity that has been impaired by bronchospasm or air trapping.

Also, they inhibit the release of slow reacting substance of anaphylaxis (SRSA) and histamine, decreasing the bronchial swelling and narrowing that occurs as a result of these two chemicals for usual indications for these drugs.

Pharmacokinetics: The xanthines are rapidly absorbed from the gastrointestinal (GI) tract when given orally, reaching peak levels within 2 hours. They are also given IV, reaching peak effects within minutes. They are widely distributed and metabolized in the liver and excreted in urine. Xanthines cross the placenta and enter breast milk

Contraindications and Cautions: Caution should be taken with any patient with GI problems, coronary disease, respiratory dysfunction, renal or hepatic disease, alcoholism, or hyperthyroidism because these conditions can be exacerbated by the systemic effects of xanthines.

Adverse Effects: Adverse effects associated with xanthines are related to theophylline levels in the blood. Therapeutic theophylline levels are from 10 to 20mcg/mL. With increasing levels, predictable adverse effects are seen, ranging from GI upset, nausea, irritability, and tachycardia to seizures, brain damage, and even death.

Table 3.12.1: Xanthines

Drug Name	Usual Dosage	Usual Indications
Aminophylline (Truphylline)	**Adult**: 6 mg/kg PO loading dose, then 3.8 mg/kg q4h × three doses. **Maintenance**: 3 mg/kg q6h Range: 600–1,600 mg/d PO in three to four divided doses Rectal: 500 mg q6–8h IV	Relief of symptoms or prevention of bronchial asthma and reversal of bronchospasm associated with chronic obstructive pulmonary disease (COPD)

	Emergency use: 1 mg/kg/h for the first 12 h after a loading dose of 0.6–3.2 mg/kg based on theophylline levels; 0.8 mg/kg/h should be used after 12 h of therapy Geriatric, renal or hepatic impaired patient: reduce dose and monitor closely Pediatric: 6 mg/kg PO loading dose, then 4 mg/kg (6 mo–9 y) or 3 mg/kg (9–16 y) q4h for three doses, then maintain at same dose q6h Range: 12 mg/kg/d PO IV emergency use: after a loading dose, administer 1.2 mg/kg/h for children 6 mo–9 y, or 1 mg/kg/h for children 9–16 y; if continued after 12 h, reduce dose to 1 mg/kg/h (6 mo–9 y) or 0.8 mg/kg/h (9–16 y) Base all doses on patient response and serum levels	

2) SYMPATHOMIMETICS

Sympathomimetics are drugs that mimic the effects of the sympathetic nervous system that include the dilation of the bronchi with increased rate and depth of respiration. The sympathomimetics that are used as bronchodilators include albuterol/salbutamol (Proventil and others), arformoterol (Brovana), bitolterol (Tornalate), ephedrine (generic), epinephrine (EpiPen), formoterol (Foradil), indacaterol (Arcapta), isoetharine (generic), isoproterenol (Isuprel and others), levalbuterol (Xopenex), metaproterenol (Alupent), pirbuterol (Maxair), salmeterol (Serevent), and terbutaline (Brethaire and others).

The therapeutic Actions and Indications: Most of the sympathomimetics used as bronchodilators are beta2-selective adrenergic agonists, beta2- receptors found in the bronchi,other systemic effects of sympathomimetics include increased blood pressure, increased heart rate, vasoconstriction, and decreased renal and GI blood flow all actions of the sympathetic nervous system

Pharmacokinetics: Sympathomimetics available only as an inhalant include the arformoterol, formoterol, indacaterol, isoetharine, levalbuterol, pirbuterol, and salmeterol. They vary in their duration of action, long-acting beta adrenergics have half-lives between 45 and 126 hours.

Other sympathomimetics are available in various forms. Albuterol and

metaproterenol are available in inhaled and oral forms. Terbutaline can be used as an inhalant and as an oral and parenteral agent. Isoproterenol is available for intravenous use.

Ephedrine is used orally and in parenteral form (for IV, IM, and subcutaneous use). These drugs are rapidly distributed after injection; they are transformed in the liver to metabolites that are excreted in the urine. The half-life of these drugs is relatively short less than 1 hour.

They are known to cross the placenta and to enter breast milk.The inhaled drugs are rapidly absorbed into the lung tissue. Although very little of the drug is absorbed systemically, any absorbed drug will still be metabolized in the liver and excreted in urine.

Contraindications and Cautions: These drugs are contraindicated or should be used with caution, depending on the severity of the underlying condition, in conditions that would be aggravated by the sympathetic stimulation, including cardiac disease, vascular disease, arrhythmias, diabetes, and hyperthyroidism. These drugs should be used during pregnancy and lactation only if the benefits to the mother clearly outweigh potential risks to the fetus or neonate.

Adverse Effects: Central nervous system stimulation, GI upset, cardiac arrhythmias, hypertension, bronchospasm, sweating, pallor, and flushing. Isoproterenol is associated with more cardiac side effects than some other drugs.

Table 3.12.2: Sympathomimetics

Sympathomimetics			
albuterol (Proventil)	**Adult**: 2–4 mg PO t.i.d. to q.i.d. or two inhalations q4–6h or two inhalations 15 min before exercise. **Pediatric**: >12 y: adult dose 6–12 y: 2 mg t.i.d. to q.i.d. oral tablets 6–14 y: 2 mg t.i.d. to q.i.d. PO oral syrup 2–6 y: 0.1 mg/kg PO t.i.d. oral syrup 2–12 y (inhalation):1.25–2.5 mg; for prevention of exercise-induced bronchospasm, 200-mcg capsule	Inhaled 15 min before exercise	Long-acting treatment and prophylaxis of bronchospasm and prevention of exercise induced bronchospasm in patients 2 y and older

ephedrine (generic	**Adult**: 25–50 mg IM, subcutaneous, or IV **Pediatric**: 25–100 mg/m2 IM or subcutaneous divided into four to six doses	Treatment of acute bronchospasm in adults and children, although epinephrine is the drug of choice	
epinephrine Sus-Phrine)	**Adult**: 0.1–0.3 mL subcutaneous q20min for 4 h as needed; may also be given by aerosol inhalation or nebulization **Pediatric**: 0.01–0.3 mL/m2 subcutaneous q20 min for 4 h as needed	Drug of choice for treatment of acute bronchospasm	

3. ANTICHOLINERGIC ANTI-ASTHMATIC DRUGS

Patients who cannot tolerate the sympathetic effects of the sympathomimetics might respond to the anticholinergic drugs ipratropium (Atrovent) and tiotropium (Spiriva). These drugs are not as effective as the sympathomimetics but can provide some relief to those patients who cannot tolerate the other drugs. Tiotropium is the first drug approved for once-daily maintenance treatment of bronchospasm associated with COPD.

Therapeutic Actions and Indications: Anticholinergics are used as bronchodilators because of their effect on the vagus nerve, which is to block or antagonize the action of the neurotransmitter acetylcholine at vagal-mediated receptor sites. Normally, vagal stimulation results in a stimulating effect on smooth muscle, causing contraction. By blocking the vagal effect, relaxation of smooth muscle in the bronchi occurs, leading to bronchodilation.

Pharmacokinetics: These drugs are available for inhalation, using an inhaler device. Ipratropium is also available as a nasal spray for seasonal rhinitis. Ipratropium has an onset of action of 15 minutes when inhaled. Its peak effects occur in 1 to 2 hours, and it has a duration of effect of 3 to 4 hours. Little is known about its fate in the body. It is generally not absorbed systemically. Tiotropium has a rapid onset of action and a long duration, with a half-life of 5 to 6 days. It is excreted unchanged in urine.

Contraindications and Cautions: Caution should be used in any condition that would be aggravated by the anticholinergic or atropine-like effects of the drug, such as narrow-angle glaucoma (drainage of the vitreous humor can be blocked by smooth muscle relaxation), bladder neck obstruction or prostatic hypertrophy (relaxed muscle causes decreased bladder tone), and conditions aggravated by dry mouth and throat. The use of ipratropium or tiotropium is contraindicated in the presence of known allergy to the drug or to soy products or peanuts (the vehicle used to make ipratropium an aerosol contains a protein associated with peanut allergies) to prevent hypersensitivity reactions. These drugs are not usually absorbed systemically, but as with all drugs, caution should be used in pregnancy and lactation because of the potential for adverse effects on the fetus or nursing baby.

Adverse Effects: Adverse effects are related to the anticholinergic effects of the drug if it is absorbed systemically. These effects include dizziness, headache, fatigue, nervousness, dry mouth, sore throat, palpitations, and urinary retention

Clinically Important Drug–Drug Interactions: There is an increased risk of adverse effects if these drugs are combined with any other anticholinergics; this combination should be avoided.

Table 3.12.3: Anticholinergics

Anticholinergics		
Drug	**Usual dose**	**Indications**
Ipratropium (Atrovent)	36 mcg (two inhalations) four times per day, up to 12 inhalations if needed; spacer not used Nasal spray: two sprays per nostril t.i.d. to q.i.d	Maintenance and treatment of bronchospasm for adults with COPD; nasal spray for rhinorrhea associated with seasonal and perennial rhinitis or the common cold
Tiotropium (Spiriva)	18 mcg/d (one capsule) using the HandiHaler inhalation device	Long-term, once-daily maintenance and treatment of bronchospasm associated with COPD in adults

Nursing Considerations for Patients Receiving bronchodilators

- Assess for possible contraindications or cautions.
- Perform a physical examination to establish baseline data for assessing the effectiveness of the drug and the occurrence of any adverse effects associated with drug therapy.

- Assess reflexes and orientation to evaluate central nervous system (CNS) effects of the drug.
- Assess the skin color and lesions to assess for dryness or allergic reaction and to evaluate oxygenation.
- Evaluate orientation, affect, and reflexes to evaluate central nervous system (CNS) effects.
- Assess pulse and blood pressure to monitor cardiovascular effects of the drug.
- Evaluate respirations and adventitious sounds to monitor drug effectiveness and possible adverse effects.
- Evaluate urinary output and prostate palpation as appropriate to monitor anticholinergic effects (anticholinergic drugs).
- Monitor respirations and adventitious sounds to establish a baseline for drug effectiveness and possible adverse effects.
- Evaluate pulse, blood pressure, and, in certain cases, a baseline electrocardiogram to monitor the cardiovascular effects of sympathetic stimulation.
- Evaluate liver function tests to assess for changes that could interfere with metabolism of the drug and require dose adjustment.
- Ensure adequate hydration and provide environmental controls, such as the use of a humidifier, to make the patient more comfortable.
- Encourage the patient to void before each dose of medication to prevent urinary retention related to drug effects.
- Provide safety measures if CNS effects occur to prevent patient injury.
- Provide small, frequent meals and sugarless lozenges to relieve dry mouth and GI upset.
- Advise the patient not to drive or use hazardous machinery if nervousness, dizziness, and drowsiness occur with this drug to prevent injury.
- Provide thorough patient teaching, including the drug name and prescribed dosage, measures to help avoid adverse effects, warning signs that may indicate problems, and the need for periodic monitoring and evaluation, to enhance patient knowledge about drug therapy and to promote compliance.
- Review the use of the inhalator with the patient; caution the patient not to exceed 12 inhalations in 24 hours to prevent serious adverse effects.
- Offer support and encouragement to help the patient cope with the disease and the drug regimen.

- Reassure patient that the drug of choice will vary with each individual. The sympathomimetics are slightly different chemicals and are prepared in a variety of delivery systems. A patient may have to try several different sympathomimetics before the most effective one is found.
- Advise the patient to use the minimal amount needed for the shortest period necessary to prevent adverse effects and accumulation of drug levels.
- Teach patients who use one of these drugs for exercise-induced asthma to use it 30 to 60 minutes before exercising to ensure peak therapeutic effects when they are needed.
- Alert patient that long-acting adrenergic blockers are not for use during acute attacks because they are slower acting and will not provide the necessary rescue in a state of acute bronchospasm.
- Provide safety measures as needed if CNS effects become a problem to prevent patient injury.
- Provide small, frequent meals and nutritional consultation if GI effects interfere with eating to ensure proper nutrition.
- Provide thorough patient teaching, including the drug name and prescribed dosage, measures to help avoid adverse effects, warning signs that may indicate problems, and the need for periodic monitoring and evaluation, to enhance patient knowledge about drug therapy and to promote compliance. Carefully teach the patient about proper use of the prescribed delivery system. Review that procedure periodically because improper use may result in ineffective therapy.
  - Offer support and encouragement to help the patient cope with the disease and the drug regimen
  - Monitor patient response to the drug (improved breathing).
  - Monitor for adverse effects (CNS effects, increased pulse and blood pressure, GI upset).
  - Evaluate the effectiveness of the teaching plan (patient can name drug, dosage, adverse effects to watch for, specific measures to avoid them, and measures to take to increase the effectiveness of the drug).
  - Monitor the effectiveness of other measures to ease breathing.

Self-assessment 3.12

1) Which of the following drugs is a xanthine?

   a) Amoxicillin

   b) Beclomethasone

   c) Aminophylline

   d) Epinephrine

2) Which of the following drugs belongs to the class of sympathomimetic anti asthmatic drugs?

   a) Amoxycilline

   b) Beclomethasone

   c) Aminophylline

   d) Epinephrine

3) During clinical practice, you receive a client with severe episode of asthma attack. After the assessment, the nurse recommends you to give aminophylline via IV route instead of oral route.

   Explain why the nurse chose the IV route instead of oral route.

3.13. National treatment guidelines for asthma

Learning Activity 3.13

The patient with known with simple intermittent episodes of asthma comes to the health facility where you are conducting the clinical practice as an associate nurse student. The patient has developed as a simple asthma attack that needs management. The nurse tasks you to manage the patient with reference to the Rwanda national guidelines of asthma management.

1) Which of the following management options may be instituted for this patient?

   a) Use an inhaled short-acting beta2 agonist (SABA) for quick relief.

   b) Use an inhaled glucocorticoid for quick relief of the asthma attack

   c) Use salbutamol, beclamethasone and aminophylline for quick relief.

   d) Use a combination of beclamethasone and aminophylline for quick relief.

2) After two days later, the patient comes with complicated episode of asthma attack and a deep assessment classifies that patient to be managed by step 2 in the national guidelines of asthma management. Which of the following drugs may be used?

a) Beclamethasone and aminophylline

b) Salbutamol and aminophylline

c) Salbutamol and beclamethasone

d) Beclamethasone and amoxicillin

CONTENT SUMMARY

Use Respiratory emergency method to treat asthma

If a patient is having an asthma attack, then classify severity based on IUATLD (International Union Against Tuberculosis and Lung Disease) guidelines below:

Table 3.13.1: asthma attack classification

Symptoms	Minor Attack	Moderate Attack	Severe Attack	Imminent Respiratory Failure
Dyspnea	With effort	While talking	All the time	All the time
Ability to Speak	In complete sentences	In short sentences	Words	Unable to speak
State of Consciousness	Normal	Normal or restless	Restless	Drowsy or confused
Respiratory Rate	20-25/min	25-30/min	>30/min	>30/min
Heart Rate	<100	100-120	>120	Bradycardia

- Position upright, give continuous salbutamol nebulizer, administer I.V hydrocortisone 100 mg or prednisolone po 60mg if I.V not available.
- Oxygen by facial mask 6l/min if O2 saturation is magnesium 2g IV x 1.
- Give amoxicillin 500mg PO x 1 if pneumonia suspected.
- Give furosemide 40mg IV x 1 if HF suspected.
- Call physician and admit to hospital.

- Intubation if decreased level of consciousness, exhaustion, silent chest, acidemia, cyanosis.
- Directed therapy if the triggering factor is evident: e.g antibiotics in case of infection.

Use the step method to treat asthma

- Drug dosages and drug classes are stepped up as needed, and stepped down when possible. Six steps are described. The basic concept is simple.
- First, all patients, starting with step 1, should use an inhaled short-acting beta2 agonist (SABA) as needed for quick relief.
- Second step all patients except those on step 1 should use a long-term control medication (preferably an inhaled glucocorticoid) to provide baseline control.
- Third, when patients move up a step, owing to increased impairment and risk, dosage of the control medication is increased or another control medication is added (typically an LABA), or both.
- Fourth, after a period of sustained control, moving down a step should be tried.
- For patients just beginning drug therapy, the step they start on is determined by the pretreatment classification of asthma severity. For example, a patient diagnosed with intermittent asthma would begin at step 1 (PRN use of an inhaled SABA), whereas a patient diagnosed with moderate persistent asthma would begin at step 3 (daily inhalation of a low-dose glucocorticoid plus daily inhalation of a long-acting beta2 agonist (LABA), supplemented with an inhaled SABA as needed).
- After treatment has been ongoing, stepping up or down is based on assessment of asthma control. Like the diagnosis of pretreatment severity, assessment of control is based on two domains: current impairment and future risk. In EPR-3, three classes of control are defined: well controlled, not well controlled, and very poorly controlled.
- Classify asthma severity: Intermittent, Persistent-Mild, Persistent-Moderate and Persistent-Severe (Asthma Attack)
  - Step-up therapy: When patient's asthma severity worsens.
  - Step-down therapy: When the patient achieves 3 months of symptom relief

STEP 5: ASTHMA ATTACK 1. Revert to Respiratory emergency

STEP 4: Persistent – Severe

1) Salbutamol Inh 2 puffs every 4 hr PRN
2) Beclamethasone 1500mcg 2 puff BD
3) Aminophylline 100mg PO 3x/day

STEP 3: Persistent – Moderate

1) Salbutamol Inh 2 puffs every 6 hrs
2) Beclamethasone 1000mcg 1puff BD

STEP 2: Persistent – Mild

1) Salbutamol Inh 2 puffs every 6 hrs PRN
2) Beclamethasone 500mcg 1puff BD

STEP 1: Intermittent

1) Salbutamol Inh 2 puffs every 6 hrs PRN

In emergency room treatment must be started while the evaluation is still going on. Position upright, give continuous salbutamol nebulizer,

- You may be given aerosolized beta-agonist medications through a face mask or a nebulizer, with or without an anticholinergic agent. Administer I.V hydrocortisone 100 mg or prednisolone po 60mg if I.V not available.
- Oxygen by facial mask 6l/min if O2 saturation is <92% RA You may be given oxygen through a face mask or a tube that goes in your nose. If symptoms uncontrolled after 30 minutes -> magnesium 2g IV x 1.
- Give amoxicillin 500mg PO x 1 if pneumonia suspected.
- Give furosemide 40mg IV x 1 if HF suspected.
- Call physician and admit to hospital.
- Intubation if decreased level of consciousness, exhaustion,
- Silent chest, acidemia, cyanosis.
- Directed therapy if the triggering factor is evident: e.g antibiotics in case of infection,

a) Use the step method to treat asthma

When symptoms improve for at least 3 months: STEP DOWN the treatment ladder

STEP #5 ASTHMA ATTACK

1. Revert to Respiratory emergency

STEP #4 Persistent – Severe

1. Salbutamol Inh 2 puffs every 4 hr PRN 2. Beclamethasone 1500mcg 2 puff BD 3. Aminophylline 100mg PO 3x/day

STEP #3 Persistent – Moderate

1. Salbutamol Inh 2 puffs every 6 hrs
2. Beclamethasone 1000mcg 1puff BD

STEP #2 Persistent – Mild

1. Salbutamol Inh 2 puffs every 6 hrs PRN
2. Beclamethasone 500mcg 1puff BD

STEP #1 Intermittent

1. Salbutamol Inh 2 puffs every 6 hrs PRN

b) Oxygen therapy

Oxygen therapy is a form of treatment that provides the body with additional oxygen, oxygen therapy used to treat various conditions, including severe asthma attacks. Typically, oxygen treatments are delivered through a face mask or nasal prongs, or sometimes an oxygen tent. Oxygen treatments can be done both in the hospital and in your home. Additionally, oxygen treatments may be required short term or long term.

Oxygen treatments can be delivered through a device like a tank of liquid or gas oxygen. (concentrators), Nasal cannula, simple face mask, nonrebreather mask, venturi mask, Bipap.

Self-assessment 3.13

The patient was admitted at the health center for signs and symptoms of asthma. When asked to provide the drugs to the patient, the student in the clinical placement consulted the national guidelines for treatment of asthma disease.

1) How is asthma classified based on national guidelines for treatment of asthma?
2) Give management options used to treat each class of asthma, and dosages of drugs used if any

End unit assessment 3

1) Diuretics alone are used to treat which of the following conditions?
   a) Severe hypertension
   b) Moderate hypertension
   c) Mild hypertension
   d) Hypertension with complication
2) Which of the following is a nursing consideration regarding the time of diuretic administration?
   a) Administer oral form early in the day so that increased urination will not interfere with sleep.
   b) Administer oral form at night so that increased urination will not disturb the work of the patient.
   c) Administer oral form at noon to ease the digestion of the patient
   d) Administer oral form early in the day so that increased urination will not interfere with other drug action.
3) Which of the following describes the mechanism of action of calcium channel blockers?
   a) Block the effects of the sympathetic nervous system are useful in blocking many of the compensatory effects.
   b) Inhibit the formation of angiotensin II and reduces vascular resistance.
   c) They increase excretion of water, sodium, chloride, and potassium.
   d) They relax and open up narrowed blood vessels.

4) Among the following is NOT a contra-indication of beta-blockers:

a) Diabetes mellitus,

b) Chronic obstructive pulmonary disease (COPD) and

c) Hypertension

d) Asthma

5) Which of the following drugs is a vasodilator?

a) Captopril

b) Hydralazine

c) Nifedipine

d) Atenolol

6) The medical management of diabetes mellitus is aimed at:

a) Regulating blood glucose levels.

b) Controlling caloric intake.

c) Increasing exercise levels.

d) Decreasing fluid loss.

7) A patient has a BP of 179/109 mmHg, which of the following IS NOT among the management measures?

a) Start two hypertensive medications

b) Start one antihypertensive

c) Encourage lifestyle modifications

d) Lifestyle Modifications

8) Which of the following drugs is an oral hypoglycemic agent?

a) Metronidazole

b) Metoclopramide

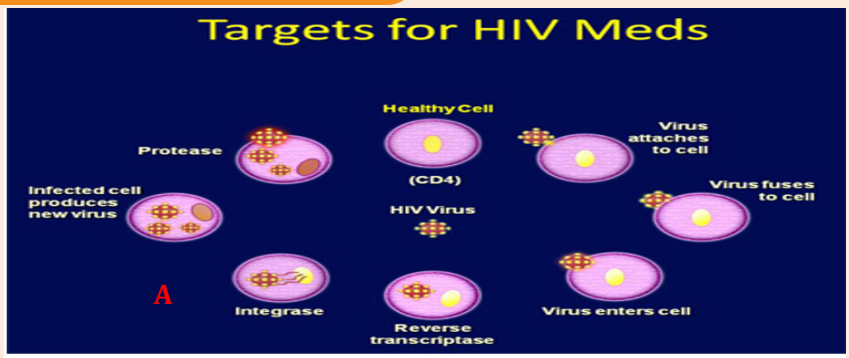
c) Metformin

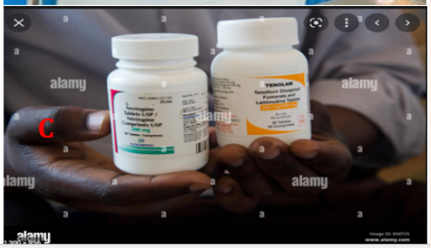
d) Methanol

Key Unit Competence

Utilize antiretroviral medications to limit HIV/AIDS transmission.

Introductory activity 4.0





Observe the images (A, B, C) above and describe briefly what they indicate for you.

4.1. Introduction to antiretroviral drugs

Learning Activity 4.1

During your clinical practice ,you receive a client in consultation. In data collection, the client reports that he is taking antiretroviral drug.

1) What is an antiretroviral drug?
2) What is a protease inhibitor?

Guidance: Use internet and library textboks.

CONTENT SUMMARY

Antiviral: An agent that kills a virus or that suppresses its ability to replicate and, hence, inhibits its capability to multiply and reproduce.

For example, amantadine (Symmetrel) is a synthetic antiviral. It acts by inhibiting the multiplication of the influenza A virus. It was used to lessen the severity of the disease, particularly in individuals at high-risk such as those who are immunosuppressed or in a nursing home.

The antivirals that have been developed are generally less effective than one would like. Viruses can replicate rapidly and, in many cases sloppily, giving rise to mutations that make them resistant to drugs. And for fast-moving viral infections like flu or a cold, a drug must be very powerful to make a difference before the disease runs its natural course.

Antivirals and Antiretrovirals are a class of medication specifically used to treat viral and retroviral infections caused by viruses like HIV, herpes viruses, hepatitis B and C. Antivirals are a class of drugs which are used to treat viral infections. The antiviral drugs target diverse group of viruses such as herpes, hepatitis, and influenza viruses. Whereas antiretroviral drugs are the drugs that are used to fight retrovirus infections which mainly include HIV. Different classes of antiretroviral drugs act on different stages of the HIV life cycle.

Retrovirus is a group of viruses that belong to the family Retroviridae and that characteristically carry their genetic blueprint in the form of ribonucleic acid (RNA). Retroviruses are named for an enzyme known as reverse transcriptase, which was discovered independently in 1971 by American virologists Howard Temin and David Baltimore. Reverse transcriptase transcribes RNA into deoxyribonucleic acid (DNA), a process that constitutes a reversal of the usual direction of cellular transcription (DNA into RNA). The action of reverse transcriptase makes it possible for genetic material from a retrovirus to become permanently incorporated into the DNA genome of an infected cell; the enzyme is widely used in the biological sciences to synthesize genes.

Integrase inhibitor: a drug that inhibits the activity of the virus-specific enzyme integrase, an encoded enzyme needed for viral replication; blocking this enzyme prevents the formation of the HIV-1 provirus.

Interferon: tissue hormone that is released in response to viral invasion; blocks viral replication nonnucleoside reverse transcriptase inhibitors: drugs that bind to sites on the reverse transcriptase within the cell cytoplasm, preventing RNA- and DNA-dependent DNA polymerase activities needed to carry out viral DNA synthesis; prevents the transfer of information that allows the virus to replicate and survive.

Nucleoside reverse transcriptase inhibitors: drugs that prevent the growth of the viral DNA chain, preventing it from inserting into the host DNA, so viral replication cannot occur.

Protease inhibitors: drugs that block the activity of the enzyme protease in HIV; protease is essential for the maturation of infectious virus, and its absence leads to the formation of an immature and noninfective HIV particle.

CCR5 coreceptor antagonist: a drug that blocks the receptor site on the T cell membrane that the HIV virus needs to interact with in order to enter the cell.

Fusion inhibitor: a drug that prevents the fusion of the HIV-1 virus with the human cellular membrane, preventing it from entering the cell.

Self-assessment 4.1

1) which of the following is a definition of antiviral drugs?

   a) Antivirals are a class of drugs which are used to treat viral infections

   b) Antivirals are a class of drugs which are used to treat viral and bacterial infections

   c) Antivirals are a class of drugs which are used to treat retroviral infections

   d) Antivirals are a class of drugs which are used to treat viral and retroviral infections

2) You receive a client with signs and symptoms of helps simplex. Among the two following groups of drugs, which one will you choose as effective to the disease?

   a) Antiretroviral drugs

   b) Antiviral drugs

3) With an example of the virus infections. Differentiate antiviral and retroviral drugs

4.2. Classification of antiretroviral drugs

Learning Activity 4.2

You are an asociate nurse carrying out the clinical placement. You receive a patient at the health facility who has been diagnosed with HIV/AIDS. What does an associate nurse will tell the patient?

1) Which classes of antiretroviral drugs can be used in HIV/AIDS management?
2) What are the five basic goals of ART?

CONTENT SUMMARY

In this lesson we discuss on classification of antiretroviral drugs. HIV infection has been transformed from a near-certain death sentence to a manageable chronic disease. Because of viruses are contained inside human cells while they are in the body, researchers have difficulty developing effective drugs that destroy a virus without harming the human host. Since the introduction of ART, the incidence of new opportunistic infections has declined dramatically. For example, the incidences of cytomegalovirus retinitis and disseminated mycobacterial infection have fallen by as much as 75% to 80%. In many patients with low CD4 T-cell counts, ART has caused CD4 counts to rise, restoring some immunocompetence and permitting withdrawal of prophylactic drugs.

Patients with HIV infection should receive ART regardless of the CD4 count or phase of HIV disease. Treatment has five basic goals: Maximal and long-lasting suppression of viral load, restoration and preservation of immune function, improved quality of life, reduction of HIV-related morbidity and mortality and prevention of HIV transmission. Most patients take several antiretroviral drugs typically two nucleoside reverse transcriptase inhibitors (NRTIs) combined with either a PI or non-nucleoside reverse transcriptase inhibitors (NNRTIs).

These highly effective regimens can reduce plasma HIV to undetectable levels, causing CD4 T-cell counts to return toward normal, thereby restoring some immune function. However, despite these advances, treatment cannot cure HIV. The HIV mutates over time, presenting a slightly different configuration with each new generation. Treatment of AIDS and ARC has been difficult for two reasons: (1) the length of time the virus can remain dormant within the T cells (i.e., months to years), and (2) the adverse effects of many potent drugs, which may include further depression of the immune system. A combination of several different antiviral drugs is used to attack the virus at various points in its life cycle to achieve maximum effectiveness with the least amount of toxicity.

Antiretroviral drugs are classified into six classes of antiretroviral drugs. Four classes: nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), integrase strand transfer inhibitors (INSTIs), and protease inhibitors (PIs) inhibit HIV enzymes.

The other two classes: HIV fusion inhibitors and CCR5 antagonists, work outside CD4 cells to block HIV entry.

NRTIs suppress HIV replication in two ways: (1) they become incorporated into the growing strand of viral DNA (through the actions of reverse transcriptase) and thereby prevent further strand growth, and (2) they compete with natural nucleoside triphosphates for binding to the active center of reverse transcriptase and thereby competitively inhibit the enzyme. To interact with reverse transcriptase, NRTIs must first undergo intracellular conversion to their active (triphosphate) forms.

The NNRTIs differ from the NRTIs in structure and mechanism of action. As their name suggests, the NNRTIs have no structural relationship with naturally occurring nucleosides. Also unlike NRTIs, the NNRTIs are active only against HIV-1. In practice, they are usually combined with an NRTI. The NNRTIs bind to the active center of reverse transcriptase enzyme. At this location, the NNRTI causes stereochemical changes (i.e., changes in the spatial arrangement of atoms forming the structure of molecules). This hampers the ability of nucleosides to bind, which inhibits DNA replication and promotes premature termination of the growing DNA strand.

NUCLEOTIDE REVERSE TRANSCRIPTASE INHIBITORS (NRTIs)

The NRTIs were the first drugs used against HIV infection. As their name suggests, the NRTIs are chemical relatives of naturally occurring nucleosides or nucleotides, the building blocks of DNA. At this time, seven NRTIs are available: Abacavir, didanosine, emtricitabine, lamivudine, stavudine, tenofovir, and zidovudine. The NRTIs are effective against both HIV-1 and HIV-2; however, their activity is greater for HIV-1. The NRTIs are ineffective as monotherapy because resistance develops rapidly. First-line antiretroviral regimens include two NRTIs and one other drug. The availability of combination antiretroviral products has simplified treatment.

Mechanism of Action

All NRTIs are prodrugs that inhibit HIV replication by suppressing synthesis of viral DNA. To do this, they must first undergo intracellular conversion to their active (phosphate) form. In their active form, they act as substrates for reverse transcriptase. However, after they become incorporated into the growing DNA strand, they prevent reverse transcriptase from adding more bases. As a result, all further growth of the DNA strand is blocked. In addition to causing premature strand termination, the activated NRTI competes with natural nucleoside triphosphates for binding to the active site of reverse transcriptase.

Adverse Effects

The NRTIs share a core of adverse effects associated with mitochondrial toxicity. Recall that mitochondria are cellular organelles that take in nutrients and convert them into ATP for energy. NRTIs can disrupt synthesis of mitochondrial DNA and can thereby impair mitochondrial function.

The main adverse effects of NRTIs are: Lactic acidosis, hepatic steatosis. Other adverse effects include: pancreatitis and myopathies, which are likely tied to lactic acidosis. Adverse effects of individual NRTIs are discussed separately.

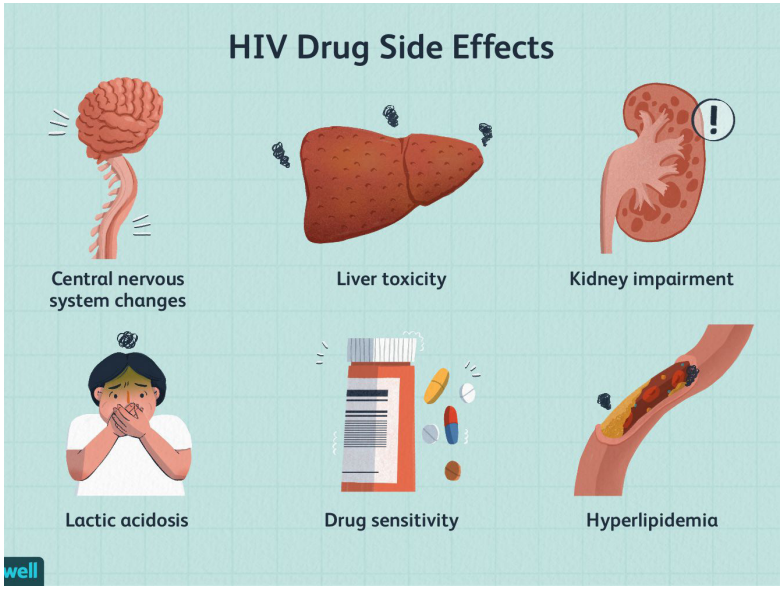
Drug Interactions

NRTIs have fewer drug interactions than most antiretroviral drugs, in part because most are not metabolized by the P450 enzymes. Interactions of individual drugs are discussed separately.

Table 4.1.1: Nucleotide reverse transcriptase inhibitors (nrtis)

Drug name	Dosage/route	Usual indications
Nucleoside reverse transcriptase inhibitors (NRTIs)		
Abacavir (ziagen)	**Adult**: 300mg PO b.i.d or 600mg/d PO **Pediatric**: 8mg/kg PO b.i.d or 16mg/kg PO once a day	combination therapy for the treatment of adults and children with HIV
Didanosine (videx)	**Adult**: 250-400mg/d PO or 125-250 mg PO b.i.d **Pediatric**: 100-120 mg/ m^2PO b.i.d	Treatment of advanced infections in adults and children with HIV as part of combination therapy
Emtricitabine (emtriva)	**Adult**: 200mg/d PO or 240mg oral solution/d **Pediatric (3mo to 17 years)**: 6mg/kg/d PO to a maximum 240mg	Part of combination therapy for treatment of HIV-1 infection
Lamivudine (epivir)	**Adult**:150mg PO b.i.d or 300mg/d PO; for chronic hepatitis B , 100mg PO qd **Pediatric (3 mo to 16 years)**: 4 mg/kg PO b.i.d	With other antiretroviral agents for the treatment of adults and children with HIV; as an oral solution for the treatment of chronic hepatitis B

Stavudine (zerit)	**Adult, child (≥60 kg)**: 40mg PO q 12h **Adult, child (30-60kg):** 30mg PO q12h **Pediatric**: other doses based on weight	Treatment of patients with HIV in combination with other antiretroviral agents
Tenofovir (viread)	**Adult**: 300mg/d PO **Pediatric (2-11 year):** 8mg/kg/d PO (for HIV not recommended for hepatitis B)	Treatment of adults/ children with HIV infection in combination with other antiretroviral drugs; treatment of chronic hepatitis B
Zidovudine (retrovir)	**Adult**: 600mgmg/d PO divided **Pediatric (6wk to 12 years):** 600mg/d PO in 2 divided doses **Maternal**: 100mg PO five per day from 14 weeks gestation until start of labor	Treatment of symptomatic HIV in adults and children as part of combination therapy; prevention of maternal transmission of HIV



NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS

The NNRTIs differ from the NRTIs in structure and mechanism of action. As their name suggests, the NNRTIs have no structural relationship with naturally occurring nucleosides. Also unlike NRTIs, the NNRTIs are active only against HIV-1. In practice, they are usually combined with an NRTI. At this time, five NNRTIs are available: efavirenz (Sustiva), nevirapine (Viramune), Delavirdine (Rescriptor), etravirine (Intelence), and rilpivirine (Edurant).

Mechanism of Action

In contrast to the NRTIs, the NNRTIs bind to the active center of reverse transcriptase enzyme. At this location, the NNRTI causes stereochemical changes (i.e., changes in the spatial arrangement of atoms forming the structure of molecules). This hampers the ability of nucleosides to bind, which inhibits DNA replication and promotes premature termination of the growing DNA strand.

Adverse Effects

Unlike NRTIs, there are no adverse effects shared by all NNRTIs. However, two of the NNRTIs, efavirenz and rilpivirine, can both cause CNS effects.

Drug Interactions

The NNRTIs have multiple drug interactions with commonly used drugs across many drug classes. These vary according to the individual NNRTI in question.

Table 4.1.2: Non-nucleoside reverse transcriptase inhibitors

Drug name	Dosage/route	Usual indications
Nonnucleoside reverse transcriptase inhibitors		
Delavirdine (Rescriptor)	**Adult**: 400mg PO t.i.d	Part of combination therapy regimens for treatment of HIV in adults
Efavirenz (Sustiva)	**Adult**:600mg/d PO **Pediatric**: dose determined by age and weight	Treatment of adults and children with HIV in combination with other antiretroviral agents
Etravirine (Intelence)	**Adult**: 200mgPO b.i.d after a meal **Pediatric**: based on weight, 100-200mg PO b.i.d	Treatment of HIV in adults with treatment experience who have evidence of viral replication and HIV strains resistant to standard therapy

Nevirapine (Viramune)	**Adult** : 200mg/d PO for 14 d, then 200mg PO b.i.d **Pediatric**: 150mg/m^2PO for 14 d, then 150 mg/m^2PO for 14 d, then 150 mg/m^2PO b.i.d	Treatment of adults or children with HIV in combination with other antiretroviral agents
Rilpivirine (edurant)	**Adult**: 25mg/d PO with food	Combination treatment of adults with HIV-1 infection

PROTEASE INHIBITORS

PIs are active against both HIV-1 and HIV-2. They are among the most effective antiretroviral drugs available. When used in combination with NRTIs, they can reduce viral load to a level that is undetectable with current assays.

As with other antiretroviral drugs, HIV resistance can be a significant problem. Mutant strains of HIV that are resistant to one PI are likely to be cross-resistant to other PIs. In contrast, since PIs do not share the same mechanism as other antiretroviral drugs, cross-resistance between PIs and these drugs does not occur. To reduce the risk for resistance, PIs should never be used alone; rather, they should always be combined with at least one reverse transcriptase inhibitor, and preferably two.

Nine PIs are available: atazanavir, darunavir, fosamprenavir, indinavir, lopinavir (with ritonavir), nelfinavir, ritonavir, saquinavir, and tipranavir.

Mechanism of Action

Maturation is necessary for HIV to infect CD4 cells; immature forms are noninfectious. Protease inhibitors prevent HIV maturation by blocking the HIV enzyme protease. It may help to look at the process of HIV maturation.

When the various enzymes and structural proteins of HIV are synthesized, they are not produced as separate entities; rather, they are strung together in large polyproteins. Protease catalyzes the cleavage of bonds in the polyproteins, thereby freeing the individual enzymes and structural proteins. Once these components have been freed, HIV uses them to complete its maturation. Protease inhibitors bind to the active site of HIV protease and prevent the enzyme from cleaving HIV polyproteins. As a result, the structural proteins and enzymes of HIV are unable to function, and hence the virus remains immature and non-infectious.

Adverse Effects

There are several adverse effects that all protease inhibitors have in common. These include hyperglycemia and the development of diabetes, lipodystrophy

(fat redistribution), elevation of serum transaminases, and decreased cardiac conduction velocity. They can also increase bleeding in patients with hemophilia.

Drug Interactions

All PIs are metabolized by cytochrome P450 enzymes, and all PIs can inhibit selected cytochrome P450 enzymes. Typically, they will also induce other enzymes. As a result, PIs can interact with drugs that inhibit or induce P450 enzymes and with drugs that are substrates for P450 enzymes. Not all interactions are harmful, of course. By inhibiting selected P450 enzymes one PI can increase the level of another PI and can thus intensify therapeutic effects. One PI—ritonavir [Norvir]—is routinely combined with other PIs with the specific purpose of increasing the therapeutic effects of the other PI. In this technique, known as ritonavir boosting, the dose of ritonavir is low: 100 to 400 mg/day. This dosage is too low to contribute significant antiviral effects, but still high enough to inhibit P450 metabolism. Unfortunately, most interactions with PIs are not beneficial. We will highlight interactions commonly experienced by patients with HIV in our discussion of individual PIs.

Table 4.1.3: Protease inhibitors

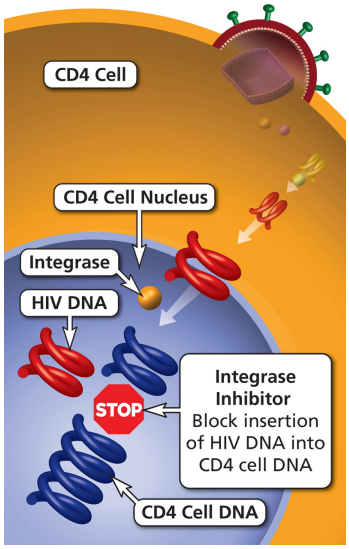
Drug name	Dosage/route	Usual indications
Protease inhibitors		
Atazanavir (reyataz)	**Adult**: 300mg/d PO with ritonavir **Pediatric**:150-300mg/d PO with ritonavir	Treatment of adults/ children with HIV as part of combination therapy
Darunavir (prezista)	**Adult**: 600mg/d PO b.i.d with ritonavir 100mg PO b.i.d **Pediatric**: dose based on weight and surface area	Treatment of adults/ children with advanced HIV disease with progression following standard treatment, used as part of combination therapy that must contain ritonavir

Fosamprenavir (lexiva)	**Adult**: 1400mg/PO b.i.d with 100mg/d ritonavir PO or 700mg PO b.i.d with ritonavir 100mg PO b.i.d **Pediatric**:18-30mg/kg b.i.d oral suspension, based on weight with ritonavir 3mg/kg PO b.i.d	part of combination therapy for the treatment of HIV
Indinavir (crixivan)	**Adult**: 800mg PO q8h; dosage adjusted based on other drugs used	Treatment of adults with HIV as part of combination therapy
Lopinavir/ ritonavir (kaletra)	**Adult**: dose varies based on indication and other antivirals: 400/100 mg-800/200mg qd or b.i.d PO **Pediatric (14 d to 12 years):** dose based on weight	Treatment of adults and children with HIV in combination with other antiretroviral agents
Nelfinavir (viracept)	Adult: 750mg PO t.id or 1250 mg PO b.i.d **Pediatric (2-13 years):** 45-55mg/kg PO b.i.d or 25-35 mg/kg PO t.i.d	Combination therapy for the treatment of adults and children with HIV
Ritonavir (norvir)	**Adult**: 600mg PO b.i.d **Pediatric**: 250mg/m2 PO b.i.d	Part of combination therapy for the treatment of adults and children with VIH
Saquinavir (Invirase	**Adult**: 1000mg PO b.i.d with ritonavir 100mg PO b.i.d	Treatment of adults with HIV as part of combination therapy
Tipranavir (aptivus)	**Adult**:500mg/d PO with 200mg ritonavir **Pediatric**: 14mg/kg PO b.i.d with ritonavir	Treatment of adults/ children with HIV in combination with ritonavir

INTEGRASE STRAND TRANSFER INHIBITORS

HIV integrase strand transfer inhibitors (INSTIs), or simply integrase inhibitors, target HIV by terminating the integration of HIV into DNA. Integrase is one of three viral enzymes needed for HIV replication. As its name implies, integrase inserts HIV genetic material into the DNA of CD4 cells. By inhibiting integrase, these drugs prevent insertion of HIV DNA and thereby stop HIV replication. They are effective against both HIV-1 and HIV-2.

We currently have three approved INSTIs: raltegravir, dolutegravir, and elvitegravir. All are indicated for combined use with other antiretroviral agents to treat adults infected with HIV-1.



Raltegravir

Actions and Use

Raltegravir [Isentress] was the first HIV integrase strand transfer inhibitor to be developed. Raltegravir stops HIV replication by preventing insertion of HIV DNA. Raltegravir is active against HIV strains resistant to some of the other drugs. Raltegravir was originally approved only for treatmentexperienced patients but is now approved for treatment-naïve patients as well. In current guidelines, raltegravir (in combination with tenofovir plus either emtricitabine or lamivudine) is considered a first-choice drug for HIV treatment. In clinical trials, raltegravir demonstrated increased viral suppression when compared to protease inhibitors and the NNRTI efavirenz. Unfortunately, HIV resistance was also more likely to develop.

Adverse Effects

Raltegravir is generally well tolerated by most. The most common adverse effect is an elevation in liver enzymes that occurs in about 10% of those taking the

drug. Approximately 4% to 5% will have elevations in serum amylase and lipase. Symptomatic adverse effects occur infrequently. In fact, the most common adverse effects, insomnia and headache, occur in only 2% to 4% of those taking this drug. In clinical trials, a few patients experienced myopathy and rhabdomyolysis, but a causal relationship has not been established. Rarely, patients have developed severe hypersensitivity reactions. Skin reactions include Stevens-Johnson syndrome and toxic epidermal necrolysis, which can be fatal. Organ dysfunction, including liver failure, may also develop.

Patients who develop signs of a hypersensitivity reaction (e.g., severe rash, or rash associated with blisters, fever, malaise, fatigue, oral lesions, facial edema, hepatitis, angioedema, muscle or joint aches) should discontinue raltegravir immediately.

Contraindications

There are no contraindications to taking raltegravir. Those with pre-existing hepatic impairment may be at risk for worsening of this condition. Caution should be maintained when taken by patients with a history of rhabdomyolysis or by those taking other drugs that have this adverse effect.

Drug Interactions

Because raltegravir is metabolized by glucuronidation, it does not have as many drug interactions as those with roles in P450 enzyme systems. Atazanavir and other inhibitors of UGT can increase levels of raltegravir. Conversely, inducers of UGT (e.g., efavirenz, fosamprenavir, rifabutin, tipranavir) can lower raltegravir levels.

HIV FUSION INHIBITORS

Unlike most other drugs for HIV, which inhibit essential viral enzymes (i.e., reverse transcriptase, integrase, protease), HIV fusion inhibitors block entry of HIV into CD4 T cells. Earlier in the chapter, we discussed the replication cycle of HIV. Recall that in step 2, the lipid bilayer envelope of HIV fuses with the lipid bilayer of the host cell membrane. HIV fusion inhibitors block this fusion process.

Enfuvirtide

Enfuvirtide [Fuzeon], widely known as T-20, is the first and only HIV fusion inhibitor currently approved by the FDA. Unfortunately, although enfuvirtide is effective, it is also inconvenient (treatment requires twice-daily subQ injections) and very expensive (treatment costs about $52,000 a year). Furthermore, injection-site reactions occur in nearly all patients.

Mechanism of Action

Enfuvirtide prevents the HIV envelope from fusing with the cell membrane of CD4 cells, and thereby blocks viral entry and replication. Fusion inhibition results from binding of enfuvirtide to gp41, a subunit of the glycoproteins embedded in the HIV envelope (see Fig. 94.1). As a result of enfuvirtide binding, the glycoprotein becomes rigid, and hence cannot undergo the configurational change needed to permit fusion of HIV with the cell membrane.

Resistance

Resistance to enfuvirtide has developed in cultured cells and in patients. The cause is a structural change in gp41. In clinical trials, reductions in drug susceptibility have ranged from 4- to 422-fold. Fortunately, the HIV mutations that confer resistance to enfuvirtide do not confer cross-resistance to NRTIs, NNRTIs, PIs, INSTIs, or CCR5 antagonists. Conversely, resistance to NRTIs, NNRTIs, PIs, INSTIs, or CCR5 antagonists does not confer cross-resistance to enfuvirtide. The rate at which resistance develops depends on the efficacy of the drugs used concurrently. When the patient's other antiretroviral drugs are still effective, resistance to enfuvirtide develops relatively slowly. However, when there is significant resistance to the other drugs, resistance to enfuvirtide develops rapidly.

Therapeutic use

Use Enfuvirtide is reserved for treating HIV-1 infection that has become resistant to other antiretroviral agents. Specifically, the drug is indicated for HIV-1 infection in patients who are treatment experienced and have evidence of HIV replication despite ongoing ART. To delay emergence of resistance, enfuvirtide should always be combined with other antiretroviral drugs.

Adverse Effects

They include injection-site reactions, pneumonia, and hypersensitivity reactions.

Drug Interactions

Enfuvirtide appears devoid of significant drug interactions. There are no interactions with other antiretroviral drugs that would require a dosage adjustment for either enfuvirtide or the other agent.

Table 4.1.4: Integrase inhibitors

Drug name	Dosage/route	Usual indications
Fusion inhibitor		
Enfuvirtide (fuzeon)	**Adult**: 90mg b.i.d by subcutaneous injection **Pediatric(6-12 years):** 2mg/kg b.i.d by subcutaneous injection	Part of combination therapy for the treatment of HIV patients with evidence of VIH replication with ritonavir
Integrase inhibitor		

Dolutegravir (tivicay)	Adult and children weighing at least 40kg: 50mg/d PO in combination with other antiretrovirals	Part of combination therapy for the treatment of infections
Raltegravir (Isentress)	**Adult, child 12 years and older**: 400mg PO b.i.d **Pediatric (6-12 years):** 400mg PO b.i.d or 300mg b.i.d chewable tablet Other pediatric dosage based on weight	Part of combination therapy for the treatment of infections

CCR5 ANTAGONISTS

CCR5 antagonists, like the fusion inhibitors, block entry of HIV into CD4 T cells. However, the mechanism by which they accomplish this is different.

Maraviroc

Maraviroc [Selzentry, Celsentri] is the first, and currently only, representative of the CCR5 antagonists. Maraviroc isn't usually used for initial treatment of HIV. It appears most effective in treating patients with drug-resistant HIV.

Mechanism of Action

CCR5 is a co-receptor that some strains of HIV must bind with to enter CD4 cells. Maraviroc binds with CCR5 and thereby blocks viral entry. HIV strains that require CCR5 for entry are referred to as being CCR5 tropic. Between 50% and 60% of patients are infected with this type of HIV. Maraviroc and enfuvirtide (a fusion inhibitor) are the only antiretroviral drugs that block HIV entry.

Therapeutic Use

Maraviroc is indicated for combined use with other antiretroviral agents to treat patients age 16 years and older who are infected with CCR5-tropic HIV-1 strains. The drug was originally approved only for treatment-experienced patients but is now approved for treatment-naïve patients as well. Before maraviroc is used, a test must be performed to confirm that the infecting HIV strain is CCR5 tropic.

Adverse Effects

The most common side effects are cough, dizziness, pyrexia, rash, abdominal pain, musculoskeletal symptoms, and upper respiratory tract infections. Intensity is generally mild to moderate. Liver injury has been seen in some patients and may be preceded by signs of an allergic reaction (e.g., eosinophilia, pruritic rash, elevated immunoglobulin E).

Patients should be informed about signs of an evolving reaction (itchy rash, jaundice, vomiting, and/or abdominal pain) and instructed to stop maraviroc and seek medical attention. During clinical trials, a few patients experienced cardiovascular events, including myocardial ischemia and MI. Maraviroc should be used with caution in patients with cardiovascular risk factors.

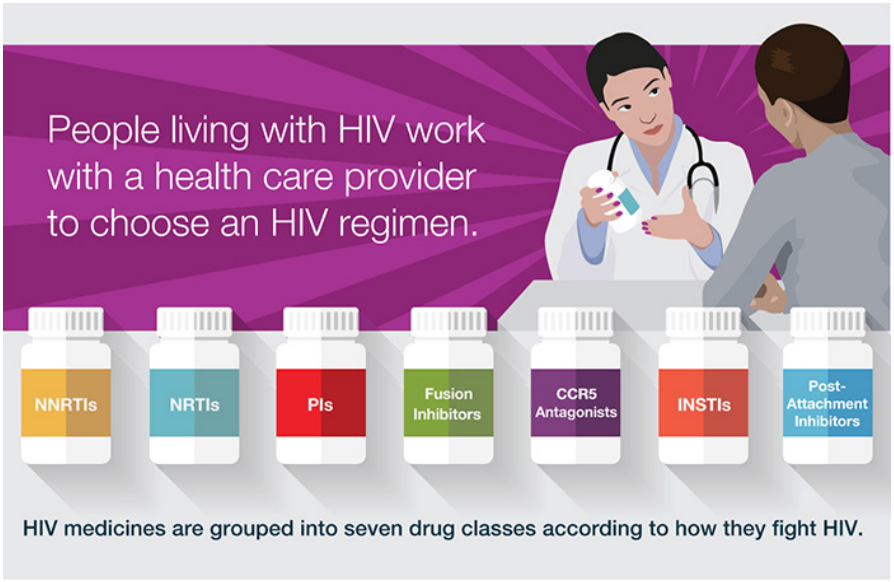
Drug Interactions

Because maraviroc is metabolized by CYP3A4, drugs that inhibit or induce this enzyme will affect maraviroc levels. Levels will be raised by strong CYP3A4 inhibitors, including protease inhibitors (except tipranavir/ritonavir) and delavirdine. Conversely, maraviroc levels will be lowered by strong CYP3A4 inducers, including etravirine and efavirenz. As always, it is important to check for interactions via a comprehensive database before administering drugs such as this one.

Table 4.1.5: FUSIOIN INHIBITORS

Drug name	Dosage/route	Usual indications
Fusion inhibitor		
Enfuvirtide (fuzeon)	**Adult**: 90mg b.i.d by subcutaneous injection **Pediatric(6-12 years)**: 2mg/kg b.i.d by subcutaneous injection	Part of combination therapy for the treatment of HIV patients with evidence of VIH replication with ritonavir
CCR5 Coreceptor antagonist		
Maraviroc (selzentry)	**Adult**: 150mg PO b.i.d ; dosage may need to be adjusted based on other drugs in the regimen	Part of combination therapy for the treatment of infections
Integrase inhibitor		

Dolutegravir (tivicay)	**Adult and children weighing at least 40kg:** 50mg/d PO in combination with other antiretrovirals	Part of combination therapy for the treatment of infections
Raltegravir (Isentress)	**Adult, child 12 years and older:** 400mg PO b.i.d **Pediatric (6-12 years)**: 400mg PO b.i.d or 300mg b.i.d chewable tablet Other pediatric dosage based on weight	Part of combination therapy for the treatment of infections



HIV medicines are grouped into seven drug classes according to how they fight HIV.

Self-assessment 4.2

1) Why is combination therapy necessary in HIV treatment?
2) Which of the following antiretroviral drugs is classified in the protease inhibitors?
   a) Enfuvirtide
   b) Raltegravir
   c) Atazanavir
   d) Nevirapine
3) What is the mechanism of action of enfuvirtide?

4.3. Antiretroviral treatment in adolescents and adults

Learning Activity 4.3

A 33-year-old newly diagnosed HIV patient was advised to start antiretroviral treatment at ART sevice where you are appointed as an associate nurse. During pre-treatment counselling, you focus on the number of combined medications to use.

1) What is the number of medications combinations is required to use in HIV/AIDS management?
2) What should the nurse include in the teaching as the ideal time to initiate ARVs after HIV diagnosis?

CONTENT SUMMARY

People with HIV should take medicine to treat HIV as soon as possible. HIV medicine reduces the amount of HIV in the body (**viral load**) to a very low level, which keeps the immune system working and prevents illness. It can even make the viral load so low that a test can't detect it. This is called an **undetectable viral load**. Getting and keeping an undetectable viral load* is the best thing people with HIV can do to stay healthy.

Initiating Antiretroviral Therapy: ART regimens typically contain at least three drugs. Regimens that contain only two drugs are not generally recommended, and monotherapy should always be avoided, except possibly during pregnancy. Additionally, all ART regimens contain drugs from at least two different classes. By using drugs from different classes, we can attack HIV in two different ways (e.g., inhibition of reverse transcriptase and inhibition of protease) and can thereby enhance antiviral effects.

Criteria for Eligibility to ART in Adults and adolescent: Antiretroviral therapy (ART) is recommended for all persons with HIV to reduce morbidity and mortality and to prevent the transmission of HIV to others. The Panel on Antiretroviral Guidelines for Adults and Adolescents recommends initiating ART immediately (or as soon as possible) after HIV diagnosis in order to increase the uptake of ART and linkage to care, decrease the time to viral suppression for individual patients, and improve the rate of virologic suppression among persons with HIV.

In addition to enhancing antiviral effects, the use of multiple drugs reduces the risk for resistance. Resistance reduction occurs because the probability that HIV will undergo a mutation that confers simultaneous resistance to three or four drugs is much smaller than the probability of undergoing a mutation that confers resistance to just one drug.

Below are key considerations in clinical management of adolescents and adults living with HIV:

- Clinical and laboratory evaluations are the cornerstones of care and treatment of HIV positive adolescents and adults.
- Renal creatinine clearance is mandatory for adolescents and adults since they initiate with TDF based regimen.
- Viral load monitoring should be conducted at 6 months and at 12 months after ART initiation, and annually thereafter. DTG-based regimen remains the preferred first-line option.
- TDF/3TC/EFV600mg is the alternative first-line regimen for adults and adolescents who cannot take TLD
- DTG-based regimen is the preferred 2nd line option for patients failing a non-DTG 1st line regimen.
- For patients failing DTG-based regimen, specialist consultation and genotyping should be considered.
- PLHIV with advanced HIV disease should be offered a package of interventions including screening, treatment and/or prophylaxis for major OIs, rapid ART initiation and intensified adherence support.
- TB screening should be done at enrolment and at each clinical visit
- Cotrimoxazole should be given to patients with advanced diseases.

Clinical evaluation

- Present and past medical history
- Comprehensive physical examination
- WHO staging
- Drug history
- Sexual history
- Nutrition status assessment
- OI screening (e.g. TB)
- NCDs screening mainly (Refer annex V).
- Cardiovascular disease: blood pressure, cardiomyopathies
- Malignancies: cervical cancer, breast cancer
- Metabolic diseases: diabetes, hyperlipidemia, hypocholesteremia
- Mental health illness

Laboratory evaluation Baseline:

- CD4 cell count,
- Cryptococcus antigen (if CD4 count < 200 cells/mm3)
- Renal function (creatinine and calculation of creatinine clearance)
- Hepatitis B surface antigen (Ag HBs)
- Hepatitis C antibody (HCV Ab)
- LFTs
- GeneXpert if TB screening is positive
- Additional investigations as clinically indicate

ART Regimen in adolescents and Adult

Treatment line	Preferred regimen	Alternative regimen
1st Line	2NRTI+Integrase Inhibitor	2NRTI+1NNRTI
2nd Line	2NRTI +1PI	2NRTI+Integrase Inhibitor
3rd Line	Optimized NRTI or ETV+1PI+1Integrase inhibitor based on genotyping results	

First line ART regimen options

There are two options recommended in first line regimen

DTG-based

NNRTI-based

Preferred 1st line regimen	Alternative 1st line regimen
*TDF/3TC/DTG	*TDF/3TC/EFV600
Note: *If TDF is contraindicated, replace with ABC	

Dosage and administration of first-line regimen

Molecule	Dosage
Tenofovir (TDF)	300 mg once a day

Abacavir (ABC 300 mg twice a day or 600 mg once a day	
Lamivudine (3TC)	300 mg once a day
Dolutegravir (DTG)	50 mg once a day
Efavirenz (EFV)	600mg once evening

Prescription of ART first line regimen

1) TDF/3TC/DTG (300/300/50 mg) (OD)
2) ABC/3TC (600/300 mg) + DTG (50 mg) (OD)
3) TDF/3TC/EFV (300/300/400mg)
4) ABC/3TC (600/300mg) + EFV 600mg

Notes:

- Encourage taking EFV based regimens in the evening before 8:00 pm to minimize dizziness
- Patients with EFV associated side effects should be advised to take it either 1-2 hours before or after meals to minimize side effects

Management of treatment failure among adolescents and adults

The monitoring of ART response and identification of treatment failure are the same as for children

- For early management of treatment failure as well as second line treatment failure refer to the treatment failure algorithm in children section.

Recommended regimens for second-line ART

Recommended regimens for 2nd line ART in adults after failure of specific first line regimens

Failing first line	**Preferred 2nd line**	**Alternative 2nd line**
TDF/ABC+3TC+DTG	AZT+3TC+ATV/r (LPV/r)	Consider specialist consultation and/or genotyping
TDF/ABC+3TC+EFV	AZT+3TC+DTG	AZT+3TC+ATV/r(LPV/r)
TDF/ABC+3TC+ PIs	AZT+3TC+DTG	

If TDF is contraindicated, replace with ABC

In case of hepatitis B co-infection, maintain TDF: TDF+AZT/3TC+ATC/r or LPV/r

Recommended regimens for third-line

- DTG 50mg BID + Darunavir/ritonavir + Optimized NRTI or Etravirine can be used based on genotyping results
- The 3rd line regimen must only be given upon expert consultation and usually with the assistance of genotyping results.
- Before prescribing third-line therapy, the patient must undergo extensive additional adherence counselling and should have a treatment partner involved in adherence assistance. Adherence counselling is critical to the success of this regimen.
- NRTI backbone may be necessary based on genotyping test or in case of Hepatitis B co-infection

Monitoring of adolescents and adults on ART

Clinical evaluation and laboratory tests play a key role in assessing adolescents and adults before ART initiation, and then monitoring their treatment response as well as possible toxicity of antiretrovirals. Note that once started, ART is a treatment for life but should be changed in the following cases:

- Drug toxicity
- Drug-drug interactions
- Co-infection
- Treatment failure confirmed by viral load

Notes:

- The follow up of CD4 count should be done whenever clinically indicated.
- For STIs management, refer to national guidelines for STIs and hepatitis.

1) TREATMENT FAILURE

Treatment failure is arguably the most compelling reason for changing the regimen. Failure is indicated if:

- Plasma HIV RNA remains above 200 copies/mL after 24 weeks
- Plasma HIV RNA remains above 50 copies/mL after 48 weeks
- Plasma HIV RNA rebounds after falling to an undetectable level
- CD4 T-cell counts continue to drop despite antiretroviral treatment
- Clinical disease progresses despite antiretroviral treatment

2) DRUG TOXICITY

If a patient experiences toxicity typical of a particular drug in the regimen, that drug should be withdrawn and replaced with a drug that is (1) from the same class and

(2) of equal efficacy. For example, if a patient taking zidovudine were to develop anemia and neutropenia, zidovudine should be discontinued and replaced with another NRTI (e.g., stavudine). Note that when toxicity is the reason for altering the regimen, changing just one drug is proper, whereas when resistance or suboptimal treatment is the reason, at least two of the drugs should be changed.

3) Promoting Patient Adherence

To achieve treatment goals and delay emergence of resistance, strict adherence to the prescribed regimen is critical. Unfortunately, several factors: duration of treatment, complex medication regimens, multiple adverse drug effects, drug-drug interactions, and drug-food interactions make adherence to ART challenging for patients.

The factors that predict poor adherence (e.g., poor clinician-patient relationship, active use of alcohol or street drugs, depression and other mental illnesses), as well as factors that predict good adherence (e.g., availability of emotional and practical support, ability to fit dosing into the daily routine, appreciation that poor adherence will cause treatment failure).

Self-assessment 4.3

1) What is the preferred 1st line regimen for adolescents and adults?
2) What is the alternative first-line regimen for adults and adolescents who cannot take TLD?
3) What can be done if a patient experiences toxicity typical of a particular drug in the regimen?

4.4. Antiretroviral treatment in Children

Learning Activity 4.4

You are an associate nurse and you receive a mother bringing her 2-year-old baby who was born with HIV. She wants the baby to be started on antiretroviral drugs, and there is a student in the clinical placement who doubts on the antiretroviral drugs to administer to the baby.

1) Which regimen should the baby start with?
2) The symptoms of HIV infection generally start later compared to the time it takes for adults to develop symptoms. TRUE or FALSE
3) The preferred 1st line ART option for children of 30kgs and above is ABC/3TC+LPV/r. TRUE or FALSE

CONTENT SUMMARY

In young children, the course of HIV infection is accelerated. Whereas adults generally remain symptom free for a decade or more, many children develop symptoms by their first birthday. Death often ensues by age 5 even with ART. Why do young children succumb so quickly?

Primarily because their immune systems are immature, and hence less able to fend off the virus. Because immune function is limited, levels of HIV RNA climb higher in toddlers than in adults, and then decline at a much slower rate.

In very young patients, diagnosis and monitoring of HIV infection employs different methods than those used in adolescents and adults. In particular, for infants under 18 months of age, diagnosis should be based on viral load assays, not on antibody tests. For children under 5 years of age, monitoring of immune status should be based on the percentage of CD4 cells, not on absolute CD4 counts.

Like older patients, young patients should be treated with a combination of antiretroviral drugs, with the goals of (1) reducing plasma viral HIV to an undetectable level and (2) stabilizing or improving immune status.

Clinical and laboratory evaluations are the cornerstones of care and treatment of HIV positive children of ≤10 years old. DTG is used for children with weight ≥ 20kgs. The preferred 1st line option for children less than 20kg is ABC/3TC+LPV/r. The preferred 1st line option for children of ≥ 20kg ABC/3TC+DTG. The preferred 1st line option for children of 30kgs and above without renal failure is TDF/3TC/DTG. For children on LPV/r, the preferred formulation is pellet (40mg/10mg, oral pellet) due to its storage and palatability reasons.

For children with more than 15kg, ATV/r can be used to replace LPV/r. For children on ABC/3TC, 120/60mg is the preferred strength. ABC is contra-indicated for children less than 3 months. If HIV is confirmed before 3 months, the recommended 1st line ART regimen is AZT+3TC+LPV/r. Switch to AZT-based regimen in case of intolerance to ABC. LPV/r is contra-indicated for new-born less than 15 days. If switching from AZT-based regimen, consider VL (viral load) suppression. If treatment failure, consider second line regimen.

TB screening is mandatory for all children at enrolment and at each clinical visit. TPT (Tuberculosis preventive therapy) should be integrated in HIV management. IPT (Isoniazid preventive therapy: Isoniazid 10mg/Kg) is used for 6 Months to all HIV children of ≤5 years old without active TB but with a history of TB contact. Anti-TB should be initiated immediately and ART within 2 to 8 weeks. The treatment failure (TF) is defined by the virological failure (plasma viral load >1000 copies/ml) based on two consecutive viral load measurements after 3 months with intensive adherence support. The management of 1st line TF is done after identifying its

probable cause and then act as shown by figure 7. The recognition of 2nd line TF is similar to the 1st line TF and the shift to 3rd line is guided by genotyping and expert consultation. The monitoring of children on ART encompasses clinical and laboratory monitoring in order to assess treatment response and potential drug toxicity.

ART Regimen for children younger than 10 years of age

Table 4.4.1 First line options for ART regimen in children:

Treatment weight range	Preferred regimen		Alternative Regimen	Comments
CHILDREN LIVING WITH HIV INITIATING ART				
<20 kg	ABC sp+3TC sp+LPV/r (40mg/10mg)pt Or ABC+3TC+LPV/r (Syrups)		ABC+3TC+NVPsp/ EFV	If less than 20kg, a child should stay on LPV/r until he reaches 20kg and shift to DTG. EFV is for children of ≥ 3 years
≥ 20 kg	20-30 kg	ABC+3TC+DTG	ABC+3TC+EFV	When reaching 30 kg, a child should be transitioned to TDF+3TC+DTG
	>30 kg	TDF+3TC+DTG	TDF+3TC+EFV	If renal impairment, consider ABC.

Table 4.4.2: Initiation of ART in children

Current regimen	Weight band	Optimal regimen for transition	Comments
CHILDREN LIVING WITH HIV ALREADY ON ART			
ABC +3TC +EFV	<20kg	No change ABC +3TC +EFV	If a child reaches 20kg shift to ABC +3TC +DTG
	20-30kg	ABC +3TC +DTG	If a child reaches 30kg shift to TDF +3TC +DTG
	>30kg	TDF +3TC =DTG	
ABC +3TC +LPV/r	<20kg	No change ABC +3TC +LPV/r	If a child raches 20kg shift to ABC + 3TC +DTG
	20-30kg	ABC +3TC +DTG	If a child reaches 30kg shift to TDF +3TC +DTG
	>30kg	TDF+3TC +DTG	

Table 4.4.3:Children who are already on ART

Second-line ART in Children

Falling first -line regimen	Preferred second-line regimen	Alternative second-line regimen	Comments
ABC or TDF +3TC +DTG	AZT + 3TC +LPV/r	HIV Expert opinion	ATV/r can be used as alternative to LPV/r for children ≥ 15kg

ABC or TDF + 3TC +LPV/r	HIV Expert opinion	AZT +3TC +DTG(in children≥ 20kg)	
ABC + 3TC + EFV	AZT + 3TC + DTG (in children ≥ 20kg)	AZT +3TC +LPV/r	ATV/r can be used as an alternative to to LPV/r for children ≥ 15kg

Self-assessment 4.4

1) When the HIV positive children should be screened for TB infection?
2) Which ART regimen should a 9-year-old child be started with?
3) Which of the following options is true with regard to treatment of patients with HIV and TB coinfection?

a) ART should be initiated immediately and anti-TB within 2 to 8 weeks
b) Anti-TB should be initiated immediately and ART within 2 to 8 weeks
c) ART should be initiated immediately and anti-TB within 6 weeks
d) Anti-TB should be initiated immediately and ART within 12 weeks

4.5. ARV Treatment in Pregnant Women

Learning Activity 4.5

A woman of 25 years of age was diagnosed for HIV positive during antenatal care at the health center. According to WHO/CDC, it is recommended that all HIV positive women should take ARTs.

Read the pharmacology book and respond the following questions

1) When a pregnant woman newly diagnosed HIV positive should start the treatment?
2) What is the ART regimen for an HIV positive pregnant woman?

CONTENT SUMMARY

In general, the management of HIV infection in pregnant women should follow the same guidelines for managing HIV infection in nonpregnant adults. Accordingly, current guidelines recommend ART for all pregnant HIV-infected women. ART is needed not only for maternal health, but also to reduce the risk for perinatal HIV transmission.

Drug selection is challenging in that information on pharmacokinetics and safety during pregnancy is limited.

When treating HIV infection in pregnant women, the goal is to balance the benefits of treatment, reducing viral load, thereby promoting the health of the mother and decreasing the risk for vertical HIV transmission (i.e., transmission to the foetus) against the risks of drug-induced fetal harm (e.g., teratogenesis, lactic acidosis, death). As a rule, the benefits of treatment outweigh the risks.

The primary determinants of therapy are the clinical, virologic, and immunologic status of the mother; pregnancy is a secondary consideration. Nonetheless, pregnancy should not be ignored.

Routine HIV testing for all pregnant women attending ANC for first time during current pregnancy together with their male partners (unless already known HIV positive status). It is preferable that these services are offered during the first trimester of pregnancy but they should be ongoing until delivery.

Every HIV-positive woman will be provided with specific counselling on family planning and getan access to a family planning method of her choice.

HIV positive pregnant and breastfeeding women should be offered index testing, partner notification and family testing services.

Every pregnant woman whose HIV status is unknown during ANC should be tested for HIV at the time of delivery.

Every pregnant woman who tested HIV negative during ANC should be retested at the time of delivery. Thereafter, retesting during postnatal period will be based on HIV risk assessment outcomes.

Women tested HIV positive during ANC or at the time of labor, should start anti-retroviral therapy immediately. In case of delay, ART initiation should not go beyond 7days.

Every pregnant or breastfeeding woman newly tested positive for HIV should start with ART regimen Tenofovir + Lamivudine + Dolutegravir.

Every pregnant or breastfeeding woman newly tested HIV-positive and on ART, should receive the first viral load test three months after ART initiation and then after every six months until the end of PMTCT follow up.

All infants born to a known HIV positive mother should receive ART prophylaxis with zidovudine and Nevirapine immediately. If not done immediately, it should be in first 72 hours post-partum or as soon as possible during the first six weeks of life.

All HIV exposed or infected children should have regular growth monitoring to enable early detection of growth retardation and undertake appropriate management.

Pre exposure prophylaxis is offered in the context of PMTCT to HIV negative pregnant and/or breastfeeding women in the following circumstances:

- Women in discordant relationship whose partners are either not on ART or are on ART but not virally suppressed
- Women practicing sex work

The regimen recommended for PrEP is a once daily TRUVADA or Tenofovir and Lamivudine for the entire pregnancy and breastfeeding period.

The use of ART for HIV positive pregnant women will depend on whether she was already on ART or not. The following situations are possible during pregnancy:

c) If the HIV-Positive pregnant woman is already initiated on ART, consider the following aspects:

- Adherence to the current ART regimen
- Viral load suppression as per the most recent viral load test results
- Consider viral load result as 'recent' if it was performed less than six months prior to the firstANC visit.
- It is mandatory to repeat the viral load test for all pregnant women not tested at the firstANC, before the third term of pregnancy (preferably at 6 months of pregnancy)
- If the woman is virally suppressed, she will be kept on her current ART regimen.
- If the woman is not virally suppressed (>200 copies/ml), she will be switched to a Dolutegravir based regimen plus two NRTIs.
- The switch to Dolutegravir- based regimen will be conducted concurrently with the adherence counselling for patients with documented poor adherence.

d) If a woman is newly diagnosed HIV positive during pregnancy:

- The woman is immediately enrolled in care and initiated on ART
- The preferred ART regimen is Tenofovir + Lamivudine + Dolutegravir (TDF+3TC+DTG)
- Any woman with impaired renal function or any contraindication to TDF will receive ABC + 3TC+DTG

NOTE: Doses are the same as in non-pregnant adults' HIV treatment. Monitoring of renal function is important.

Self-assessment 4.5

1) Any pregnant woman whose HIV status is unknown during ANC doesn't need to be tested for HIV at the time of delivery. TRUE or FALSE
2) Given their fragile status, the pregnant women with HIV positive status should benefit from lower doses of ARTs compared to the non-pregnant adults. TRUE or FALSE
3) Which of the following treatment regimens is used as ART initiation among pregnant women in Rwanda?

   a) Abacavir + Lamivudine + Dolutegravir.
   b) Tenofovir + Lamivudine + Dolutegravir.
   c) Efavirenz + Lamivudine + Dolutegravir.
   d) Nevirapine + Lamivudine + Dolutegravir.

4.6. Prophylaxis in new-borns with Perinatal HIV Exposure or HIV Infection

Learning Activity 4.6

Visit library and read pharmacology books /use internet and respond to following question:

When should the newborn exposed perinatally to HIV start taking newborn ARV regimens?

CONTENT SUMMARY

A child is considered as 'exposed to HIV', if he/she is born to an HIV positive mother. The initiation of infant prophylaxis depends on the time the mother was diagnosed HIV positive. Children born to HIV negative mothers in discordant couple will not receive any prophylaxis as long as their mothers remain HIV negative.

Infant born to a known HIV-positive mother:

All children born to a known HIV positive mother (before or during labour) will receive zidovudine and Nevirapine (AZT+ NVP) as soon as possible within 72 hours after birth up to six weeks of life. The baby will also start cotrimoxazole prophylaxis at the age of 6 weeks until the final confirmation of HIV negative status at the age of 24 months.

Infant born to a mother diagnosed for HIV after delivery

If the mother is identified to be HIV-positive at the time of breastfeeding, she should be put on ART. The child will start a combined AZT and NVP as soon as possible for six weeks. At the end of 6 weeks ART prophylaxis; the child will also start cotrimoxazole prophylaxis until the final confirmation of HIV negative status at 24 months of life.

All Breastfed infants who are at high risk of acquiring HIV, including those first identified as exposed to HIV during the postpartum period, should continue infant prophylaxis for an additional 6 weeks (total of 12 weeks of infant prophylaxis) using NVP and AZT.

High-risk infants are defined as:

Infant born to women with established HIV infection who have received less than four weeks of ART at the time of delivery; or born to women with established HIV infection with viral load >1000 copies/mL in the four weeks before delivery, if viral load measurement available; OR identified for the first time during the postpartum period, with or without a negative HIV test prenatally.

Self-assessment 4.6

1) During clinical practice in maternity ward, you receive a woman with baby at the second day of home delivery. You take blood sample for HIV testing. After 3 hours you receive a laboratory technician' s call informing you that the mother is HIV positive. Explain the management of mother and her baby to prevent mother to child transmission.

4.7. HIV Prevention among Discordant Couples

Learning Activity 4.7

1) A couple consults the healthcare facility where you are carrying out the clinical placement, and they report they are discordant. The senior nurse tasks you to explain to the couple the overall interventions package for that discordant couple. What is that package?
2) What are the objectives of these interventions?

CONTENT SUMMARY

Evidence-based interventions package for HIV sero-discordant couples can be provided through facility based and/or community interventions. Although these interventions are delivered in a package, providers must ensure that they contextualize the specific, particular needs of the couple since different couples may have different needs.

The objectives of these interventions are:

- To protect the negative partners from acquiring HIV infection
- To provide care and treatment to HIV positive partners, allowing them access to early treatment that improves clinical outcomes
- To protect future children from HIV infections
- To offer the appropriate HIV prevention package for children and other family members of the HIV positive individuals
- To support the prevention of unwanted pregnancies in discordant couples

The overall intervention package for discordant couples consists of the following:

- Risk reduction counselling and condom provision
- Initiation of pre-exposure prophylaxis for those whose HIV positive partner is not yet on ARV or are not virally suppressed
- Family planning counselling and service provision
- Repeat HIV testing for the uninfected partner every 12 months
- Care and treatment for the HIV-positive partner
- STI screening and treatment

In case of a pregnant HIV-negative partner:

- The HIV testing shall be done every three months
- A pre-exposure prophylaxis should be offered in case of non-viral suppression for the positive partner.
- At labor a single dose of TDF+3TC+DTG will be offered for all women who are not taking the pre-exposure prophylaxis.

The health care provider should encourage the discordant couple to follow up in the same health facility and synchronize with pharmacy refills and appointment schedule. Ongoing psychosocial support and counselling shall be offered to the discordant couple.

Self-assessment 4.7

1) The health care provider should encourage the discordant couple to follow up in the same health facility and synchronize with pharmacy refills and appointment schedule. TRUE or FALSE
2) Pregnant HIV-negative partner in discordant couples should receive a single dose of TDF+3TC+DTG at labor if they are not taking the pre-exposure prophylaxis. TRUE or FALSE

4.8. ART for Post-Exposure Prophylaxis (PEP)

Learning Activity 4.8

1) While he was giving IM injection to a known HIV positive patient, an associate nurse injured himself with a needle after injecting the drug. The senior nurse sends him to the ART service for post exposure prophylaxis. Which drugs may preferably be administered to this patient?

2) An HIV serology test should be performed for the exposed caregiver as soon as possible (ideally within 72 hours). TRUE or FALSE

CONTENT SUMMARY

Every person who has experienced exposure to blood/body fluids, victim of sexual assault, or accidental sexual exposure (i.e., condomless, sex with a known HIV-positive person; condom breakage) must have access to an early evaluation of the risk of HIV infection and antiretroviral prophylaxis if indicated. It is therefore necessary to have PEP services. Evidence shows that initiating ART prophylaxis soon after exposure to HIV reduces the risk of HIV infection by about 80%. Postexposure prophylaxis (PEP) is short-term ART to reduce the likelihood of acquiring HIV infection after potential exposure.

Post-exposure prophylaxis should be provided immediately or preferably within 72 hours of exposure. An HIV serology test should be performed on the exposed individual as soon as possible (ideally within 48 hours).

Case of Accidental Exposure to Blood (AEB) or Other Biological Fluids

In case of accidental exposure to blood, always clean the exposed area immediately. In case of exposure through needle stick or skin injury, clean the wound immediately with clean water and soap. In case of splash on the mucous membranes (particularly the conjunctiva), rinse at least for 5 minutes with copious amounts of water or preferably physiological saline or any available saline and do not apply disinfectant on the mucous membranes. One of the health care providers from the health facility must evaluate the actual risk for a given patient. This evaluation includes:

- The severity of the exposure, which is directly linked to the depth of the wound and the type of needle that was responsible for the injury (venipuncture needle, needle for injection, non sharp instrument).
- For external contact of secretions with the skin or mucosa (splash), the risk is higher with blood than with any other body secretions (amniotic fluid, serous fluid). The person assumed to be the source should be assessed on his or her HIV status, clinical and immunological status and history of ART. If the HIV status is not known, it is important to establish it with his/her free consent. If the HIV status of the source person cannot be obtained within 4 hours, prophylaxis for the exposed person should be started immediately

after a negative HIV test. If eventually the person assumed to be the source is proven to be HIV-negative, then ARV prophylactic treatment may be stopped

Case of Sexual Assault or Rape

In case of rape, the provider must first follow the HIV counselling and testing.PEP should be offered to the sexual assault victim once the clinician has assessed all the factors involved in the likelihood of HIV transmission (suspicion of HIV positivity in the assailant, probability of HIV transmission). PEP might help the victim gain a sense of control and decrease their anxiety about acquiring HIV. Consider HIV post-exposure prophylaxis for survivors of sexual assault presenting within 72 hours of the assault. In addition to HIV post-exposure prophylaxis, women should be offered emergency contraception to prevent unintended pregnancy immediately or preferably within 72 hours after sexual exposure.

ART Prophylaxis in PEP

The current recommended duration of post-exposure prophylaxis for HIV infection is 28 days. Treatment should start as early as possible, within the first 4 hours following the exposure, without waiting for results of HIV serology of the source person. A limit of 72 hours is reasonable in seeking maximum efficacy, however the sooner the better.

The recommended post-exposure prophylaxis drugs are based on the current second and first line regimen:

1. TDF+ 3TC / FTC +ATV/r
2. AZT + 3TC/ FTC + ATV/r(If noTDFor a contraindication)

NB: The recommended ART Prophylaxis is the same in rape/sexual assault and exposure to biological fluids

Self-assessment 4.8

1) When HIV post-exposure prophylaxis for survivors of sexual assault is taken into consideration?
2) What are the actual risks the health care providers from the health facility must evaluate in case of exposure through needle stick or skin injury?

End unit assessment 4

I. Complete the empty spaces with the appropriate terms.

a) Antiretroviral drugs

b) Antiviral

c) Retrovirus

1) ……An agent that kills a virus or that suppresses its ability to replicate and, hence, inhibits its capability to multiply and reproduce.

2) ……is a group of viruses that belong to the family Retroviridae and that characteristically carry their genetic blueprint in the form of ribonucleic acid (RNA).

3) …….. are the drugs that are used to fight retrovirus infections which mainly include HIV. Different classes of antiretroviral drugs act on different stages of the HIV life cycle.

II. Respond by true or false

1) Abacavir (Ziagen), lamivudine (Epivir) and stavudine (Zerit XR), tenofovir (Viread).

2) Efavirenz (Sustiva), nevirapine (Viramune) are drugs in the class of protease inhibitors

3) Abacavir (Ziagen) lamivudine (Epivir), stavudine (Zerit XR), tenofovir (Viread), and zidovudine (Retrovir) drugs in the class of Nonnucleoside reverse transcriptase inhibitors .

4) Atazanavir, indinavir and lopinavirare drugs in protease inhibitors.

5) Like older patients, HIV positive young patients should be treated with a combination of antiretroviral drugs.

6) Antiretroviral therapy (ART) is recommended for all persons with HIV to cure the patient by killing the virus.

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