PHARMACOLOGY

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MPH/BSC/MED EDUC’/pharm

(Complete NOTES)

Learning Objectives

By the end of this Module, the learners should be able to administer drugs professionally to patient’s.

INTRODUCTION TO PHARMACOLOGY

- **Definition of terms:**

❖**Pharmacology** is the study of effects of chemical substances on the function of living systems.

❖ **pharmacology** is the science of drugs which includes their preparation, use and effects.

❖It is also the science that deals with the **origin, chemistry, effects** and **uses** of drugs.

❖**Pharmacy:** Branch of health science that deals with preparation and dispensing of drugs.

❖**pharmacotherapy:** The study of therapeutic uses and effects of drugs.

Terminology

- **Pharmacognosy:** the study of drugs that come from natural sources e.g. plants, animals and minerals as well as search for new drugs from natural sources.
- **Pharmacokinetics** :this is the study of the body acts on the drugs; it is characterized by absorption, distribution, metabolism(biotransformation)and excretion/elimination. It can further be described as how the body handles a drug from site of administration to the site of action and elimination.
- **Pharmacodynamics/mechanism of action:** the study of how drugs act on the body.

Terminologies Cont…

- **Pharmacogenetics:** the study of the effects that genetics have on an individuals response to drugs.
- **Contra-indication:** A health condition/ state that will prelude the administration of a drug e.g. aspirin is contraindicated in peptic ulcer disease.
- **Half life or half time (t1/2):**Time taken for plasma concentration to fall by half following its elimination in the body.

Terminologies Cont…

- **Toxicology:** This branch of pharmacology which deals with the an desirable effects of chemicals on living systems from individual cells to complex body systems.

- **Drug:** Any substance used in diagnosis, cure, treatment and prevention of disease/condition or any substance that brings a change in biological functions through its chemical actions. The term drug, medication, and medicine are used synonymously.

Terminologies Cont…

- **Drug interactions** :effects produced when some drugs are given concurrently.
- **Desired therapeutic effect**: This should indicate the mechanism of action of a drug e.g.an analgesic is for pain relief, accompanied by central nervous system depression inhibition of inflammation, neutralization of acid in the stomach, vasodilation in angina or muscle relaxation.
- **Placebo:** Any component of therapy that is without specific biological activity e.g. inactive substance such as normal saline or distilled water usually used in clinical trials research and for psychological treatment.

Drug Reactions and Interactions

Any physiologically active drug has the potential to cause an undesirable reaction that may induce illness in the recipient. These include toxic reaction, side effects, allergic reactions, cumulative reaction, tolerance and dependence and detrimental drug reaction.

- **Side effects:** these are physiological effects exerted by the chemicals that are not related to the desired therapeutic effects. you must therefore be familiar with serious side effect and commonly occurring effects.
- **Adverse drug reaction:** this an injury occurring by taking medication .It may occur following a single dose or prolonged administration of a drug or result from a combination of two or

Drug reactions and Interactions Conti….

- **Drug interaction:** this is when **an interactant chemical** modifies the therapeutic results that are anticipated with a drug the interact may be another drug, some combination **of a drug, natural or artificial components in the diet, pollutants chemical from the environment, endogenous body chemicals and Chemicals used for diagnostic** laboratory test. Drug interaction may be **detriment or beneficial** drug and may vary from one person to another. This may affect the **absorption, distribution , metabolism or excretion** of the drugs.
- **Allergic reactions:** This the body's immunological response to a drug following previous exposure to the same drug.

Drug reactions and Interactions Conti…..

- **Idiosyncratic reactions:** this is genetically determined, un expected response to a drug. The response may take the form of extreme sensitivity to low doses or extreme insensitivity to high doses to the drug.
- **Chain reaction:** Medication are often added to a regime to control side effects of other drugs. This can initiate a chain reaction e.g. cortisone is prescribed to treat a serious inflammatory condition it can cause hypertension, ulcers, diabetes and a reactivation of arrested tuberculosis.
- **Cumulative reaction:** Drugs accumulate in the body whenever the dosage exceeds the amount the body can eliminate through metabolism or excretion
- **Tolerance and dependence: Tolerance** occurs when a person no longer responds to the drug in the way that person initially responded as a result of continued use of the drug causing a need to increase dose of a drug to achieve the same effect.

Drug reactions and Interactions Conti….

- There three basic types of tolerance.

metabolic /pharmacokinetics tolerance this occurs due to increased metabolism of a drug leading to reduction in drug concentration at the receptor site.

cellular/pharmacodynamic tolerance this caused by adaptive changes that take place at the receptor site or drug action site.

cross tolerance when tolerance to one drug confers tolerance to another drug. Drugs that have the same chemical structure tend to portray cross tolerance e.g. people tolerance to one barbiturates are usually tolerant to all barbiturates e.g., phenobarbital, thiopental. However drugs of similar class can also portray cross-tolerance.

- **Intolerance:** low threshold to normal pharmacological response. A drug causes an exaggeration of a normal pharmacological response e.g. morphine may cause coma instead of respiratory distress which occurs with administration of a normal dose.

Drug reactions and Interactions Conti…..

- **Dependence**: A state arising from repeated periodic or continuous administration of a drug that results in harm to the individual or sometimes society. People feel desire or compulsion to continue using the drug and feel ill if abruptly withdrawn or an antidote is used. Substance that cause dependence are taken to induce a good feelings or avoid discomfort of their absence.

Types dependence:

a. psychological dependence: usually first to appear, where the individual have a craving for the effect the drug produces motional distress like fear, anxiety and irritability occur when the drug is withdrawn.

b. Physical dependence: this dependence is usually defined in terms of withdrawal/abstinence syndrome that are physical in nature e.g. tremors, ataxia, shivering.

Drug reactions and Interactions Conti…..

- **Iatrogenic responses:** these are responses produced an intentionally during the cause of treatment e.g. penicillin may cause hepatic toxicity, steroid may cause Cushing's syndrome.
- **Anaphylaxis:** A sudden serious life threating allergic reaction and should be treated as a medical emergency, it causes more than one of the following ; an itchy rash throat and tongue swelling, shortness of breath ,vomiting, lightheadedness and low blood sugar.

Drug development

- After a chemicals that has shown therapeutic value has been identified, it must undergoes a series of scientific test to evaluate its actual therapeutic and toxic effects. The process is controlled by legally established bodies e.g. pharmacy and poisons board and food & drug administration (FDA)development IN Kenya and USA respectively. Before receiving legal approval to be marketed to the public ,drugs must pass through several sequential stages of development.

Pre-clinical trials: this phase involves testing the drug on laboratory animals to test their pharmacodynamics, pharmacokinetics and toxicology. The toxicity studies include mutagenic, carcinogenic and reproductive studies.

Drug Development Conti....

Phase I: clinical pharmacology

This is first phase human volunteers, usually 20-50 (healthy volunteers or volunteer patients depending on the class of drug and its safety)are used to test the drug. Pharmacodynamics and pharmacokinetics era tested. Toxicity and therapeutic effects are further tested.

Phase II: therapeutic exploration

Tests are done on patients who have the disease usually 100-200 patients are involved in the study. Pharmacodynamics and pharmacokinetics era determined as well as dosing requirements and efficacy of the drug at the given dose

Phase III: Therapeutic confirmation

The drug is used on Avast clinical market 300-3000 patients are involved. Prescriber observes patients closely for drug adverse effects and therapeutic effects.

Drug Development Conti….

Phase IV: continuous evaluation

the prescribers are expected to report to the regulatory bodies any unexpected effects which then evaluates this information. A drug may be withdrawn from the market if it produces toxic effects e.g. thalidomide.

- **Orphan drug :** drugs that have been discovered but are not financially viable and therefore have not been adopted by any drug company. may be useful in treating a rare disease or may have potentially dangerous adverse effects. They are often abandoned after **preclinical trials** or **phase I** studies.

Sources of drugs

a)**Plants sources:** plants have been used as a source of drugs since pre-historic times. Plants are an important source of chemicals that are developed into drugs. Any part of a plant; including **leaves, roots** and **back** can be used. Drug can be processed using the synthetic version of the active chemical found in plants e.g. **dronabinol** which contains the active ingredients **delta-9-tetrahydrocannabinol** found in marijuana.it prevents nausea and vomiting in cancer patients but does not cause adverse effects as when one smokes marijuana.

Examples of active ingredients in plants.

i)Alkaloids: Taste bitter and are poorly absorbed in water but become soluble if dissolved in acids examples of drugs derived from alkaloids includes; atropine, caffeine, cocaine, quinine, codeine and morphine.

Sources of drugs Conti….

ii)Glycosides: these are digitalis products e.g. digoxin, digitoxin which are gotten from digitalis purpureal or foxglove plants.

iii)**Gums:** these are polysaccharides exudates that can be used for bulk laxatives and dental adhesives.

iii)**Resins**: the most common resins is **benzoin** which is used as an antiseptic.

iv)**Oils:** These can be volatile oils like **peppermint, spearmint, menthol**, **cinnamon, lemon camphor**. They have pleasant fragrance and evaporate easily. The other types of oils is fixed oils which include **castor oil** used as a laxative, **olive oil** for cooking, **emollients** used in cosmetics and **solvents** for injections.

Sources of drugs Cont….

b) **Animal sources: these** are used to replace human chemicals that are not produced adequately due to disease or genetic problems e.g. **insulin** from pancreases of pigs and cows. **Thyroid drugs** and **growth** hormone **preparations** from animals hypothalamus. Despite these animal sources most of these products are being currently produced synthetically which provides purer and safer products than animal sources.

c)**Inorganic sources:** salts of various elements have therapeutic effect in the human body e.g., **aluminum** (used as antacids), **fluoride(** used to prevent dental cavities and osteoporosis), **gold(** used for rheumatoid arthritis), **iron(** used for anemia) and **potassium** (used in potassium K+ supplements.)

Sources of drugs Cont....

d)**Synthetic sources:** Many drugs are developed synthetically after chemicals in plants ,animals or other environment have been screened for signs of therapeutic activity. This eliminates side effects and increases drug potency. Drugs have genetic engineering are used to produce chemicals that have therapeutic effects.

e)**Microbiological sources:** example penicillins,tetracycline

f)**recombinant DNA technology.**

Uses of drugs

1. **curative:** this is the primary therapy e.g. in treating infections or auxiliary therapy e.g. application of anaesthetic medication.
2. **suppress signs and symptoms**, hence improve quality of life without attaining cure e.g. anti diabetics.
3. **prevent/prophylaxis-** this could be primary e.g. use of vaccines to prevent one from getting a disease or secondary to stop progression of an existing disease.
4. **diagnosis-** for instance the use of tuberculin test to diagnose PTB

Drug nomenclature

Nomenclature is the systematic naming of drugs especially pharmaceutical drug

Drugs in majority of circumstances have three types of names.

1. i)**Chemical/molecular/ scientific name:** this is the chemical/ molecular structure of a drug. It states the structure in terms of atoms and molecules accompanied by a diagram of the chemical structure. Most useful to a few technically trained personnel e.g. chemist or research pharmacist the names are unsuitable for general use since they are long. e.g. **acetyl-p-amino-phenol** is for **paracetamol** or **acetaminophen**

Drug Nomenclature Conti……

ii)**Generic/non-proprietary/approved name;** this is the abbreviated and approved name. it is the official medical name assigned by the producer in collaboration with the food and drugs board and nomenclature committee. The generic name can be used by any interested party and it removes confusion of giving several names to the same drug regardless of who manufactures them once they have the same chemical structure. A generic name is not capitalized e.g. **acetylsalicylic acid** commonly known as **aspirin,**

iii) Trade name/proprietary/brand name: name given to the drug by the manufacturing and marketing company. One drug may have so many trade name e.g. acetaminophen has about 30 names some are paramol, Tylenol, Panadol etc. they are usually capitalized.

Example of drugs chemical name, generic name and trade name.

Chemical name	Generic name	Trade names
2-(4-isobutylphenyl)propanoic acid	ibrufen	Brufen, advil, nurofen
N-acetyl-para-aminophenol	Paracetamol, acetaminophen	Calpol, Panadol, tylenol
2-(2-methl-5-nitro-1h-imidazol1-y)ethyl benzoate.	metronidazole	Flagyl ,metrogyl

Two major methods of dispensing drugs

- **Over the counter drugs (OTC):**they do not need a prescription and can be purchased at the chemical shops; examples pain relief, blood tonics, vitamin preparation, ORS, antacids, antimalarial.
- **Prescription drugs:** They need a prescription and must be controlled from abuse and dependence; e.g. antibiotics, anti-hypertensives, sedatives, diabetics drugs etc.

Patients education -about OTC drugs

- You need to give your attention to all the drugs the patient is taking whether prescription or OTC.
- Caution patient not to treat themselves with OTC drugs.
- Inform them that most of the OTC medication contain more than one active ingredient.
- Tell he patient that interactions can occur when takes more than one OTC medication at a time or takes one with a prescription drugs.

Patients education about drugs

Prescription drugs

- Inform patient about special consideration and drug safety precaution.
- Encourage: complete medication list complete adverse reaction list.
- Patients compliance.

Pharmacokinetics

- Pharmacokinetics is the process by which the body, sick or well, handles and affects the drug. O*r is the study of the bodily absorption, distribution, metabolism, and excretion of drugs.*

It is characterized by four processes

1) Absorption ;This is the process by which a drug is transferred from the site of administration into the circulating fluids of the body e.g. Blood and lymph.

2) The rate of absorption is vital because it determines when the drug is available to exert its action.

3) Bioavailability: This is the fraction extent to which a dose of drug reaches its site of action .**for example;1.** hepatic metabolism and biliary excretion may occur before a drug taken orally reaches systemic circulation.**(first pass effect)**

4) Drug given intravenously its bioavailability is 100%thus bioavailability must be considered when calculating none intravenous routes of administration.

Factors affecting absorption

- Route of drug administration.
- Dose.
- Dosage formulation.
- Food and fluids administered with the drugs.
- Status of the absorptive surface.
- Rate of blood flow to the small intestines.
- acidity of the stomach
- Status of GI motility.

Factors influencing drug administration

- ✓The nature of the absorbing surface.
- ✓Blood flow to the site of administration; increase in blood flow facilitates abortion ; and e.g. sublingual route and pulmonary epithelium.
- ✓The health status of the person taking the drug. This affects the rate of absorption and transportation.
- ✓The lipid solubility of drugs the higher the solubility the more a drug is absorbed especially in the GIT.
- ✓The PH of the drug.
- ✓Drug concentration and critical concentration.

Routes of drug administration

- A drugs route of administration affects the rate and extend of absorption.
- **Enteral route** : drugs given along any portion of the GIT.it is most **common, safe, convenient. and economical**. but it is the **slowest,** it can be orally, sublingually, and rectally.
- **Parenteral route:** intradermally, subcutaneous, intramuscular, intrathecal intravenous.
- **Pulmonary route**: administered by in halation.
- **topical:** applied on the skin, mucus membrane of eyes, ears, nasal mucosa, bladder, vagina and the penis.

Factors to consider when choosing the route of drug administration

1. The time at which the effect of the drug is required.
2. The method most suitable for the drug required.
3. The site of drug action.
4. Patients status whether conscious or unconscious.
5. Desire off the patient.

Conti……

- When prescribing drugs the dose may vary with certain factors ; **age, route, assimilation.**

ii)**distribution:** this is the transport of a drug in body fluids to various tissues of the body and ultimately site of action.

The rate of distribution depends on;

- The permeability of the capillary to the drug.
- Lipid solubility and ionization of the drug. lipid soluble drugs are more rapidly absorbed and distributed than their lipid insoluble drugs
- Cardiac function e.g. cardiac out put and regional blood, drug are fast distributed to areas with rich blood flow(**Heart, kidneys, brain**) later to areas of low blood flow (**muscle**, **fat tissue).**

Conti…..

- Drugs are widely distributed in body water (**free fraction of drug**)and partly as bound to **plasma proteins** and or tissues.
- Plasma protein and tissue binding of drug reservoirs that sustain pharmacological action of a drug. The bound fraction and the free fraction are usually in a state of equilibrium
- other proteins involved in drug binding include; **lipoproteins, glycoprotein and globulins.**

Biological membranes which limit the distribution of drugs

- **Blood brain barrier:** allows distribution of only lipid soluble drugs e.g. **general anesthetics, barbiturates** into the brain and spinal cord.
- **Placenta barrier:** lipid soluble and some lipid insoluble can diffuse through hence some drug meant for the mother may pass through and harm the baby e.g. **steroids ,narcotis** and **anaesthetics.**
- **Blood-testes barrier:** this may limit some chemotherapeutic agents used for treating testicular neoplasms.

Metabolism

iii)metabolism/biotransformation:

the biological transformation of a drug into an inactive metabolite, a more soluble compound ,or a more potent metabolite.

The **Liver** is the main organ of metabolism.

The **Kidneys, gut mucosa, lungs** and **the skin** are also involved in drug metabolism.

NB: Delayed drug metabolism results in accumulation of drug in the body and prolonged effect of the drug

Factors influencing metabolism

- **Physiological factors** like starvation, liver diseases, cardiovascular problems, these depress microsomal enzyme systems.
- **Age** people with extreme ages have decreased metabolism
- **Genetic predisposition** genetic differences in the rate of metabolism of some drugs exist.
- **Prior administration of the particular drugs or other drugs** e.g. repeated administration of a particular drug may cause induction or inhibition

Enzyme induction or inhibition

- enzyme induction this is a situation whereby the re is an increase in amount and activity of the liver microsomal enzymes usually due to exposure to certain substances such as drugs and endogenous substances.
- A drug may induce its own metabolism

pharmacological Importance of enzyme induction

1. Drug interaction may occur.
2. Disease may result .
3. Tolerance (metabolic) to the drug.

Enzyme induction or inhibition Conti.

- **Enzyme inhibition** this refers to decrease synthesis and activity of liver microsomal enzymes.it results in reduced metabolism of other drugs/inhibiting drug and endogenous substance.
- General enzyme inhibition(beyond liver enzymes)has a greater pharmacological importance utility than enzyme induction.
- Examples of drugs that inhibit enzymes include **chloramphenicol** and **cimetidine**.

Excretion

iv) Excretion: this the process by which drugs and pharmacologically active or inactive metabolites are eliminated from he body primarily through the **Kidneys.**

Net renal excretion of a drug is as a result of 3 processes

1. **filtration (passive glomerular filtration)**
2. **re-absorption,**
3. **active tubular secretion.**

other routes through which drugs are eliminated include

intestines or biliary excretion e.g. neomycin

Pulmonary elimination e.g. volatile liquids (general anaesthetics)

Sweat and saliva elimination e.g. thiazides.

Breast milk elimination e.g. narcotics.

Pharmacodynamics/mechanism of action

The study of how drugs act on the body. It is the chemical changes or effects that a drug has on body cell and tissues.

- **Drug action**: the cellular process involved in the drug and cell interaction.
- **Drug effects**: the physiology reaction of the body to the drug.

The common drug molecules (targets) on which drugs bind to produce therapeutic effects include **enzymes, carrier molecules, ion channels, and receptors.**

- **The receptor :** these are proteins that are found within or on the surface of cells

Two terms related to receptors are **affinity and efficacy.**

- **Efficacy** the tendency of a drug to activate the receptor once bound.
- **Affinity** the tendency of a drug to bind to the receptor.

Drug interactions

Harmful interactions-

-Oral contraceptives and anti TB drugs – contraceptive failure.

-Tetracycline and antacids – cimetidine renders tetracycline ineffective.

-Anticoagulants warfarin and aspirin – may result to bleeding.

Beneficial drug interactions-

-Amino glycoside & penicillin's achieve **synergic** antimicrobial effects

-probenecid plus penicillin prolong action of penicillin..

-Morphine poisoning-naloxone is used as an antidote.

Continuation.....

Synergism

This can either be

summation- this occurs when the effect of two drugs having the same action are additive e.g. beta blockers plus thiazide diuretics have an additive anti hypertensive effects.

Potentiating- this means to make more powerful, occurs when the action of one drug increases the action of another. e.g trimethoprim plus sulfamethoxazole.

Antagonism

- **Agonist**- drug binds to a receptor there is a response.
- **Antagonist**-drug binds to a receptor-no response, prevents binding of agonist(alphæ*and* beta blockers)
- **Partial agonist-a** drug that is able to both stimulate and block at receptor.
- **Antagonism-** occurs when two or more drugs oppose the action of one another producing opposite pharmacodynamic effects e. g.

Antacids and tetracycline form a complex which is excreted in feaces chemical antagonism.

Administration of Medications/Drugs

- Administration of medication involves all the activities related to safe drug use which include;-

✓Assessing the risk to a client of a new drug order.

✓Delivering the drug dose to the proper body tissues.

✓Assessing the client's response to drug therapy.

✓Treatment of adverse reactions to drugs.

✓Consulting with the doctor about adjusting the prescribed regime.

✓Educating the client about proper use of drugs substances.

Principles of Drug Administration

- For a Clinical officer to administer any medication, it is important to avoid errors to adhere to the principles of drug administration.
- To provide safe administration of drugs a Clinical officer should practice the rights of drug administration... they are;-

➢*Right patient.*

➢*Right drug.*

➢*Right dose.*

➢*Right time.*

➢*Right route.*

Principles of Drug Administration Conti…..

Five additional right are essential in Clinical practice; These includes;-

- The right assessment e.g. patients ability to swallow, allergies, contraindication, new signs and symptoms that may indicate adverse effects of administration, heart, liver or kidney disorders etc.
- The right documentation.
- The clients right to information of name, purpose, action and potential side effects.
- The right evaluation.
- The clients right to refuse medication regardless of the consequences.

Principles of Drug Administration Conti…..

- **Right client or patient:**

✓You should make sure that the right client receives the right drug.

✓You should only give drugs to the person for whom they are prescribed or recommended for.

✓If the patient is wearing an identification bracelet, check the clients name on the identification bracelet with the name, hospital number on the medication card in your hand.

✓Alternatively if the patient is conscious and sane simply call out the patients name.

Principles of Drug Administration Conti…..

Right drug

- You must check and double check the package label of the drug.
- The right drug label should be read at list three times;

--Before preparing or measuring the actual prescribed does.

-Before replacing the drug on the shelf just before administering the drug to the client.

- You must prepare the medication you give yourself and **DO NOT** giver drugs prepared by someone else.

A Mentally alert person will notice a change in medication or mention problems that have arisen from the medication.

Ensure that you take the following precaution when administering medicine.

- All doses are best prepared from the original container.
- Medicines should not be prepared in the dark
- You should caution clients about the use of non-labelled pillboxes
- Do not mix supplies of several tablets or capsules in a single container
- make sure you check medication label before removing from the shelf before pouring or measuring and when returning to the shelf.

The right dose:

- To obtain the right dose you must carefully measure the medicine.
- when pouring solid drugs such as capsules and tablets use proper technique to avoid contaminating the drugs. you should pour the medication in the container cap, and transfer the number of units required from the cap to the medication cup

Right route:

- The right route must be used for drug delivery.
- Most drugs are given orally or by topical application .
- Ensure the patient understands how the drug is to be taken.
- sub lingual or chewable tablets should **NOT BE** swallowed whole.
- Crush oral drugs if swallowing is difficult or if they are to be taken in liquid form.
- Demonstrate to the patient the procedures for application of topical drugs.
- Always check the doctors orders ,the cardex and the treatment sheet to verify the medication route.

Right time:

- For example;

The hourly interval between doses

The relationship of dose to the clients activity ,such as before or after meals, on rising or retiring, every 4hours, hour, 12 hours.

Medication in children

Take great care when administering drugs in children;

- There is high risk of errors due to changes in weight and age.
- Most drugs have not been tested in children.
- Many drugs are marked in dosage forms and concentration suitable for adults. Therefore this requires dilution, calculation preparation and administration of very small doses.
- Children have limited sites for IV (intravenous)administration , several drugs may be given through the same site.
- This increases the need for small volumes of fluid and flushing between sites.

Medication errors

- Wrong client
- Wrong route
- Wrong medication or IV fluids
- Wrong dose or IV rate
- Omission of dose
- Incorrect discontinuation of treatment.

Drug storage

- Many factors can change your medication including heat, .air , light, and moisture. This will infective or even harmful.
- Drugs require careful storage and handling to maintain their safety and potency.
- Every medication has its owner recommended storage condition from room temperature, refrigeration and freezing thus check the specific storage condition.
- They must be kept in special spaces secured from access by unauthorized persons.
- Storage areas should be kept clean, cool, and dry with no direct sun light.
- Drugs should not be placed on the floor.
- Sterile substances should be protected from contamination.

- Drugs are best kept in their original containers. original containers protect their content.
- Do not transfer sterile substances from container to container as it increases the probability of contamination. Protect the label from soiling to ensure it remains legible.
- Drugs should only be labeled in pharmacy.

Classification of drugs

Classification systems enable us to readily identify the similarities and differences among a large number of medications within or outside a classification.

Drugs can be classified according to;

1. **Body systems as follows;**

-Respiratory system medications

-Cardiovascular system

-Nervous system

-GIT medications.

1. **Their functions or usage e.g.**

✓Antidepressant

✓Diuretics

✓Analgesics

✓Antibiotics

3.**Their chemical make up**

✓Estrogens

✓Opioids

Antibiotics Agents

- Antibiotics are among the most commonly used and misused of all drugs.
- The inevitable consequence of their widespread use has been the emergence of **antibiotic-resistance pathogens.**
- There different groups of antibacterial agents based on molecular structure and members of each group have a comparable pharmacokinetic and pharmacodynamics.

Classification of Antibiotics

- Beta- lactam antibiotics
- tetracycline
- Aminoglycoside
- Macrolides
- Quinolones
- Azoles
- Antimycobacterial
- Sulphonemides
- lincosamides
- Unclassified antibiotics like chloramphenicol, spectinomycin and vancomycin

Beta –lactam Antibiotics

All beta –lactam compounds ,so named because of their unique four membered lactam ring as a basic chemical structure.

They are sub divided into the Following;-

- Penicillins
- Cephalosporins
- Others like;-carbapenems and monobactams

Penicillins

Classification of penicillins

- **Narrow spectrum** e.g. benzyl penicillin(Xpen), phenoxy methyl penicillin, penethicillin etc.
- **Antistaphylococcal penicillin** also called beta-lactamase resistant penicillin, or penicillinase resistant penicillin's e.g. nafcillin, cloxacillin, flucloxacillin, methicillin etc.
- **Broad spectrum penicillin e.g.** ampicillin, amoxicillin, bacampicillin etc
- **Antipseudomonal (extended spectrum penicillin) e.**g. carbecillin, carfecillin, ticarcillin, temocillin etc.

Mechanism of action

- All beta lactam anti biotics inhibit bacteria cell wall synthesis.

this is by inactivating enzymes located in the bacteria cell membrane .

- They are **bactericidal** agents acting against multiplying bacteria (diving cells) as resting bacteria do not make new cell walls.

Mechanism of bacterial resistance

General mechanism of bacteria resistance to antibiotics including beta –lactams are;

- Decreased penetration to the target cells
- Alteration of the target site
- Inactivation of the antibiotics by a bacterial enzyme e.g. beta – lactamase.

Pharmacokinetics

- Benzylpenicillin is destroyed by gastric acid hence it is parenterally administered.
- Phenoxymethylpenicillin can be orally given.
- **Metabolism** is in the liver.
- Half life less than 2hours.
- Poor lipid solubility hence they don’t cross the BBB.
- **Distribution** in body fluids and tissues with a few exception. they are polar hence extracellular concentrations exceed he intracellular.
- **Elimination** in the kidneys by glomerular filtration and tubular secretion.

Benzyl penicillin G

- Penicillin G is gastric acid unstable is used where high plasma concentration era required.
- Maximum plasma concentration is reached after 15 minute of administration
- Half life 0.5 hours hence reasonably spaced doses have to be large to maintain a therapeutic concentration high doses can be maintained by use of probenecid.

Indication for penicillin G

It is generally active against gram positive and gram negative cocci, hence indicated for treatment of the following conditions;

- Otitis media
- Gonococcus infection
- Throat infections
- Streptococcal endocarditis
- Meningococcal meningitis
- Pneumonia meningitis
- actinomycosis

Cloxacillin

- *Half live is 30 minutes*

Indication for infections due to penicillinase (enzyme against penicillin) producing staphylococci especially skin infections and soft tissue infections e.g. **cellulitis, otitis externa, impetigo**

Dosage;

Adults by oral 500mg every 6 hours at least 30 minutes before meals because food decreases absorption.

IM 500mg every 4-6 hours.

IV injection or infusion 500mg every 4-6 hours .

The dose may be increased in severe Conditions.

Ampicillin

- ✓Is gastric stable, it is moderately 50 % absorbed orally as food interferes with absorption..
- ✓The drug is concentrated in the bile and it undergoes enteral hepatic recycling.
- ✓Excretion is through the kidneys 1/3 of the administered drug appears unchanged in urine.
- ✓Almost all staphylococcus aureus,50% of E.coli, and 50% of haemophilus influenza are now resistant.

Indications of Cloxallin

- Urinary tract infections.
- Sinusitis .
- Chronic bronchitis.
- Invasive salmonellosis gonorrhea
- Boils and septic wounds

Side effects

Diarrhea is quiet common, nausea

Macular rashes resembling measles/rubella – discontinue treatment

Dosage

- ✓Adults oral 0.25 to 1g 6 hourly at least 30 minutes before food.
- ✓Different dose are used in treating different condition.
- ✓Gonorrhea 2-3g is administered as a single dose with probenecid.
- ✓UTI :500mg every 8 hours IM/IV/infusion.
- ✓ Children under age 10 years give half the adult dose.

Amoxicillin

- This is a broad spectrum penicillin.
- A derivative of ampicillin and differs by only one hydroxyl (OH) group.
- Have similar anti bacteria spectrum as ampicillin.
- when given orally absorption is better than ampicillin.
- Absorption is not affected by food in the stomach.
- Half life is 1 hour’

Indication

- ✓UTI, otitis media, sinusitis, chronic bronchitis, inversive salmonellosis and gonorrhea.

Dosage

- Adult dose orally 250mgs 8 hourly which can be doubled in severe infections.
- Children up to 10 years of age get 125mg 8 hourly this is doubled in severe infections.
- IM/IV adults 500 mg 8 hourly.
- IM/IV children get 50-100mg /kg daily in divided doses.

Side effects

Diarrhea is less frequent with the use of amoxicillin than ampicillin

Co- amoxiclav

- Amoxicillin (250mg or 500mg)can be combined with clavulanic acid (125mg) to make co- amoxiclav.
- Clavulanic acid itself has no significant anti bacteria activity but binds to beta-lactamase and there by competitively inhibits its activity hence protecting the penicillin. This potentiate the action of penicillin.

Indication

Active against beta-lactamase producing bacteria that are resistant to amoxicillin which include; staphylococcus aureus, 50% of E-coli, 15% of H. influenzae strains and klebsiella spp,

Adverse Effect of Penicillin's

- 1gE –Mediated allergic reactions.
- serum sickness.
- Dermatological reactions e.g. eryema multiforme ,steven johsons syndrome and exfoliative dermatitis.
- Neurologic reactions.
- Gastrointestinal reactions.
- Hepatobiliary reaction.
- Renal reactions.

Precautions

- Instruct clients that penicillin V, amoxicillin, and amoxicillin-clavulanate may be taken with meals. All others should be taken with a full glass of water 1 hours before meals or 2 hours after.
- Instruct clients to report any signs of an allergic response such as skin rash, itching, and/or hives.
- IM injection should be done cautiously to avoid injection into a nerve or an artery.
- Advise clients to complete the entire course of therapy regardless of presence of *absence of symptoms* .

Cephalosporins

- Cephalosporins are the most frequently prescribed class of antibiotics.
- They are structurally and pharmacologically related to the penicillins. they have a wider spectrum of activity than penicillins hence they are more expensive.

Mechanisms of action

- ✓They are bactericidal, interfere with the bacterial cell wall synthesis.

Classification of cephalosporins

- ✓They are grouped in “generations” based on their spectrum of antimicrobial activity.
- ✓The first cephalosporins were designated first generation while later, more extended generation cephalosporins.
- ✓Each newer generation of cephalosporins has a significantly ***greater gram negative antimicrobial*** properties than the preceding generation, in most cases with decreased activity against gram positive organism.
- ✓The newer agents have a much longer half life resulting in the decreased of dosing frequency.

First Generation Cephalosporins

These are generally active against gram positive bacteria. They have moderate activity against gram negative bacterial. Examples;-

Used for upper and lower respiratory tract infnxs.

- ✓ Cephalexin.
- ✓Cephaloridine
- ✓Cephalothin
- ✓Cephapirin
- ✓Cefazolin
- ✓Cephradine
- ✓Cefadroxil.

Second Generation Cephalosporin

- They have a greater gram-negative spectrum eg H.influenza n. gonorrhea, E.coli, shigella.
- Also some gram-positive organism e.g. clostridium, staphylococcus, streptococcus and pneumococcus.
- they are more resistant to beta lactamase.

Indications of Cephalosporins;-

- Upper and lower respiratory tract infection ie tonsolitis, pharyngitis etc
- Sinusitis
- Acute bacterial Otitis media
- Impetigo

Third generation cephalosporins

- They are especially better than 1st and 2nd generation cephalosporin against gram negative bacteri

Uses;- Meningitis, lung infections,otitis media,peritonitis, bones and joint infections, UTI, Soft tisue infxns, some heart conditions which bacterial, gonorrhea and syphilis, neutrophenia and lyme dse.

- Cefriaxone
- Cefperazone
- Cefotaxime
- Ceftazidine
- Cefodizime

Ceftriaxone (Rocephin) 3rd gen'

- Half life 4hours hence requires to be administered Twice a daily.

Indications;

Septicemia, Pneumonia, UTI, RTI, soft tissue infections.

Contraindication;

- ➢Penicillin sensitivity
- ➢Administer with caution in renal impairment.
- ➢Do not administer to infants below 6 weeks.
- ➢Cephalosporin hypersensitivity.

Fourth generation cephalosporin

These drugs has excellent activity on gram positive and gram negative bacteria such as methicillin susceptable staphylococci, penicillin restistant pneumococco and varidins group streptococci.

Examples includes;-

- Cefepime
- Cefditoren and cefpirome.

Pharmacokinetic of cephalosporins

Usually given parenterally, though few may be given orally e.g.

cephalexin

cephradine

cefadroxil

Distribution- Wide distribution because of lipid solubility.

Metabolism- in the liver with half life of 1-4 hours.

Excretion- excreted unchanged in urine especially tubular secretion.

- Dosage should be reduced for patients with renal impairment.
- Active excretion in the kidneys can be blocked by probenecid.

Additional Indication; Septicemia, Pneumonia, Meningitis, Biliary tract infection, Peritonitis, Urinary tract infection, sinusitis.

Unwanted effects of most cephalosporins

- **Hypersensitivity** is the most common
- 10% of the patients sensitive to penicillin are sensitive to cephalosporin.
- **Hemorrhage** due to interference with blood clotting factors.
- Use of cephalosporin for more than two weeks causes **thrombocytopenia, neutropenia, interstitial nephritis and abnormal liver function tests.**

Drug interactions

- Cephalosporin with **alcohol**- disulfiram like effects.

Patient should avoid alcohol when taking these class of drug.

- Cephalosporin with high f**rusemide** and **torsemide** are likely to cause nephrotoxicity.
- Cephalosporin with **aminoglycoside** – nephrotoxicity.
- Cephalosporin with **oral anticoagulant** like warfarin may cause bleed because both interfere with clotting factors.

Precautions of Cephalosporins in general;-

- ✓Instruct clients to complete the prescribed course of therapy, even though symptoms may resolve before the full course of antimicrobial treatment is completed.
- ✓ Advise clients to take oral cephalosporins with food.
- ✓ Instruct clients to store oral cephalosporin suspensions in a refrigerator.

Tetracyclines

- First isolated in 1948, isolated from Streptomyces fungi.

Naturally occurring;

✓Tetracycline

✓Chlortetracycline

✓Oxytetracycline

✓Demeclocycline

Semi-synthetic

Doxycycline, lymecycline, meclocycline, methacyline, minocycline, rolitetracycline etc.

Pharmacokinetics

- Tetracyclines are partially absorbed in the alimentary tract EXCEPT minocycline and doxycycline which have a good absorption.
- Absorption is increased in absence of food
- antacids and milk decrease absorption as they contain metals like **magnesium, calcium, aluminum ,iron** which chelate with them.
- **Distribution** is narrow but they cross the placenta barrier.
- **Metabolism** is in the liver
- **Excretion** in urine via glomerular filtration unchanged.

Pharmacodynamics

- Tetracyclines are broad spectrum bacteriostatic.
- They inhibit protein synthesis by binding to the 30s sub unit of the bacterial ribosomes.

Indication;

Psittacosis, pneumonia, brucellosis, shigellosis, rickettsia diseases e.g. Q fever, typhus, cholera, borrelia (lame disease, relapsing fever)acne ,amoebic dysentery, spirochetes, protozoa, bacillary dysentery and chlamydia infections

Aminoglycosides

Examples;

Gentamycin, kanamycin, amikacin, tobramycin, streptomycin, neomycin,

They are always used in combination of beta lactam antibiotic because of their synergism effect.

Pharmacokinetics; they are water soluble hence hey not absorbed through the gut .

They are given IM/IV route

Distribution; narrowly distributed hence do not cross the blood brain barrier.

Pharmacodynamics/Mechanism of action

- They are bactericidal- they act by binding to the 30s ribosomal sub unit and they inhibit bacterial protein synthesis.

Drug interaction;

- ❑Synergic effect when give with beta lactam antibiotic .
- ❑Bone marrow depression when give with bone marrow depressing agents.
- ❑Muscle weakness or paralysis when given with neural muscular blocking agent.
- ❑Ototoxicity when given with ototoxic agent.

Side effects /unwanted effects

- Have serious un wanted effects and that are dose dependent

These are; nausea, vomiting, diarrhea , lethargy, hypersensitivity and headache.

Others are ,nephrotoxicity, ,ototoxicity, bone marrow depression, neuromuscular blockade, palpitation, numbness, tingling sensation, depression and disorientation.

Contraindication

- Patients with **hearing deficit** because thy damage the 8th cranial nerve(vestibular cochlear/auditory nerve)
- **Myasthenia gravis** since they cause neural muscular blockade.
- Patients with **severe renal disease** as they are nephrotoxic
- Hypersensitivity
- Neonates, geriantrics, infant, botulism and patients with packinsonism

Gentamycin

✓This is the most active aminoglycoside.

✓Half life 2-3 hours and reaches peak plasma concentration within 30 minute.

Route of administration;- IM/IV.

- **Indication;**

Gram negative and gram positive; septicemia, meningitis, endocarditis, UTI, neonatal sepsis and acute pyelonephritis among other infections.

Contraindications;

Like other aminoglycoside.

Children below 2wks 7.5mg/kg body weight every 12 hrly. (od)

Gentamycin Cont…

- Aminoglycoside can replace penicillin in penicillin sensitive patients
- **Gentamycin** combine with penicillin have a synergic antibiotic effect expands the spectrum of antibiotics activity and prevent emergence of resistance..
- **Neomycin** and **kanamycin** can be used for hepatic coma to reduce normal flora and therefore ammonia gas formation.
- **Amikacin** has broadest antibacterial spectrum because it is stable to 8 of the 9 classified aminoglycoside inactivating enzymes whereas gentamycin is inactivated by five of them.
- **Amikacin** is indicated for serious gram negative infections resistant to gentamycin.
- Neomycin and framycetin are too toxic for systemic use hence used topically for treatment of **aer, nose** and **skin** infections,

Quinolones

These are broad spectrum antibiotic though some like nalidixic acid and cinoxacin have a narrow antibacterial spectrum.

Most popular quinolones are fluoroquinolones Which include;-

- Norfloxacin
- Ciprofloxacin
- Moxifloxacoin
- Ofloxacin
- Levofloxacin
- Acrofloxacin
- Pefloxacin

Pharmacodynamics/Mode of Action

- They are act by inhibiting bacterial DNA gyrase the enzyme that maintains the Helical twist/structure of the DNA.
- They are **bactericidal** but some are **bacteriostatic.**

Pharmacokinetics

- Quinolones are absorbed in the gut though aluminum and magnesium antacid interfere with the **absorption**.
- **Distribution** wide distribution such that they cross the placenta and are distributed in breast milk.
- They are concentrated in the lungs, kidneys, prostate, and phagocytes.
- They don't cross the BBB except ofloxacin and pefloxacin.
- **Metabolism** they under go hepatic metabolism with a variable half life
- Norfloxacin and ciprofloxacin half life of 2-3 hours, 5 hour ofloxacin, perfloxacin10 hour.
- **Excretion**/elimination via renal and biliary.

Adverse effects of Quinolones

- GIT effects like nausea, vomiting, and diarrhea
- CNS effects like dizziness, headache, confusion and convulsions.
- Allergic reactions in form of skin rashes,

They are reported to cause arthropathy in immature animals hence not recommended for children and adolescence unless the benefit out ways the risk.

- Photosensitivity
- Bone marrow suppression.

Contraindications of Quinolones

- ✓History of epilepsy or seizures.
- ✓Glucose-7-phosphatedehydrogenase deficiency.
- ✓Myasthenia gravis.
- ✓Pregnancy and breast feeding.

Indications; quinolones are basically indicated for UTI ciprofloxacin has a broader spectrum of antibacterial activity.

These are often caused by gram negative organisms like E.coli, proteus spp. Therefore infections like complicated UTI, inversive otitis externa, salmonella typhi infection, gonorrhea, bacteria prostatitis and cervicitis.

They are also indicated for anthrax which has been used as a biological warfare.

So the soldiers can take quinolones just before they go to war just in case they are at risk of exposure to anthrax.

Drug Interactions

These antibiotics are enzyme (cytochrome p-450) inhibitor hence interact with other drugs at metabolism e.g. theophylline, warfarin, and caffeine.

- NSAIDs and quinolones causes an increase in the risk of convulsion.
- NSAIDs tends to potentiate the effect.

Ciprofloxacin

- Half life is 3hrs

Indications

It is mostly effective against gram negative bacteria e.g. salmonella, shigella, Campylobacter, pseudomonas, enterobacteria,chlamydia and some mycobacteria, UTIs and genital urinary tract infections.

Dosage

- **Oral** 250-750mg bd depending with what is being treated.
- **IV** infusion (adult) 500mg bd daily.....

Drug Interactions

- Cationic compounds (aluminum-magnesium antacids, iron salts, sucralfate, milk and dairy products) decrease absorption of ciprofloxacin;
- Administer cationic compounds 6 hrs. before or 2 hrs after ciprofloxacin
- Plasma levels of theophylline can be the increased with concurrent use of ciprofloxacin;
- Monitor levels and adjust dosage accordingly.
- Plasma levels of warfarin can be increased with concurrent use of ciprofloxacin;
- Monitor prothrombin time and INR, and adjust the dosage of warfarin accordingly.

Precautions of Quinolones

- Ciprofloxacin is available in oral and intravenous forms.
- Decrease doses of ciprofloxacin in clients with renal dysfunction.
- Intravenous ciprofloxacin should be administered slowly over 60 min.
- For inhalation anthrax infection, ciprofloxacin is administered every 12 hrs for 60 days.
- Instruct clients to complete the prescribed course of antimicrobial therapy, even though symptoms may resolve before the full course is completed.

MACROLIDES

- These broad spectrum antimicrobials including;
- Erythromycin
- Azithromycin(brand name is Zithromax)
- Spiramycin
- Clarithromycin (Klacid) en Telithromycin (ketec)

Pharmacodynamics; they **inhibit protein synthesis** by irreversibly binding to ribosomal 50s sub unit of the sensitive micro-organism hence they are bacteriostatic.

But sometimes can be bactericidal if the dose is high.

Example azithromycin is bactericidal against streptococcus pyogenes, streptococcus pneumonia and hemophilus influenza

Pharmacokinetics

They can be administered orally though erythromycin is unstable in acidic environment.

Distribution;-

Is good except that the drugs do not cross the BBB

Metabolism;-

Tiz in the liver and have variable half life.

e.g. clarithromycin has 4.5 hours , azithromycin less than 3.5 hours and erythromycin has 1.4 to 2 hours.

Therapeutic Uses/indication

- Used to treat infections in **clients with a penicillin allergy**, such as for **prophylaxis against rheumatic fever** and **bacterial endocarditis**.
- Used for clients **with Legionnaires' disease, whooping cough** (pertussis), **and acute diphtheria** (eliminates the carrier state of diphtheria) .
- Used for chlamydia infections (**urethritis and cervicitis; pneumonia** caused by Mycoplasma pneumoniae; **respiratory tract infections** caused by **Streptococcus pneumoniae and Neisseria gonorrhea.**

Side/Adverse Effects;

Gastrointestinal discomfort

- (nausea, vomiting, epigastric pain) Administer erythromycin with meals.
- Observe for GI symptoms and notify the provider.

Hepatotoxicity (abdominal pain, lethargy, jaundice) . Instruct clients to notify the provider because the medication should be discontinued. Prolonged QT interval causing dysrhythmias and possible sudden cardiac death

- Use in clients with prolonged QT intervals is not recommended.
- Avoid concurrent use with medications that affect hepatic drug metabolizing enzymes.

Contraindications/Precautions.

- pre-existing liver disease

Erythromycin

- Erythromycin is the most commonly used macrolide.

Pharmacokinetic;

Erythromycin is inactivated by gastric enzymes hence it is administered as protected enteric coated tablets.

It is hydrolyzed in the 1st phase metabolism to release the active erythromycin.

It is dissolved and absorbed in the small intestines where it undergoes enetro hepatic recirculation.

- **Distribution;-** is very good as it is well distributed in the spleen, liver, placenta, breast milk and inflamed meninges.
- **Excretion;-** 90% in feaces and small amounts in urine.

Dosage and Route of Administration

- Orally adults and children above 8years 250-500mg 6 hourly.
- Maximum dose is 4g in severe infections.
- Children up to 2years 125mg 6hourly.
- IV infusion 25-50/kg body wt. daily as continuous infusion.

Drug interaction

Macrolides are enzyme inhibitor and they interfere with the metabolism of*drugs like warfarin, carbamazepine, theophylline , corticosteroids, oral contraceptives, digoxin, and cyloserine and odium valproate*

- Food tends to decrease the absorption of macrolide, hence should be given one hour before food or 2-3 hours after meals.

Azithromycin

Azithromycin is derived from erythromycin by adding a methylated nitrogen into the lactogen ring.

- Its specrum of activity and clinical uses are virtually identical to those of clarithromycin.
- Azithromycin is active against mycobacteria avium complex and toxoplasma gondii.

SULPHONAMIDE

Are a group of man-made medicines that contain the sulfonamide chemical group. They are called sulfa drugs.

- Examples
- Trimethoprim and Sulfamethoxazole
- Sulphadiazine,
- Sulfisoxazole,
- Sulphadimidine,
- Sulfasazine,
- Sulfametopyrazine,
- Sulphaloxate

Pharmacokinetics of sulfa drugs

- They inhibition of other metabolic processess.They interfere with folic acid synthesis by preventing addition of para-aminobenzoic acid (PABA) int the folic acid molecule through competing for the enzyme dihydropteroate synthesis
- they have good absorption except a few of them sulpadiazine and which are poorly absorbed in the gut.
- Distribution widely distributed in body tissues and fluid including crossing the BBB.
- They are metabolized in the liver withhalf life of 10 hours.
- Majority are excreted in urine hence dose should be reduced in renal impairment.

Side and adverse effects

- **Hypersensitivity including Stevens-Johnson syndrome**

- Do not administer TMP-SMZ to clients with allergies to: Sulfonamides (sulfa), Thiazide diuretics [hydrochlorothiazide (HCTZ)] , Sulfonylurea-type oral hypoglycemics [tolbutamide (Orinase)], Loop diuretics [furosemide (Lasix)]

- Stop TMP-SMZ at the first indication of hypersensitivity, such as rash.

- **Blood dyscrasias (hemolytic anemia, agranulocytosis, aplastic anemia)** •

-Draw the client's baseline and periodic CBC levels to detect any hematologic disorders.

- Observe for any bleeding episodes, sore throat, or pallor. • If the above symptoms occur, instruct clients to notify the provider.

- **Crystalluria**

- Maintain adequate oral fluid intake.

- Instruct client to drink 2 to 3 L/day.

- **Kernicterus (jaundice, increased bilirubin levels)**

- Avoid administering TMP-SMZ to women who are pregnant near term, breastfeeding mothers, and infants younger than 2 months.

- Monitor the client's liver function. Photosensitivity

- Avoid prolonged exposure to sunlight, use sunscreen, and wear appropriate

Cotrimoxazole (serpin

This has replaced use of sulphonamide due to resistance.

Dosage for children

It's a bd drug

Indications

- Pneumocystic carinii pneumonia
- Toxoplasmosis
- UTI
- Chronic bronchitis
- Others sulphonamides are used for topical application for prophylaxis **of burns, leg ulcers, pressure sores** because of their wide anti bacteria spectrum

Drug Interactions

- Sulfonamides can increase the effects of **warfarin (Coumadin), phenytoin** (Dilantin), **sulfonylurea oral hypoglycemic**, and **tolbutamide** (Orinase) by inhibiting hepatic metabolism.
- dosages of these medications may be required during therapy.

Precautions; Instruct patient***not to take*** the drugs on an empty stomach plus to use a full glass of water.

- Instruct clients to complete the prescribed course of antimicrobial therapy, even though symptoms may resolve before the full course is completed.

Depending on therapeutic intent, effectiveness may be evidenced by:
Improvement of infection symptoms, such as improvement of urinary tract symptoms (decreased frequency, burning, and pain during urination) and negative urine cultures…….

AZOLES

- Azoles are synthetic antifungals with broad-spectrum fungistatic activity against yeasts and fungi, including candidal species. By blocking fungal cytochrome P450-dependent enzymes, azoles disrupt the synthesis of ergosterol, which is the principal sterol in fungal cell membranes.
- Are 5 membered heterocyclic compounds containing a nitrogen atom and at least one other non carbon atom as part of the ring.
- Classified into two groups: those with two nitrogens in the azole ring (the imidazoles; examples include clotrimazole, econazole, ketoconazole, miconazole, and tioconazole) and those with three nitrogens in the azole ring (the triazoles; examples include fluconazole, itraconazole, posaconazole.

AZOLES cont....

Names of azoles maintain the prefix upon reduction (e.g., pyrazoline, pyrazolidine). The numbering of ring atoms in azoles starts with the heteroatom that is not part of a double bond, and then proceeds towards the other heteroatom.

Imidazole and other five-membered aromatic heterocyclic systems with two nitrogens are extremely common in nature and form the core of many biomolecules, such as histidine.

AZOLES cont....

Compound classes

Nitrogen only

Imidazole

Pyrazole

1,2,3Triazole

1,2,4Triazole

Tetrazole

Pentazole

AZOLES cont....

- **N,O compounds**
- Oxazole
- Isoxazole
- 1,2,3-oxadiazole (unstable)
- Oxadiazole (1,2,4-Oxadiazole)
- Furazan (1,2,5-oxadiazole)
- 1,3,4-oxadiazole

AZOLES cont....

N,S compounds

- Thiazole
- Isothiazole
- Thiadiazole (1,2,3-Thiadiazole)
- 1,2,4-thiadiazole
- 1,2,5-thiadiazole
- 1,3,4-thiadiazole

Azoles mechanism of action

- The generally accepted **mode of action** of **azoles** is the inhibition of 14α-lanosterol demethylase, a key enzyme in ergosterol biosynthesis, resulting in depletion of ergosterol and accumulation of toxic 14α-methylated sterols in membranes of susceptible yeast species.

Classes of antifungal drugs

Class	Mechanism of action	Drugs
	What are the classes of antifungal drugs? Tables	
Azole	Impairs ergosterol synthesis	Voriconazole
Echinocandin	Impairs ß 1,3 glucan synthesis	Caspofungin
Nucleoside analog	Impairs pyrimidine metabolism	Flucytosine

AZOLES

- Are 5 membered heterocyclic compounds containing a nitrogen atom and at least one other non carbon atom as part of the ring.
- This includes several classes of drugs e.g. **metronidazole and tinidazole** which have both anti bacteria and anti protozoal activity.
- Others are **fluconazole, itraconazole econazole, ketoconazole**, and miconazole which are anti fungal drugs .(to be covered under anti fungal drugs)
- others are **mebendazole, thiabendazole,** which are anti helminths (to be covered under ant-helminths).

Metronidazole

- It is very effective against anaerobic bacterial and protozoa.

Pharmacodynamics/MOA

- metronidazole is converted into an active form and bind to the bacterial DNA and prevents nucleic acid formation which consequently interferes with bacterial replication hence its bacteriostatic.

Pharmacokinetics;

- well absorbed after oral and rectal administration

Distribution;- is wide.

Metabolism;- is in the liver.

- **Excretion;-** in urine partly unchanged and partly as metabolite.

Half life is 8 hours.

Indications

- used for treatment of sepsis caused by orgasms like Bacteroides
- and anaerobic cocci.
- Intra-abdominal infections
- Septicemia, wounds, pelvic infection
- Osteomyelitis.
- pelvic infections
- Infections of the brain and lungs.

Indications cont…

- Used in prevention of post operative infection especially after bowel, antibiotic related colitis, eg pseudomembranous colitis , amoebiasis EH
- other indications include giardiasis, acute ulcers, gingivitis, and dental infections. and anaerobic vaginosis
- Treatment of protozoal infections (**intestinal amoebiasis, giardiasis, trichomoniasis**) and obligate anaerobic bacteria (**Bacteroides fragilis, antibiotic-induced Clostridium difficile, Gardnerella vaginalis**)
- Treatment of H. pylori in clients who have peptic ulcer disease in combination with tetracycline and bismuth salicylate.

Dosage and route of administration

Established anaerobe are usually treated for 7 days.

- The dose per oral is then 4oomgs 8 hourly for 7 days.
- By infusion 500mg 8 hourly.

For surgical prophylaxis

- Per oral 400mg 8 hourly started 24 hours before surgery then continued postoperatively by IV infusion for 5—7days.

Adverse Effects

Gastrointestinal discomfort (nausea, vomiting, dry mouth, and metallic taste) Advise clients to observe for symptoms and to notify the provider.

Dark urine Advise clients that this is a harmless effect of metronidazole.

CNS symptoms (numbness of extremities, ataxia, and seizures)

Advise clients to notify the provider if symptoms occur.

Stop metronidazole.

Contraindications/Precautions

- Use cautiously in clients with renal dysfunction to prevent accumulation of toxic levels with prolonged use.
- Avoid use during the first trimester of pregnancy and use with caution during the rest of pregnancy because metronidazole can pass through the placenta.

Interactions

- Alcohol causes a disulfiram-like reaction/ Advise clients to avoid alcohol consumption.
- Metronidazole inhibits inactivation of warfarin.
- Monitor prothrombin time and INR, and adjust warfarin dosage accordingly.

Precautions

- Administer by oral or IV route.
- Instruct clients to complete the prescribed course of antimicrobial therapy, even though symptoms may resolve before the full course is completed.

Nursing Evaluation of Medication Effectiveness

- Depending on therapeutic intent, effectiveness may be evidenced by: Improvement of symptoms (resolution of bloody mucoid diarrhea, formed stools, negative stool results for ameba and Giardia, , decrease or absence of watery vaginal/ urethral discharge, negative blood cultures for anaerobic organisms in the CNS, blood, bones and joints, and soft tissues).

Chloramphenicol

- It is soluble in water and poorly soluble in alcohol
- Chloramphenicol succinate which is used for parenteral administration is highly water soluble.

Pharmacokinetics

- The usual dosage of chloramphenicol is 50-100mg/kg/d.
- After oral administration crystalline chloramphenicol is rapidly and completely absorbed.
- A 1g oral dose produces blood levels between 10and 15mcg/ml
- Chloramphenicol palmitate is a pro drug that is hydrolyzed in the intestine to yield free chloramphenicol.

Pharmacodynamic

chloramphenicol potent inhibitor of microbial protein synthesis.

It binds to the 50s sub unit of the bacteria ribosome

It is bacteriostatic, broad spectrum against both aerobic and anaerobic gram positive and gram negative bacterial.

Indications

- It is rarely used due to it potential toxicity and bacterial resistance.
- Used to treat; serious rickettsia infections such as typhus and rocky mountain spotted fever.
- Alternative for beta lactam antibiotics for treatment of meningococcal meningitis and pneumococcal meningitis
- Topical eye infections.

Adverse reactions

GIT disturbance nausea, vomiting and diarrhea.

- ✓This rare in children.
- ✓Oral and vaginal candidiasis may occur due to alteration of the normal flora.

Born marrow disturbance

- ✓Suppression of the born marrow
- ✓Aplastic anemia it is irreversible and fatal

Toxicity for new born infants:

- ✓New born infants lack glucuronic acid for the conjugation and detoxification of chloramphenicol.
- ✓Therefore drugs may accumulate resulting in **gray baby syndrome** with vomiting flaccidity, hypothermia, gray colour, shock and collapse

ANTI-FUNGAL DRUGS

- Fungi are saprophytic organism as they lack chlorophyll which is present in plants.
- Many fungi are commensals in the bodies of healthy people but pose a problem when immune system is compromised.

Fungal infections has increased due to the following reasons

- ✓Increase use of broad spectrum antibiotics which decrease non pathogenic bacterial that compete with the fungi.
- ✓Increases number of people with immunosuppression, use of cancer chemotherapy, and immunosuppressants, diabetes mellitus or have burns.
- ✓Inversive procedures may introduce fungi into systemic circulation.

Therapeutic Uses

- Antifungals are the treatment of choice for systemic fungal infection (Candidiasis, Aspergillosis, Cryptococcosis, Mucormycosis) and non opportunistic mycoses, (Blastomycosis, Histoplasmosis, Coccidioidomycosis)

Resistant is usually due;-

- ❑Decrease in membrane ergosterol content
- ❑Change in membrane structure

Classification of anti fungal drugs

1. **Topical anti-fungal**

- ❑Polyenes anti-fungal agents e.g. nystatin
- ❑Benzoic acid

2. **Systemic anti fungal**

- ❑Polyenes anti-fungal agents e.g. amphotericin B
- ❑Fluorinated pyramids e.g. only flu cytosine
- ❑Azoles ;imidazole and triazoles

-Imidazole's include clotrimazole and econazole, sulconazole, fenticonazole, **ketoconazole,** and miconazole

-triazole include fluconazole, itraconazole and voriconazoles among others

3. **Miscellaneous**; terbinafine and Griseofulvin

- ✓Polyenes anti-fungal agents**; nystatin** and **amphotericin B** are the only ones in clinical use.
- ✓**MOA;** they act by binding to the **ergostel** in fungal cell walls forming pores or channels which increase permeability and allow leakage of fungal cellular molecules e.g. potassium and magnesium

Therapeutic uses

- ✓Antifungals are the treatment of choice for systemic fungal infection (Candidiasis, Aspergillosis, Cryptococcosis, Mucormycosis) and non-opportunistic mycoses, (Blastomycosis, Histoplasmosis, Coccidioidomycosis).
- ✓Some antifungals treat superficial fungal infections:
- ✓ dermatophytic infections (tinea Pedis [ringworm of the foot], tinea cruris [ringworm of the groin]); candida infections of the skin and mucous membranes; and fungal infections of the nails (Onychomycosis).

Amphotericin B

Amphotericin B has been available for use since 1950s

MOA/PHARMACODYNAMICS

- Amphotericin B deoxycholate is an antifungal agent that acts on fungal cell membranes to cause cell death.
- Depending on concentration, these agents can be fungi static (slows growth on the fungus) or fungicidal (destroys the fungus).

PHARMACOKINETICS

- administered intravenously
- **wide distribution** though poor penetration to the CNS
- 90% bound to plasma, **half life** of 24 and 15 days
- **excretion** predominantly via the biliary route(slow excretion over a period of days)

Therapeutic Uses

- ✓Antifungals are the treatment of choice for systemic fungal infection (Candidiasis, Aspergillosis, Cryptococcosis, Mucormycosis) and non-opportunistic mycoses, (Blastomycosis, Histoplasmosis, Coccidioidomycosis).

Adverse reactions

Infusion reactions (fever, chills, rigors, and headache) 1 to 3 hr. after initiation

- Pretreat with diphenhydramine (Benadryl) and acetaminophen.
- Meperidine (Demerol), Dantrolene, or hydrocortisone may be given for rigors.

Thrombophlebitis Observe infusion sites for signs of erythema, swelling, and pain.

- Rotate injection sites.
- Administer in a large vein and administer heparin before infusing amphotericin B

Nephrotoxicity

- Obtain baseline kidney function (BUN and creatinine) and do weekly kidney function test, Monitor I&O.
- Infuse 1 L of saline on the day of amphotericin B infusion.

Hypokalemia

- Monitor electrolyte levels, especially potassium.
- Administer potassium supplements accordingly.

Bone marrow suppression • Obtain baseline CBC and hematocrit, and monitor weekly.

Ketoconazole

Hepatotoxicity (anorexia, nausea, vomiting, jaundice, dark urine, and clay-colored stools)

- ❑ Obtain baseline liver function studies and monitor liver function monthly.
- ❑ If symptoms occur, notify provider and discontinue medication.

Effects on sex hormones:

- ❑In males, gynecomastia (enlargement of breast), Impotence, erectile dysfunction
- ❑ In females, irregular menstrual flow

Advise clients to observe for these symptoms and to notify the health provider.

Contraindications/Precautions

- Antifungals are contraindicated in clients with renal dysfunction because of the risk **for nephrotoxicity**.

Interactions Medication/Food Interactions Nursing Interventions/Client Education

- Aminoglycosides (gentamicin, streptomycin, cyclosporine) have additive nephrotoxic risk when used concurrently with antifungal medications.

Avoid use of these antimicrobials when clients are taking amphotericin B due to additive nephrotoxicity risk.

- Antifungal effects of Flucytosine (Ancobon) are potentiated with concurrent use of amphotericin B.

Potentiating the effects of flucytosine allows for a reduction in amphotericin B dosages.

Nursing Administration

- Amphotericin B is highly toxic and should be reserved for severe life-

Systemic infection for mucocutaneous infections

Griseofulvin

- Griseofulvin is a very insoluble fungistatic drug derived from a species of penicillium.
- It is only used in the systemic treatment of dermatophytosis.
- It is administered in a microcrystalline at a dose of 1g per day.
- **Absorption** is improved when it is given with **fatty foods.**
- Nail infections may require therapy for months to allow regrowth of the new protected nail and is often followed by relapse.

Topical anti fungal

Nystatin

- Nystatin is a polyene macrolide much like amphotericin B.
- it is too toxic for parenteral administration and is only used topically
- nystatin is currently available in creams, ointments, suppositories and other forms for application to skin and mucous membrane.
- nystatin is active against most candida species and is most commonly used for suppression of local candida infections.

Anti mycobacterial agents (anti-tuberculosis)

The main mycobacterial infection are the **tuberculosis** and **leprosy.** The treatment of tuberculosis assumes the principle of combination therapy for two main reasons,

- To prevent emergency of resistance (tubercle bacilli develops resistant very fast when monotherapy is used).
- To reduce the rate of spread by reducing bacterial population rapidly.
- For this reason the available tablets contain multiple drugs in a fixed dose combination (FDC).

Anti-TB conti’

Anti TB are divided into two **first line** and **second line**

I. **First line;** this is not a universal principle but depend on local scientific evidence.

The drugs include isoniazid, ethambutol, pyrazinamide and streptomycin.

ii Second line drugs include capreomycin, cycloserine, clarithromycin and ciprofloxacin

Anti TB cont.'

- **First initial phase**: takes two months and three drugs are used concomitantly.
- These includes **Isoniazid (H), Rifampicin (R) Pyrazinamide (Z) plus (Ethambutol or streptomycin)** if resistant organism are suspected. This combination reduces bacterial population rapidly.
- **Continuation phase** takes four months and two drugs are used these are isoniazid and rifampicin.

ISONIAZID

Expected Pharmacological Action

- This medication is highly specific for mycobacteria. Isoniazid inhibits growth of mycobacteria **by preventing synthesis of mycolic acid** in the **c**ell wall.
- **Therapeutic Uses**; Indicated for active and latent tuberculosis
- ***Latent:*** INH only – 6 to 9 months
- ***Active:*** Multiple medication therapy including INH, for a minimum of 6 months
- **The initial phase (induction phase)**; focuses on eradicating the active tubercle bacilli, which will result in non infectious sputum.
- **The second phase (continuation phase)** works toward eliminating any other pathogens in the body.

Isoniazid cont.

- ✓Length of treatment varies and may be as short as 6 months for medication-sensitive tuberculosis (2 months for the initial phase and 4 months for the continuation phase) or as long as 24 months for medication-resistant infections.

Adverse Effects

- **Allergic skin eruptions** are the commonest side effects
- Others are fever , GIT disturbance
- **Peripheral neuropathy (tingling, numbness, burning, and pain resulting from deficiency of pyridoxine, vitamin B6).**

Instruct clients to observe for symptoms and to notify the provider if symptoms occur.

Administer 50 to 200 mg of vitamin B6 daily.

- **Hepatotoxicity (anorexia, malaise, fatigue, nausea, and yellowish discoloration of skin and eyes).**

Instruct clients to avoid consumption of alcohol.

Medication may need to be discontinued if liver function test results are elevated.

Contraindications/Precautions

INH is contraindicated for clients with liver disease.

INH inhibits metabolism of phenytoin, leading to buildup of medication and toxicity.

Ataxia and incoordination may indicate toxicity.

Monitor the client's levels of phenytoin.

Dosage of phenytoin may need to be adjusted based on phenytoin levels.

Concurrent use of alcohol, rifampin, and pyrazinamide increases the risk for hepatotoxicity.

Instruct clients to avoid alcohol consumption.

Monitor liver function.

Interactions cont.’

- ✓Induce liver enzymes,hence affect the metabolism of warfarin, glucocorticoids, narcotics, oral anti diabetes, dapsone and estrogens and oral contraceptives.
- ✓Advice clients on oral contraceptives to change method of family planning or use a back up method.

Rifampicin

- This is one of the most active anti TB .it is also active against gram positive and gram negative bacteria.
- **Mechanism of action:** Rifampin is bactericidal as a result of inhibition **of protein synthesis**.
- **Indications:**

Rifampin is a broad-spectrum antibiotic effective for gram-positive and gram-negative bacteria,

M. tuberculosis, and M. Leprae.

Pharmacokinetics

- ✓Given orally
- ✓Has a wide distribution
- ✓It causes orange tinge coloration to saliva ,sputum, tears, sweat and urine.
- ✓It is excreted in urine and under goes enterohepatic recycling.
- ✓Metabolism is in the liver and the metabolites has anti bacterial activity but poorly absorbed from the gut.
- ✓Half life is one to five hours but reduces during treatment since it induces microsomal enzymes, hence its own metabolism.

Side/adverse effects

i) **Discoloration of body fluids**.

- Inform clients of expected orange color of urine, saliva, sweat, and tears.

ii)Hepatotoxicity (jaundice, anorexia, and fatigue)

- Monitor the client's liver function.
- Inform clients regarding symptoms of anorexia, fatigue, and malaise, and instruct them to notify the provider if symptoms occur.
- Avoid alcohol.

iii) Mild gastrointestinal discomfort associated (anorexia, nausea, and abdominal discomfort.

- Abdominal discomfort is mild and usually does not require intervention

Contraindications/Precautions

-
- Use cautiously in clients with liver dysfunction.

Interactions

Rifampin accelerates metabolism of warfarin (Coumadin), oral contraceptives, protease inhibitors, and NNRTIs (medications for HIV), resulting in diminished effectiveness.

- ✓ Increased dosages of HIV medications may be necessary.
- ✓ Monitor PT (prothrombin time) and INR (international normalized ratio)
- ✓ Clients may need to use alternative form of birth control.

Concurrent use with INH and pyrazinamide increases risk of hepatotoxicity.

- ✓ Instruct clients to avoid alcohol consumption. Monitor liver function.

Attention

Depending on therapeutic intent, effectiveness may be evidenced by:

- Improvement of tuberculosis symptoms such as clear breath sounds, no night sweats, increased appetite, no afternoon rises of temperature
- 3 negative sputum cultures for tuberculosis, usually taking 3 to 6 months to achieve.

Ethambutol

Pharmacodynamics;

- Mechanism of action through inhibiting inhibition of bacterial growth through suppression of RNA synthesis. Resistance emergence occurs rapidly if used on its own.

Pharmacokinetic

- Good absorption from GIT.
- Metabolism is in the liver.
- Excretion in urine.
- It can reach therapeutic concentrated with CSF for tuberculosis.

Side Effects

These are common.

- **Optic neuritis** dose related especially if renal function decreases.

this leads to visual disturbances, **red/ green color blindness** followed by decreased visual acuity.

Monitor color vision in long treatments

Contraindication

- **Patients with known optic neuritis**

Patients who are unable to appreciate and report visual side effects or changes in vision e.g.

- **young children and unconscious patients**

Pyrazinamide

- It is often inactive in neutral PH.

Pharmacodynamics.

- its mechanism of action is unknown but it is tuberculostatic at acidic PH.
- it is very effective against intracellular organism in macrophages since after phagocytosis, in which PH is low.

Pharmacokinetic

- it has good gut absorption .
- it is widely distributed in that it crosses the BBB
- excreted in the kidneys

Dapsone

Pharmacodynamics

- DAPSONE is chemically related to sulphonemides and it acts by inhibiting the enzyme dihydrofolate reluctance hence inhibits folate synthesis.
- Its action is antagonized by PABA. resistance to this drug
- Has increased, hence it ‘s combined with other drugs during treatment.

Pharmacokinetic

- Good oral absorption.
- It under goes enteral hepatic recycling.
- It has a half life of 24 to 48 hours
- it is excreted in feces

Side effects

- ✓Hemolysis of white blood cells .
- ✓Anorexia , nausea and vomiting.
- ✓Fever and allergic dermatitis,
- ✓ neuropathy
- ✓Leprareation where there is exacerbation of lepromatous lesions can occur and a syndrome resembling infectious mononucleosis which can be fatal.

Antiviral agents

- Viruses present a more difficulty problem of chemotherapy than do higher organisms, e.g. bacteria, for they are intracellular parasites that use the metabolism of the host cells.
- Antiviral agents are most active when virus are replicating.
- The earlier the treatment is given the better.
- Apart from primary infections ,viral illness is often the consequences of reactivation of latent virus in the body.
- Patients whose immune system is compromised may suffer particular severe illness.
- Viruses are capable of developing resistance.

Antiviral and antiretroviral cont.....

Drug	viruses	Chemical type	target
Non nucleotide reverse transcriptase inhibitor. (NNRTIs);Nevirapine, Delavirdine.	HIV Virus	Non nucleotide analogue	Reverse transcriptase
protease inhibitors; Saquinavir, Ritonavir, Indinavir, Nelfinavir.	HIV virus	Peptide analogue	HIV protease
Ribavirin	Broad spectrum: HCV, HSV, Measles, Lasa fever, SARS	Triazole carboxamide	RNA mutagen
Amantadine/ Rimantadine	Influenza A strains	Tricyclic amine	Matrix protein/ hemagglutinin
Zanamivir, oseltamivir phosphate	Influenza strains A and B	Neuraminic acid mimetic	Neuraminidase inhibitor
Pleconaril	picornaviruses	Small cyclic	Blocks attachment and coating
Interferons	Hepatitis B and C virus	protein	Cell defense

Drug(	viruses	chemical	Target
vidarabine	herpesvirus	Nucleoside analogue	Virus polymerase
acyclovir	Herpes simplex (HSV)	Nucleoside analogue	Virus polymerase
Ganciclovir and valganciclovir	Cytomegalovirus (CMV)	nucleoside analogue	Virus polymerase
Nucleoside reverse transcriptase inhibitor (NRTI) zidovudine(AZT) didanosine (ddI), zalcitabine (ddC), stavudine (D4T), lamivudine (3TC)	Retroviruses (HIV)	Nucleoside analogue	Reverse transcriptase
Non nucleotide reverse transcriptase inhibitor (NNRTI) nevirapine and delavirdine	HIV virus	Non nucleotide analogue	Reverse transcriptase
Protease inhibitors saquinavir, Ritonavir, indinavir, nelfinavir	HIV virus	Peptide analogue	HIV protease

Acyclovir

Expected Pharmacological Action

- Acyclovir prevents the reproduction of viral DNA and thus interrupts cell replication.

Therapeutic Uses

- Acyclovir is used to treat **herpes simplex** and **varicella-zoste**r viruses

Ganciclovir is used for treatment and prevention of cytomegalovirus (CMV).

- Prevention therapy using ganciclovir is given for clients who have HIV/ AIDS, organ transplants, and other immunocompromised states.
- **Interferon alfa-2b** and **lamivudine** are used to treat hepatitis.
- **Oseltamivi**r is used to treat influenza A and B.
- **Ribavirin** is used to treat respiratory syncytial virus (RSV) and influenza.

Side/Adverse Effects

Acyclovir Phlebitis and inflammation at the site of infusion

✓ Rotate IV injection sites.

✓ Monitor IV sites for swelling and redness.

Nephrotoxicity

✓Administer acyclovir infusion slowly over 1 hr.

✓Ensure adequate hydration during infusion and 2 hr. after to minimize nephrotoxicity by administering IV fluids and increasing oral fluid intake as prescribed.

Mild discomfort associated with oral therapy (nausea, headache, diarrhea)

- Observe for symptoms and notify the provider.

Side/Adverse Effects cont….

Ganciclovir

Granulocytopenia and thrombocytopenia

- Obtain baseline CBC and platelet count.
- Administer granulocyte colony-stimulating factors.
- Monitor WBC, absolute neutrophil, and platelet counts.

Contraindications/Precautions

- Acyclovir should be used cautiously in clients with renal impairment or dehydration, and clients taking nephrotoxic medications.
- Ganciclovir is Pregnancy Risk Category C;
- contraindicated in clients with a neutrophil count below 500/mm3 or platelet counts less than 25,000/mm3, and should be used cautiously in clients with pre-existing low white and platelet counts.

Drug Interactions

Acyclovir

- ❑ Probenecid may decrease elimination of acyclovir.
- ❑ Monitor for medication toxicity.
- ❑Concurrent use of zidovudine may cause drowsiness.
- ❑ Use with caution

Ganciclovir

- ❖Cytotoxic medications may cause increased toxicity.
- ❖ Use together with caution.

Precautions

Acyclovir:

For topical administration, advise clients to put on rubber gloves to avoid transfer of virus to other areas of the body.

Administer IV infusion slowly over 1 hr or longer.

Inform clients to expect symptom relief but not cure.

Instruct clients to wash affected area with soap and water 3 to 4 times/day and to keep the lesions dry after washing.

Advise clients to refrain from sexual contact while lesions are present.

Clients with healed herpetic lesions should continue to use condoms to prevent transmission of the virus.

Precautions

Ganciclovir

Administer IV infusion slowly, with an infusion pump, over at least 1 hr.

Administer oral medication with food.

Administer intraocular for CMV retinitis.

Instruct clients to complete the prescribed course of antimicrobial therapy, even though symptoms may resolve before the full course is completed.

Antiretroviral drugs

- **Antiretroviral** therapy goal is to delay disease progression and to prolong survival by suppressing the replication of the virus.
- Two types of antiretroviral combination are recommended for initial HIV therapy;

1. **First line ;** 1 NNRTI plus 2NRTI.
2. **Second line;** 1PI plus 2 NRTI.
3. protease inhibitors are preserved for second line

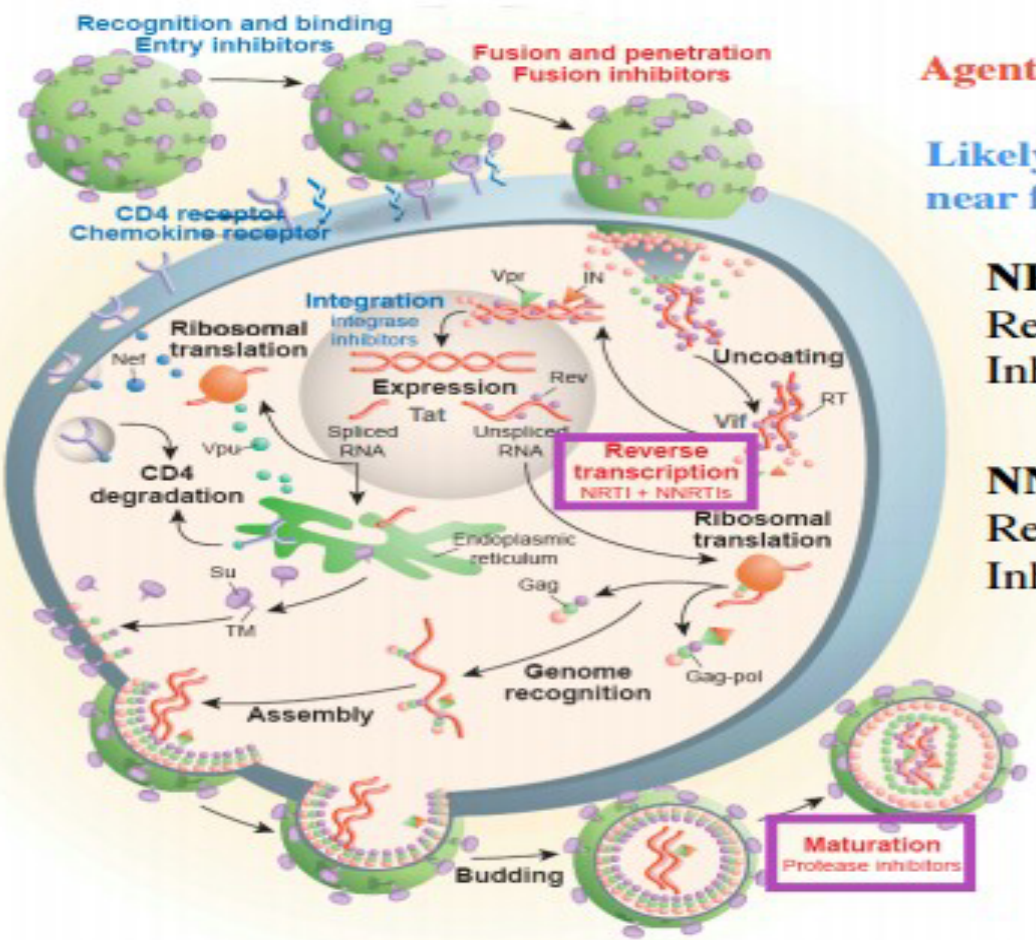
Five goals of ART

1. To reduce amount of HIV virus in the body.
2. Support and restore the immune system.
3. Improve the quality of life.
4. Reduce HIV related illness and deaths.
5. Reduce general risk of transmission.

Mechanism of action of ARVs

1. Block reverse transcriptase to disrupt copying of HIV genetic cord(NRTIs, NNRTIs).
2. Block protease enzyme, preventing maturation of new virions.(PIs).
3. Prevent fusion of HIV with cell membranes (fusion inhibitors).
4. Block CCR5 co receptor (CCR5 antagonist)

HIV life cycle: Targets for antivirals



Agents approved by FDA

Likely to be available in the near future

NRTI: Nucleoside Reverse Transcriptase Inhibitor

NNRTI: Non-nucleoside Reverse Transcriptase Inhibitor

ZIDOVUDINE (RETROVIR)

Other Medications

- ✓Didanosine (Videx)
- ✓ Stavudine (Zerit)
- ✓ Lamivudine (Epivir)
- ✓Abacavir (Ziagen)

Combination Medications:

Abacavir, lamivudine zidovudine (Trizivir)

Abacavir, lamivudine (Epzicom)

Lamivudine, zidovudine (Combivir)

Expected Pharmacological Action

✓ Reduces HIV symptoms by inhibiting **DNA synthesis** and thus viral replication.

Therapeutic Uses

✓Used to treat HIV infection

✓ Route of Administration: Oral, IV

Side/Adverse Effects

Suppressed bone marrow resulting in anemia, agranulocytosis (neutropenia) and thrombocytopenia

- Monitor CBC and platelets. Advise clients that transfusions may be needed.

Lactic acidosis

- Monitor for symptoms of lactic acidosis, such as hyperventilation, nausea, and abdominal pain. Pregnancy increases the risk of lactic acidosis.

Nausea, vomiting, diarrhea

- Clients may take the medication with food to reduce gastric irritation. Monitor fluids and electrolytes.

Hepatomegaly/fatty liver so Monitor liver enzymes

Precautions

Probenecid, valproic acid, and methadone may increase zidovudine.

- Reduce dosage
- Monitor for medication toxicity.

Ganciclovir or medications that decrease bone marrow production may further suppress bone marrow.

- Use together with caution.

Rifampin and ritonavir may reduce zidovudine levels.

- Adjust dosage if needed.

Phenytoin may alter both medication levels.

- Monitor medication levels.

Non-nucleoside reverse transcriptase inhibitors (NNRTI s)

- Select medication: delavirdine (Rescriptor), efavirenz (Sustiva)
- Other Medications: nevirapine (Viramune), etravirine (Intelence)

Expected Pharmacological Action

- NNRTIs act directly on reverse transcriptase to stop HIV reprication

Therapeutic Uses

- Primary HIV-1 infection
- Often used in combination with other antiretroviral agents to prevent medication resistance

Route of administration:

- Oral
- Monitor for rash.

Adverse Effects

Rash, which may become serious and lead to Steven's-Johnson syndrome

- ✓ Monitor for rash.
- ✓Treat with diphenhydramine (Benadryl), if prescribed.
- ✓ Notify the provider for fever or blistering.

Flu-like symptoms, headache, fatigue

- ✓ Monitor for adverse reactions.
- ✓ Encourage rest and adequate oral fluid intake

Contraindications/Precautions

- NNRTIs are Pregnancy Risk Category C.
- These medications are contraindicated in clients with medication hypersensitivity.
- Use with caution in clients who have liver disease.

Precautions

Antacids may decrease absorption of delavirdine.

- Allow 1 hr. between medications.

NNRTIs may increase effects of amphetamines, antihistamines, calcium channel blockers, ergot alkaloids, quinidine, warfarin, and others.

- Monitor for medication toxicity.

Rifampin and phenytoin may cause decrease in levels of delavirdine.

- Do not use together.

Didanosine may reduce both medications' absorption.

Allow 1 hour between medications.

NNRTIs hypotension and changes in vision.

- may cause increase in sildenafil level.
- Monitor for Use together with caution.

Protease inhibitors

Members of this group are;

ritonavir (Norvir)

Saquinavir (Invirase)

Indinavir (Crixivan)

Amprenavir (Agenerase)

Nelfinavir (Viracept)

Mechanism Of Action

Protease inhibitors act against HIV-1 and HIV-2 to alter and inactivate the virus by inhibiting enzymes needed for HIV replication.

Indication

Used to treat HIV infections

Should be used with another antiretroviral medication to reduce medication resistance

Route of administration: Oral

Adverse Effects

- **Diabetes mellitus/hyperglycemia ;** Monitor serum glucose,

Adjust diet and administer anti-diabetic medications as prescribed. Advise clients to monitor for increased thirst and urine output.

- **hypersensitivity reaction;**

Monitor for rash.

Notify the provider if rash develops.

- **Nausea and vomiting;** Take medication with food to reduce GI effects and increase absorption.
- **Elevated serum lipids**

Monitor for hyperlipidemia.

Adjust diet.

- **Thrombocytopenia, leukopenia**

Monitor CBC. Monitor for signs of infection (fever, sore throat). Monitor for bleeding, blood in stool and bruising

Precautions

- Ritonavir may cause these medications to accumulate to toxic levels: Bupropion, carbamazepine, diazepam, lidocaine, prednisone clozapine, lovastatin, simvastatin, alprazolam, and ergotamine.

Avoid concurrent use.

- Ritonavir may increase medication levels of sildenafil, tadalafil, and vardenafil.

Use with caution. Dosages of these medications may need to be reduced.

- Ritonavir decreases levels of ethynyl estradiol in oral contraceptives. Instruct clients to use an alternative form of birth control.

Fusion inhibitors

Enfuvirtide this is the first antiretroviral to target the host cell attachment.

Mechanism of action/pharmacodynamics

- It inhibits fusion of the cellular and viral membranes.

Pharmacokinetic

- It is give by S.C. injection half life is 4hours.

adverse effects

- Limited to mild injection site reactions
- Hypersensitivity and peripheral neuropathy may occur.

Standard 1st line regime for adults in Kenya

- Stavudine (D4T)/Zidovudine (AZT)+ Lamivudine(3TC)+Nevirapine (NVP)

OR

- Stavudine (D4T)/Zidovudine (AZT) +Lamivudine (3TC)+ Efavirenz.

Assignment

Find out the standard 1st line and the 2nd line ART regime in children.

ANALGESICS and NSAIDS)

- Analgesics may be defined as any member or group of drugs used to achieve analgesia, relief from **pain.** They relieve pain without causing any loss of consciousness.
- Analgesics drug works in various ways on the periphery and the CNS.
- NSAIDs are referred to as non narcotic analgesics or non-opioid analgesics.

They differ from opioids in the aspects;

- They are less potent
- Fail to produce drowsiness or CNS depression
- Non additive in nature
- Posses anti inflammatory/antipyretic activities

NSAIDs cont.'

1st generation NSAIDs (COX-1 and COX-2 inhibitors):

- ✓ Aspirin
- ✓ Ibuprofen (Motrin, Advil)
- ✓ Naproxen (Naprosyn)
- ✓ Indomethacin (Indocin)
- ✓ Diclofenac (Voltaren)
- ✓Ketorolac (Toradol)
- ✓ Meloxicam (Mobic)

2nd generation NSAIDs (selective COX-2 Inhibitor):

- ✓ Celecoxib (Celebrex)

Mechanism of action

- ✓Inhibition of prostaglandin synthase, also known as cox — Inhibition of COX-1 can result in decreased platelet aggregation and kidney damage.
- ✓ Inhibition of COX-2 results in decreased inflammation, fever, and pain.

Therapeutic Uses /indication (analgesic , antipyretic, and anti inflammatory)

- ✓ Inflammation suppression.
- ✓ Analgesia for mild to moderate pain, such as with osteoarthritis and rheumatoid arthritis.
- ✓ Fever reduction.
- ✓ Dysmenorrhea.
- ✓ Inhibition of platelet aggregation, which protects against stroke and myocardial infarction. (aspirin)
- ✓The exception of acetaminophen which is an analgesic and antipyretic.

Adverse Effects

- **Gastrointestinal discomfort (dyspepsia, abdominal pain, heartburn, nausea)**
- **Damage to gastric mucosa may lead to GI bleeding and perforation, especially with long-term use. •**
- Advise clients to take medication with food or with a full glass of water or milk.
- Advise clients to avoid alcohol.
- Observe for signs of bleeding (passage of black or dark-colored stools, severe abdominal pain, nausea, vomiting).
- Administer a proton pump inhibitor, such as omeprazole (Prilosec), or an H2 receptor antagonist, such as ranitidine (Zantac) to decrease the risk of ulcer formation. Use prophylaxis agents such as misoprostol (Cytotec) .

Side/adverse effects cont.'

Renal dysfunction (decreased urine output, weight gain from fluid retention, increased BUN and creatinine levels)

- Use cautiously with older adults and clients who have heart failure.
- Monitor I&O and kidney function (BUN, creatinine).

Increased risk of heart attack and stroke (non aspirin NSAIDs)

- Use the smallest effective dose for clients with known cardiovascular disease.
- Salicylism may occur with aspirin. Signs and symptoms include tinnitus, sweating, headache and dizziness, and respiratory alkalosis.
- Advise clients to notify the provider and to stop taking aspirin if symptoms occur.
- Reyer syndrome is rare, but serious in childhood.
- This occurs when aspirin is used for fever reduction in children who have a viral illness, such as chickenpox or influenza
- Advise clients to avoid giving aspirin when a child has a viral illness, such as chickenpox or influenza.

Adverse effects cont....

Aspirin toxicity

- ✓ Aspirin toxicity should be managed as a medical emergency in the hospital.

Therapy includes:

- ✓ Cooling with tepid water.
- ✓Correction of dehydration and electrolyte imbalance with IV fluids.
- ✓ Reversal of acidosis and promotion of salicylate excretion with bicarbonate.
- ✓ Gastric lavage Activated charcoal may also be given to decrease absorption.
- ✓ Hemodialysis may be indicated.

Contraindications for aspirin and other 1st generation NSAIDs include

- Pregnancy (Pregnancy Risk Category D)
- Peptic ulcer disease
- Bleeding disorders such as hemophilia, vitamin K deficiency
- Hypersensitivity to aspirin and other NSAIDs
- Children with chickenpox or influenza (aspirin)
- Use NSAIDs cautiously in older adults, clients who smoke cigarettes, and in clients with H. pylori infection, hypovolemia, asthma, chronic urticaria, and/or a history of alcoholism.
- Celecoxib is contraindicated in clients with allergy to sulfonamides.
- Ketorolac is contraindicated in clients with advanced renal dysfunction
- Use should be no longer than five days because of the risk for kidney damage.
- 2nd generation NSAIDs should be used cautiously in clients who have known cardiovascular disease.

Acetaminophen

Mechanism Of Action;

- Acetaminophen slows the production of prostaglandins in the central nervous system.

Therapeutic Uses

- Analgesic (relief of pain) effect
- Antipyretic (reduction of fever) effects

Adverse Effects

Acute toxicity that results in **liver damage** with early symptoms of nausea, vomiting, diarrhea, sweating, and abdominal discomfort progressing to, **hepatic failure**, **coma** and **death**

- Advise clients to take acetaminophen as prescribed and not to exceed 4 g/day.
- Administer the antidote**, acetylcysteine** (Mucomyst).

Contraindications/Precautions

- Use cautiously in clients who consume three or more alcoholic drinks/day and those taking warfarin (interferes with metabolism).

Drug Interactions

Alcohol increases the risk of liver damage.

- Advise clients about the potential risk of liver damage with consumption of alcohol.

Acetaminophen slows metabolism of warfarin (Coumadin) leading to increased levels of warfarin.

- This places clients at risk for bleeding.
- Instruct clients to observe for signs of bleeding (bruising, petechiae, hematuria).
- Monitor prothrombin time and INR levels and adjust dosages of warfarin accordingly

Opioid analgesics/narcotic analgesics

- Opioids are classified as agonists, agonist-antagonists, and antagonist.

Opioid Agonists

- ❑ morphine sulfate
- ❑ Fentanyl (Sublimaze, Duragesic)
- ❑ Meperidine (Demerol)
- ❑ Methadone (Dolophine)
- ❑ Codeine, oxycodone (OxyContin)

Mechanism of action

- Opioid agonist produce analgesia by binding to specific proteins-coupled receptors that are located in the brain and the spinal cord regions involved in the transmission and modulation of pain

Indication/Therapeutic Uses

- ❑ Relief of moderate to severe pain **(postoperative, myocardial infarction, cancer)**
- ❑ Sedation
- ❑ Reduction of bowel motility
- ❑ Codeine: cough suppression

Route of administration

- Morphine sulfate – Oral, subcutaneous, IM, rectal, IV, epidural, and intrathecal
- Fentanyl (Sublimaze, Duragesic) – IV, IM, transmucosal and transdermal
- Meperidine (Demerol) – Oral, subcutaneous IM, and IV
- Codeine – Oral, subcutaneous IM, and IV
- Methadone (Dolophine) – Oral, subcutaneous, and IM
- Oxycodone (OxyContin) – Oral, rectal
- Hydromorphone (Dilaudid) – Oral, subcutaneous, IM, IV

Adverse Effects (morphine sulphate)

Respiratory depression.

- ✓ Monitor the client's vital signs.
- ✓ Stop opioids if the client's respiratory rate is less than 12/ min, and then notify the provider.
- ✓ Have **naloxone (Narcan)** and resuscitation equipment available.
- ✓ Avoid the use of opioids with CNS depressant medications (barbiturates, benzodiazepines, and consumption of alcohol).

Constipation

- ✓ Increased fluid intake and physical activity.
- ✓ Administer a stimulant laxative, such as Bisacodyl (Dulcolax), to counteract decreased bowel motility, or a stool softener, such as docusate sodium (Colace), to prevent constipation.

Side/ adverse effects cont….

Orthostatic hypotension

- ❑ Advise clients to sit or lie down if symptoms of lightheadedness or dizziness occur.
- ❑ Avoid sudden changes in position by slowly moving clients from a lying to a sitting or standing position.
- ❑ Provide assistance with ambulation as needed.

Urinary retention

- ❑ Advise clients to void every 4 hr.
- ❑Monitor I&O.
- ❑ Assess the client's bladder for distention by palpating the lower abdomen area every 4 to 6 hr. side and adverse effects

Adverse effects cont....

Cough suppression

Advise clients to cough at regular intervals to prevent accumulation of secretions in the airway.

Auscultate the client's lungs for crackles, and instruct clients to increase intake of fluid to liquefy secretions.

Sedation

Advise clients to avoid hazardous activities such as driving or operating heavy machinery.

Biliary colic

Avoid giving morphine to clients who have a history of biliary colic. Use meperidine as an alternative.

Adverse effects cont….

Emesis

- Administer an antiemetic such as promethazine (Phenergan).

Opioid overdose triad of coma, respiratory depression, and pinpoint pupils

- Monitor the client's vital signs.
- Provide mechanical ventilation.
- Administer opioid antagonists, such as naloxone (Narcan) or nalmefene (Revex)

Contraindications/Precautions

- Morphine is contraindicated after biliary tract surgery.
- Morphine is contraindicated for premature infants during and after delivery because of respiratory depressant effects.
- Meperidine is contraindicated for clients with renal failure because of the accumulation of normeperidine, which can result in seizures and neurotoxicity.

Use cautiously with: Clients who have asthma, emphysema, and/or head injuries; infants, and older adults.

Caution

- Clients who have asthma, emphysema, and/or head injuries; infants, and older adult clients (risk of respiratory depression).
- Clients who are pregnant (risk of physical dependence of the fetus).
- Clients in labor (risk of respiratory depression in the newborn and inhibition of labor by decreasing uterine contractions)
- Clients who are extremely obese (greater risk for prolonged side effects because of the accumulation of medication that is metabolized at a slower rate)
- Clients with inflammatory bowel disease (risk of megacolon or paralytic ileus)
- Clients with an enlarged prostate (risk of acute urinary retention)

Opioid Agonist-Antagonist

- Butorphanol (Stadol)
- Nalbuphine hydrochloride (Nubain)
- Buprenorphine hydrochloride (Buprenex)

Expected Pharmacological Action

- These medications act as antagonists on mu receptors and agonists on kappa receptors.

Compared to pure opioid agonists, agonist-antagonists have:

❖ A low potential for abuse causing little euphoria.

❖ In fact, high doses can cause adverse effects (anxiety, restlessness, mental confusion).

❖Less respiratory depression.

- Less analgesic effect

Opioid Agonist- Antagonist Cont……

Indication

- ❑Relief of moderate to severe pain
- ❑Treatment of opioid dependence (buprenorphine)
- ❑ Adjunct to balanced anesthesia
- ❑Relief of labor pain (butorphanol)

Route of administration

- ❖ Butorphanol – IV, IM, intranasal
- ❖Nalbuphine – IV, IM, subcutaneous
- ❖ Buprenorphine – IV, sublingual, epidural

Side Effects

- Abstinence syndrome (cramping, hypertension, vomiting)
- Sedation respiratory depression
- Dizziness
- Increased intracranial pressure, headache

Contraindications/Precautions

- Use cautiously in clients who have a history of myocardial infarction, renal or liver disease, respiratory depression, or head injury, and clients who are physically dependent on opioids.

Drug Interactions

- CNS depressants and alcohol may cause additive effects.
- Use together cautiously.
- Monitor respirations.
- Opioid agonists may antagonize and reduce analgesic effects of the opioid. Do not use concurrently.

Opioid Antagonist

- Naloxone (Narcan) Naltrexone (Re Via, Depade),
- nalmefene (Revex)

Mechanism of Action Opioid antagonists interfere with the action of opioids by competing for opioid receptors. Opioid antagonists have no effect in the absence of opioids.

Therapeutic Uses

Treatment of opioid overdose Reversal of effects of opioids, such as respiratory depression

Reversal of respiratory depression in an infant

Route of administration:

Naloxone- IM, IV, subcutaneous

nalmefene – IV, IM, subcutaneous

Naltrexone – Oral

Opioid antagonist cont.....

Therapeutic Uses

Treatment of opioid overdose Reversal of effects of opioids, such as respiratory depression

Reversal of respiratory depression in an infant

Route of administration:

- Naloxone,
- Nalmefene – IV, IM, subcutaneous
- Naltrexone – Oral

Opioid anti-agonist cont…..

Side Effects

- ❑ Tachycardia and tachypnea
- ❑ Abstinence syndrome (cramping, hypertension, vomiting)
- ❑ Pulmonary edema

Contraindications/Precautions

- ❖ Opioid antagonists are Pregnancy Risk Category B.
- ❖ These medications are contraindicated in clients with opioid dependency.

Adjuvants medication for pain

- Tricyclic antidepressants: amitriptyline (Elavil) – oral/IM
- Anticonvulsants: carbamazepine (Tegretol) – gabapentin (Neurontin) oral
- CNS stimulants: methylphenidate (Ritalin) – oral
- Antihistamines: hydroxyzine (Vistaril) – oral/IM
- Glucocorticoids: dexamethasone (Decadron) – oral, IV, IM
- Bisphosphonates: etidronate (Didronel) – oral
-

Adjuvants medication for pain cont..

- NSAIDs: ibuprofen (Motrin) – oral
- Other Medication: Tricyclic antidepressants: imipramine (Tofranil) – oral
- Anticonvulsants: phenytoin (Dilantin) – oral, IV, IM
- CNS stimulants: dextroamphetamine (Dexedrine) – oral
- Glucocorticoids: prednisone (Deltasone) – oral
- Bisphosphonates: pamidronate (Aredia) – IV
- NSAIDs: ketorolac (Toradol)

Expected Pharmacological Action

✓Adjuvant medications for pain enhance the effects of opioids

Therapeutic Uses

- These medications are used in combination with opioids and cannot be used as a substitute for opioids.
- NSAIDs are used to treat inflammation.
- Tricyclic antidepressants are used to treat depression and neuropathic pain such as cramping, aching, burning, darting, and lancinating pain.
-

Therapeutic Uses cont…

- Anticonvulsants are used to relieve neuropathic pain.
- CNS stimulants augment analgesia and decrease sedation.
- Antihistamines decrease anxiety, prevent insomnia and relieve nausea.
- Glucocorticoids decrease pain from intracranial pressure and spinal cord compression.
- Bisphosphonates manage hypercalcemia and bone pain

ANTI HELMINTHIC

- **Benzimidazole (BZAs)**

These are broad spectrum anthelmintic agents.

Thiabendazole., **Mebendazole** and **Albendazole** have been used extensively for human helminth infections.

- Other drugs are ;**pyrantel pamoate, ivermectin, praziquental, piperazine citrate , benzdiazepines and diethylcarbamazine.**

Indication/uses;

Thiabendazole is active against a wide range of nematodes that infect the GI tract but it clinical use has declined due to its toxicity.

Mebendazole is used for the treatment of intestinal roundworm infections.

Anthelminthic cont…..

- Albendazole is used primarily against a variety of intestinal and tissue nematodes but also against Larva forms of certain cestodes (cysticercosis, hydatidosis)
- Used with **ivermectin** or **diethylcarbamazin**e for control of helminthes.

Anthelminthics mechanism of action

- The **BZAs** inhibit microtubule polymerization by binding to b-tubulin.
- **Mebendazole** and **Albendazole** are highly effective in treating the major infections (ascariasis, enterobiasis, trichuriasis, and hookworm)'

-These drugs are active against both larva and adult stages of the nematodes, and they are ovicidal for ascaris and trichuris .

-Immobilization and death of susceptible GI parasites occur slowly and their clearance from the GI tract may not be complete until several days after treatment.

Albendazole is more effective than mebendazole for strongyloidiasis, cystic hydatid disease caused By Echinococcus Granulosus And Neurocysticercosis

Anthelminthic mechanism of cont….

- The choice of drug depends on specific helminths involved
- Example cestodes infestations e.g. echinococcus granulosus the drugs used are thiabendazole, Albendazole, piperazine citrate, pyrantel pamoate, ivermectin and diethylcarbamazine (hetrazan).

Absorption, fate, and excretion

- **Thiabendazole** is absorbed rapidly after oal ingestion and reaches peak plasma concentration after 1 hour. Most of the drug is excreted in urine.
- **Mebendazole** is rapidly metabolized resulting to low systemic bioavailability.
- **Albendazole** is variably absorbed after oral administration, a fatty meal enhances absorption. It is well distributed into various tissues including hydatid cysts. It excreted in urine.

ANTI PROTOZOA AND ANTIMALARIA

- ✓The common protozoa infection include;
- ✓Amoebiasis ,
- ✓Trypanosomiasis,
- ✓Giardiasis,
- ✓Malaria,
- ✓Cutaneous and visceral leishmaniasis
- ✓ Chagas disease,
- ✓ toxoplasmosis and
- ✓ trichomoniasis

Antimalarial

Examples include; **quinine, Artesunate,chloroquine, mefloquine, proguanil, pyrimethamine/sulfadoxine, tetracycline, doxycycline & minocycline, primaquine, and also artemether-Lumefantrine (coartem)**

- The first line treatment of uncomplicated malaria in Kenya is Artemether-Lumefantrine.
- The second line treatment for uncomplicated malaria in Kenya is dihydroartemisinic-piperaquine (DHA-PPQ)
- This is available in a fixed dose combination with adult tablets containing 30mg/320mg of DHA-PPQ
- Pediatric tablets containing 20mg/160mg of DHA-PPQ

Dosage; Artemether Lumefantrine

WEGHT IN KG	AGE IN YEARS	NUMBER OF TABLETS PER DOSE					
		day 1		day 2		day 3	
		1st dose	8hours	24hours	36hours	48 hours	60 hours
5-14	5/12- 3 years	1	1	1	1	1	1
15-24	3-7 years	2	2	2	2	2	2
25-34	8-11 years	3	3	3	3	3	3
Above 34	Above 12 years	4	4	4	4	4	4

Anti-malaria cont….

- Other anti-malarial drugs for uncomplicated malaria are;
- Amodiaquine plus artesunate
- Mefloquine plus artesunate
- Halofantrine (halfan) .this drug can cause arrhythmias, and is contraindicated in patients with heart disease.

Quinine

✓Quinine is an alkaloid derived from cinchona tree.

Indication

Reserved for severe and complicated malaria.

Pharmacodynamics/mechanism of action

✓It binds to plasmodium DNA to prevent protein synthesis but its exact mode of action remains uncertain.

✓It is used to treat plasmodium falciparum in areas of multiple drug resistant.

Pharmacokinetics

- Quinine is well absorbed in the gut but absorption is delayed by antacids. It can be given via slow IV Infusion.
- Metabolism occurs in the liver, the excretion is in the kidneys.
- It is used for the treat of chloroquine resistant P . falciparum often With Combination Of Pyrimethamine/ Sulfadoxine

Side Effects

- Has a low therapeutic widow and it produces effects in the skeletal muscles and can cause; **GI irritation, renal damage, hemolytic anemia** (rarely)associated with "**black water fever**" in previously sensitized patients.
- Black water fever has a fatality rate of 25% due to intravascular coagulation and renal failure.

Side effects cont…..

- ✓Hypotension
- ✓Hypoglycemia
- ✓Cinchonism

Dosage;

Loading dose IV Quinine 20mg/kg body wt. in 500mls of 5% or 10% dextrose (MAX 1200MG) for 4 hours then 10mg/kg body wt. as intravenous infusion in 500mls of 5% or 10% dextrose to run for 4hrs every 8 hourly (maximum 600mgs)

After 3 IV doses of quinine, one should try to change into oral treatment and treatment should continue for 7 days.

Dosage cont….

- For children loading dose is 20mg /kg body wt. in 15mls/kg of isotonic fluid to run over 4 hours and maintenance dose 10mg/ kg body wtin 10mls /kg of isotonic fluids to run over 4 hours every 12 hourly un til the patient can take orally.
- Oral quinine is given 10mg/kg body wt 8 hourly to complete a total of (parenteral + oral) 7 days.

Prevention of malaria

- Chemoprophylaxis; mefloquine or atovaquone-proguanil or doxycycline.
- Intermittent presumptive treatment (IPT) in recommended for pregnant women in areas of high malaria transmission.
- Current recommended IPT medication is sulphadoxine 500mg , pyrimethamine 25mg given as a dose of 3 tablets.

Amoebicidal drugs

Metronidazole was covered under azoles antibiotics.

SEDATIVES-HYPNOTICS

- ✓Also known as anti **anxiety drugs**
- ✓Sedative hypnotics refers to drugs that depress the **CNS activity, relieve anxiety** and **induce sleep**.
- ✓**Effective Sedatives** (anxiolytic) drug should reduce anxiety and exert a calm effect.
- ✓**Hypnotics** drug should produce drowsiness and encourage the onset and maintenance of a state of sleep.
- ✓All sedative hypnotics cross the **placenta barrier** and may contribute to the **depression neonatal vital function.**
- ✓Sedative-hypnotics are detectable in *breast milk* and may exert depressant effects in the nursing infant.

Classification of Sedative Hypnotics

- **Benzodiazepine**s; clonazepam, diazepam, midazolam, lorazepam, triazolam, flurazepam, alprazolam, chlordiazepoxide.
- **Barbiturates;** phenobarbital, metharbital, thiopental sodium
- **Newer generation**; zopiclodine, zolpidem.
- **Miscellaneous;** chloral hydrate
- **B-adrenoreceptor antagonist;** Flumezanil
- The most commonly used are **benzodiazepines** and **barbiturates** medications.

Pharmacological actions

- ✓Useful predominantly as **anticonvulsants, muscle relaxant and in status epilepticus.**
- ✓Abrupt withdrawal causes precipitation of epileptiform seizures.
- ✓They potentiate analgesics .
- ✓Wide margin of safety
- ✓ Give rise to drug dependency (abuse liability)
- ✓Obliterate moments of sequential events

Pharmacodynamics of benzodiazepines, barbiturates &new hypnotics

- Molecular pharmacology of **GABA** (gamma aminobutyric acid) receptor (GABA is an inhibitory neurotransmitter)
- The benzodiazepine, barbiturates , zolpidem, zaleplon and other drugs bind to molecular component of GABA, a receptor in neuronal membrane in the CNS. improving the symptoms of sleep disturbance, tremors and muscle tension.

Organ level Effects

- **Sedation;** exert calming effects with reduction of anxiety at relatively low doses.
- **Hypnosis;** all sedative hypnotics induce sleep if high enough doses are given.
- **Muscle relaxation**
- **Effects on respiratory and cardiovascular** functions especially on patients with pulmonary disease
- **Anticonvulsant effects e.g**. phenobarbitone
- **anesthesia**, e.g. barbiturates thiopental
- **Tolerance** ; psychological & physiological Dependence

Clinical Indications

- Insomnia
- Sedation and amnesia before and during medical surgical procedures.
- Treatment of epilepsy and seizure state.
- as a component of balanced anesthesia.
- For control of ethanol and other sedative hypnotic withdrawal states.
- For muscle relaxation in specific neural muscular disorders

Direct toxic action

- Relatively low doses may lead to **Drowsiness , impaired judgement, diminished motor skills**. sometimes with impact on driving, working and personal relationship.
- Criminals use BZDs in cases of “date rape” is based on their dose dependent amnestic effects.
- At higher dose toxicity may present as **lethargy or state of exhaustion** or as **gross symptoms** equivalent to those of **ethanol intoxication**.

Benzodiazepines Common Indications

- Most commonly used sedatives hypnotics.

MOA exert their action as the other CNS depressants.

Classification

Short acting e.g. midazolam, triazolam, half life five hours.

Intermediate e.g. lorazepam, oxazepam, clonazepam. Half life five to 24 hours.

Long acting e.g. diazepam, chlordiazepoxide, prazepam. Half life 24 hours.

Side Effects of Benzodiazepines

- Daytime drowsiness, ataxia, rebound insomnia on withdrawal
- The elderly develop blurred vision, tremors , constipation, and anterograde amnesia.
- Respiratory depression which may worsen in COPD
- Decrease BP and heart rate.
- Paradoxical effects in the first 2 weeks of therapy such as hostility, aggression, excitement, antisocial behavior
- cross tolerance with other sedative/hypnotics agents e.g. alcohol/ barbiturates.
- withdrawal symptoms may develop any time after stopping E.G. anxiety, insomnia, GIT disturbance, tinnitus, perceptual disturbance, lack of appetite and perspiration. treat with **flumazenil**

Contraindication

- In pregnancy, shock, acute alcohol intoxication and neonatal withdrawal symptoms, in the elderly and during lactation

Drug interaction

- **Alcohol plus benzodiazepines** cause severe CNS depression.
- **Cimetidine, disulfiram and oral contraceptives** cause increase benzodiazepines effects.
- **Ranitidine** and **theophylline** decrease benzodiazepine effects.

Barbiturates

Include;-

- Mephobarbital (mebaral)
- Pentobarbital (Nembutal)
- Phenobarbital (luminal, solfoton)
- Amobarbital
- Thiopental sodium.

Pharmacological Effects

CNS

- Depression of CNS
- Sedative hypnotic
- Anticonvulsant
- General anesthetic (sodium thiopental)
- Enhance analgesic effect of morphine

Therapeutic Application

- ✓Sedatives
- ✓Hypnotic
- ✓Anticonvulsant
- ✓ pre anesthetic medicament
- ✓Potentiate analgesic activity
- ✓anti epileptic; phenobarbitone, metharbital
- ✓ general anesthesia ;thiopental sodium

Adverse Reaction

- ❑ Acute drug dependence
- ❑ Drug tolerance
- ❑ Withdrawal symptoms

Contraindication

- Renal damage
- Hepatic ailments
- Pulmonary insufficient

Anticonvulsant/seizure /anti epileptic medication

- **Barbiturates**: Phenobarbital (Luminal) , Primidone (Mysoline) amobarbital, metharbital.
- **Hydantoins: phenytoin (Dilantin)**
- **Benzodiazepines:** Diazepam (Valium), Lorazepam (Ativan)
- **Carboxamide**: Carbamazepine (Tegretol, carbatrol) , oxcarbazepine **(Trileptal)**
- **Phenyltriazine**: Lamotrigine (lamictal)
- **Pyrrolidines:** levetiracetam (Keppra)
- **Succinimides**: ethosuximide (zorontin)
- **Miscellaneous:** acetazolamide (Diamox), primidone(mysoline), valproic acid(depakene, Depakote), zonisamide (zonegran)

Mechanism of Action

- Unfortunately the mechanism of seizure activity is not well understood.
- AEDs control seizure disorders by various mechanisms, which include:
- Slowing the entrance of sodium and calcium back into the neuron and, thus extending the time it takes for the nerve to return to its active state.
- Suppressing neuronal firing, which decreases seizure activity and prevents propagation of seizure activity into other areas of the brain.
- Decreasing seizure activity by enhancing the inhibitory effects of gamma butyric acid (GABA

Therapeutic uses

Phenobarbital

- Phenobarbital is used for partial seizures and generalized tonic clonic seizures.
- This medication is not effective against absence seizures.

Phenytoin

- phenytoin effective against all major forms of epilepsy except absence seizures.
- Use IV route for status epilepticus.

Phenytoin is an ant dysrhythmic.

Carbamazepine

Carbamazepine is used for the treatment of partial (simple and complex) seizures, tonic-clonic seizures, bipolar disorder, and trigeminal and glossopharyngeal neuralgias.

Therapeutic use Cont…..

Ethosuximide is only indicated for absence seizures.

Valproic Acid

✓ Valproic acid is used for partial, generalized, and absence seizures; bipolar disorder; and migraine headaches.

Gabapentin

✓Gabapentin is used as a single agent for control of partial seizures.

✓ This medication is also used for neuropathic pain and the prevention of migraine headaches.

Diazepam

Diazepam is used in status epilepticus.

Adverse drug reaction of anti epileptics/ anticonvulsant medication

- Almost all cause undesired effects
- All cross the placenta barrier;
- **Cleft lip, cardiac malformation;** phenobarbitone, phenytoin.
- **Spina bifida**; folate deficiency induced by sodium valproate, phenytoin, phenobarbital

Phenytoin

- This is the oldest non sedative anti seizure drug introduced in 1938.

Mechanism of action

It blocks sodium channels and inhibit the generation of rapidly repetitive action potentials.

Pharmacokinetics

- oral ,IM, IV.

Metabolism;

- Is in the liver.

Side /Adverse Effects of Phenytoin

- ❑CNS effects (nystagmus, sedation, ataxia, double vision, cognitive impairment)
- ❑Monitor for symptoms and notify the provider if symptoms occur.
- ❑ Gingival hyperplasia (softening and overgrowth of gum tissue, tenderness, and bleeding gums)
- ❑Advise clients to maintain good oral hygiene (dental flossing, massaging gums).
- ❑ Skin rash • Stop medication if rash develops.
- ❑ Teratogenic (cleft palate, heart defects)
- ❑ Avoid use in pregnancy..

Side /adverse Effects of Phenytoin

- Cardiovascular effects (dysrhythmias, hypotension)
- Administer at slow IV rate and in dilute solution to prevent adverse CV effects.
- Endocrine and other effects (coarsening of facial features, hirsutism, and interference with vitamin D metabolism)
- Instruct clients to report changes.
- Encourage clients to consume adequate amounts of calcium and vitamin D.

PSYCHOTHEPEUTIC AGENTS

❑These are*Antipsychotics, Antidepressants and Mood Stabilizers*

ANTIDEPRESSANTS

❖ Depression is a mood (affective) disorder and is a widespread problem, ranking high among causes of disability.

❖ Clients starting antidepressant medication therapy for depression need to be advised that symptom relief can take 1 to 3 weeks and possibly 2 to 3 months for full benefits to be achieved. Encourage continued adherence.

❖Clients with major depression may require hospitalization with close observation and suicide precautions until the antidepressant medications reach their peak effect.

Antidepressants Cont…….

Antidepressant mediations are classified into four main groups:

- Tricyclic antidepressants
- Selective serotonin reuptake inhibitors (SSRIs)
- Monoamine oxidase inhibitors (MAOIs)
- Atypical antidepressant

a)Tricyclic antidepressant;

Amitriptyline (Elavil), Imipramine (Tofranil), Doxepin (Sinequan), Nortriptyline (Aventyl), Amoxapine (Asendin),

Trimipramine (Surmontil)

Mechanism of Action of Antidepressants

- ✓Tricyclic antidepressant medications block reuptake of **norepinephrine** and **serotonin** in the synaptic space, thereby intensifying the effects of these neurotransmitters.

Therapeutic Uses

- ✓ Depression
- ✓Chronic pain
- ✓ Childhood Enuresis
- ✓Obsessive compulsive disorders (clomipramine)

Side Effects of Antidepressants

Sedation

Anticholinergic Effects

✓ Dry mouth

✓Blurred vision

✓ Photophobia

✓ Urinary hesitancy or retention

✓ Constipation

✓Seizures and impotence

- older patients; dizziness, postural hypotension, constipation, delayed micturition, edema, muscle tremors.

Tricyclic Overdose

- ❑Lethal 70 to 80 percent die before reaching the hospital
- ❑CNS and cardiovascular systems are affected.
- ❑death results from seizures and dysrhythmias

No specific antidote

- ✓Decrease drug absorption with activated charcoal
- ✓Speed elimination by alkalinizing urine
- ✓Manage seizures and dysrhythmias
- ✓Basic life support

Drug Interactions

- Antipsychotics and steroids may inhibit TCAs
- Aspirin may displace TCAs from binding site
- TCAs and alcohol potentiate the effects of each other hence death due to severe respiratory distress.

Monoamine Oxidase Inhibitors (MAOI s)

- Phenelzine (Nardil)
- Isocarboxazid (Marplan)
- Tranylcypromine (Parnate)
- Selegiline (Emsam) – transdermal MAOI

Mechanism of action

- MAOIs inhibit the MAO enzyme system in the CNS.
- Amines (**Norepinephrine**, **Dopamine** And **Serotonin)** resulting in higher levels in the brain to transmit impulses.

Therapeutic use

- ✓Highly effective considered second line treatment for depression not responsive to cyclics.
- ✓Atypical depression
- ✓Bulimia nervosa
- ✓Obsessive compulsive disorders (OCD)

Side effects

Few side effects most common; **orthostatic hypotension.**

Tachycardia, dizziness, insomnia, anorexia, blurred vision, palpitation, drowsiness, headache, nausea, impotence

MAOIs overdose

• Symptoms appear 12 hours after ingestion.

these are; tachycardia, circulatory collapse, seizure, coma.

Treatment ;

- gastric lavage
- Urine acidification
- hemodialysis

Maois Hypertensive Crisis And Tyramine

- Ingestion of food/drinks with amino acid **tyramine** leads to hypertensive crisis, which may lead to cerebral hemorrhage, stroke, coma, or death
- Avoid foods that contain tyramine;
- Aged mature cheese
- Smoked/pickled or aged meat, fish, poultry(herring ,sausages, corned beef, salami, pepperoni).
- Red wine(chianti, sherry, vermouth)
- Italian broad beans (fava).

Contraindications/Precautions

- ✓ MAOIs are Pregnancy Risk Category C.
- ✓These medications are contraindicated in clients taking SSRIs and in those with pheochromocytoma, heart failure, cardiovascular and cerebral vascular disease, and severe renal insufficiency.
- ✓ Use cautiously in clients with diabetes and seizure disorders or those taking TCAs.
- ✓ Transdermal selegiline is contraindicated for clients taking carbamazepine (Tegretol) or oxcarbazepine (Trileptal), which may increase blood levels of the MAOI.

Selective Serotonin Reuptake Inhibitors (SSRIs)

- ❑Fluoxetine (Prozac)
- ❑Citalopram (Celexa)
- ❑Escitalopram oxalate (Lexapro)
- ❑Paroxetine (Paxil)
- ❑Sertraline (Zoloft)

Pharmacodynamics

- ✓SSRI inhibit the reuptake of only serotonin at the part of the amine pump that is specifically for reuptake of serotonin.
- ✓This explains why these drugs have lesser unwanted effects compared to TCAs.
- ✓ the drug of choice for Depression.

Therapeutic Uses

- ❑ Major depression
- ❑Obsessive compulsive disorders (OCD)
- ❑Bulimia nervosa
- ❑ Premenstrual dysphoric disorders
- ❑ Panic disorders
- ❑ Posttraumatic disorder (PTSD)

Pharmacokinetics

- SSRIs are well absorbed orally
- Wide distribution and half life of fifteen to 24 hour but fluoxetine has a half life of 24 to ninety six hours.
- They achieve effects within 2 to 4 weeks.
- **Paroxetine** and **fluoxetine** are not used with TCAs since they inhibit TCA hepatic metabolism
- **Unwanted effects**

This include nausea and vomiting, diarrhea, agitation, anorgasmia priapism.

Drug interaction

- MAOIs, TCAs, and St. John's wort increase the risk of serotonin syndrome.
- Fluoxetine can displace warfarin (Coumadin) from bound protein and result in increased warfarin levels.
- Fluoxetine can increase the levels of tricyclic antidepressants and lithium.
- Fluoxetine suppresses platelet aggregation and thus increases the risk of bleeding when used concurrently with NSAIDs and anticoagulants.

Second Generation Antidepressants

Newer

- Fewer side effects than tricyclic but not superior in overall efficacy or onset of action.

Examples are

- Trazodone,
- Bupropion
- Duloxetine

Mechanism of Action

- selective inhibition of serotonin uptake
- Advantage over tricyclic and MAOIs little or no effect on cardiovascular system.

Therapeutic uses

Depression, bipolar affective disorders, obesity, eating disorders, obsessive compulsive disorders, panic attacks, myoclonus, treatment for various substance abuse problems (bupropion is used for smoking cessation treatment)

Side Effects

- **CNS;** headache, dizziness, nervousness, insomnia, fatigue and tremors.
- **GI;** nausea, diarrheal, constipation, dry mouth, sweating, sexual dysfunction .

ANTIPSYCHOTIC/ TRANQUILIZERS/NEUROLEPTICS

- Classification of neuroleptic is based on chemical structure or severity of resulting unwanted effects.
- Based on unwanted effect;

Conventional (typical, first generation)

Examples;

Chlorpromazine, haloperidol, and fluphenazine

Newer (atypical, second generation)

Example; clozapine, loxapine, asenapine, olanzapine, quetiapine, paliperidone, risperidone, sertindole.

Classification cont.'

- The distinction between typical and atypical neuroleptic is not clear but rest on ; receptor profile , incidence of extrapyramidal effects which are less in the atypical group, efficacy in treatment and efficacy in negative symptoms.

Classification according to chemical structures;

Phenothiazines; chlorpromazine 100 to 1500mg , trifluoperazine, fluphenazine 1 to 10 mg

Butyrophenones; haloperidol 2 to 20mg

Dibenzodiazepine; clozapine 25 to 900mg

Thienobenzodiazepines; olanzapine

Thioxanthene's; flupentixol 6 to 18mg

Benzisoxazole; risperidone 1to 12mg

Pharmacodynamics

- ✓They act by blocking the dopamine receptor.

Indication

- ✓Treatment of acute and chronic psychosis
- ✓ Schizophrenia
- ✓ Bipolar disorders (primarily the manic phase)
- ✓Tourette's syndrome
- ✓ Delusional and schizoaffective disorders
- ✓Dementia
- ✓Prevention of nausea/vomiting through blocking of dopamine in the chemoreceptor trigger zone of the medulla
- ✓hiccups

Side Effects Typical Antipsychotic

- Extrapyramidal effects (dystonia, parkinsonism, tardative dyskinesia)
- Anticholinergic effects; (dry mouth, blurred vision, urinary retention, constipation and impotence)
- Cardiovascular effects; tachycardia, arrhythmias, postural hypotention
- Galactorrhea,
- gynecomastia

Side Effect Atypical Antipsychotics

- **Clozopine**; weight gain, agranulocytosis
- **Risperidone**; insomnia anxiety, agitation
- **Olanzapine**; weight gain, dizziness, sedation, anticholinergic effect

Mood Stabilizers

lithium carbonate

Expected Pharmacological Action

Lithium produces neurochemical changes in the brain, including serotonin receptor blockade.

There is evidence that the use of lithium can show a decrease in neuronal atrophy and/or an increase in neuronal growth.

Therapeutic Uses

- Lithium is used in the treatment of **bipolar disorders.** Lithium controls episodes of **acute mania**, helps prevent the return of mania or depression, and decreases the incidence of suicide.
- Other uses:
- Alcoholism
- Bulimia
- Schizophrenia

Pharmacokinetics

- **Absorption** :rate and extent vary with dose form. absorption is complete within hours of oral use.
- **Distribution** :wide distribution in the body, concentration in thyroid gland, bone and brain tissue exceed serum levels.
- **Metabolism** :not metabolized
- **Excretion** : excreted unchanged in urine. Half lif18 hours (adolescence)to 3 hour (elderly).
- **Dosage adults** :300mg to six hundred mg up to q.i.d increasing to achieve optimal dosage.

Adverse reaction

- Gastrointestinal distress (nausea, diarrhea, abdominal pain).
- Fine hand tremors that can interfere with purposeful motor skills and can be exacerbated by factors such as stress and caffeine.
- Polyuria, mild thirst.
- Weight gain
- Renal toxicity
- Goiter and hypothyroidism with long-term treatment Brady dysrhythmia, hypotension, and electrolyte imbalances .

Contraindications/Precautions

- Lithium is Pregnancy Risk Category D. This medication is teratogenic, especially during the first trimester.
- Discourage clients from breastfeeding if lithium therapy is necessary.
- Use cautiously in clients with renal dysfunction, heart disease, sodium depletion, and dehydration

Medication/Food Interactions

- Sodium is excreted with the use of diuretics. Reduced serum sodium decreases lithium excretion, which can lead to toxicity.
- Concurrent use of NSAIDs (ibuprofen [Motrin] and celecoxib [Celebrex]) will increase renal reabsorption of lithium, leading to toxicity.
- Avoid use of NSAIDs.

Use aspirin as a mild analgesic .

- Anticholinergics (antihistamines, tricyclic antidepressants) can induce urinary retention and polyuria, leading to abdominal discomfort
- Advise clients to avoid medications with anticholinergic effects. rt.

Precaution during Administration

- Monitor plasma lithium levels while undergoing treatment. At initiation of treatment, monitor levels every 2 to 3 days and then every 1 to 3 months. Lithium blood levels should be obtained in the morning, usually 12 hr. after the last dose.
- During initial treatment of a manic episode, levels should be between 0.8 to 1.4 mEq/L.
- Maintenance level range is between 0.4 to 1.0 mEq/L.
- Plasma levels > 1.5 mEq/L can result in toxicity.
- Care for clients who have a toxic plasma lithium level in an inpatient setting and provide supportive measures. Hemodialysis may be indicated.
- Advise clients that effects begin within 7 to 14 days.

Precaution during Administration cont….

- ✓Advise clients to take lithium as prescribed. Lithium must be administered in 2 to 3 doses daily due to a short half life. Taking lithium with food will help decrease GI distress.
- ✓ Encourage clients to adhere to laboratory appointments needed to monitor lithium effectiveness and adverse effects. Emphasize the high risk of toxicity due to the narrow therapeutic range.
- ✓Provide nutritional counseling. Stress the importance of adequate fluid and sodium intake.
- ✓ Instruct clients to monitor for signs of toxicity and when to contact the provider. Clients should stop taking medication and seek medical attention if experiencing diarrhea, vomiting, or excessive sweating.

Other mood stabilizing drugs

- Carbamazepine (Tegretol)
- Valproic acid (Depakote)
- Lamotrigine (Lamictal) Purpose

Expected Pharmacological Action:

AEDs help treat and manage bipolar disorders by various mechanisms, which include:

- Slowing the entrance of sodium and calcium back into the neuron and, thus extending the time it takes for the nerve to return to its active state.
- Potentiating the inhibitory effects of gamma butyric acid (GABA)
- Inhibiting glutamic acid (glutamate) which in turn suppresses CNS excitation

Therapeutic Uses

- Treatment of manic and depressive episodes, prevention of relapse of mania and depressive episodes.
- Especially useful for clients with mixed mania and rapid cycling bipolar disorders.

CNS STIMULANTS

MEDICATION	SHORT ACTING	INTERMEDIATE ACTING	LONG ACTING
Methylphenidate	Ritalin, Methylin	Ritalin SR, Methylin ER	ethylin ER Ritalin LA, Concerta, Daytrana (transdermal)
Dexmethylphenidate	Focalin		
Dextroamphetamine	Dexedrine		Dexedrine Spansule
Amphetamine mixture	Adderall		Adderall-XR

CNS Stimulants Cont…..

Expected Pharmacological Action **:**

These medications raise the levels of norepinephrine, serotonin, and dopamine into the CNS.

Therapeutic Uses:

- ADHD (Attention Deficit Hyperactivity Disorder)
- Conduct disorder

Side Effects

- CNS stimulation (insomnia, restlessness)
- Weight loss
- Cardiovascular effects (dysrhythmias, chest pain, high blood pressure) • These medications may increase the risk of sudden death in clients with heart abnormalities.
- Development of psychotic symptoms such as hallucinations, paranoia Withdrawal reaction.
- Hypersensitivity skin reaction to transdermal methylphenidate (hives, papules)

Contraindications/Precautions

- These medications are contraindicated in clients who have a history of drug abuse, cardiovascular disorders, severe anxiety, and psychosis.

Medication/Food Interactions:

Concurrent use of MAOI s may cause hypertensive crisis.

Concurrent use of caffeine may increase CNS stimulant effects.

Methylphenidate inhibits metabolism of phenytoin (Dilantin), warfarin (Coumadin), and phenobarbital, leading to increased serum levels.

OTC cold and decongestant medications with sympathomimetic action can increase CNS stimulant effects.

MUSCLE RELAXANT/ NEUROMUSCULAR BLOCKING AGENTS

- Neuromuscular blocking agents have various uses including assisting with:
- sedation during general anesthesia,
- control of seizures during electroconvulsive therapy,
- suppression of gag reflex during endotracheal intubation.
- Medications include **succinylcholine (Anectine)** and **vecuronium (Norcuron)**

Anti -Parkinson's drugs

Neuromuscular Agents Cont…..

Muscle relaxants and antispasmodic agents can affect both the central and peripheral nervous systems.

- These agents are used with spasticity related to muscle injury, cerebral palsy, spinal cord injury, and multiple sclerosis.
- Agents include **diazepam** (Valium), **baclofen** (Lioresal), and **dantrolene** (Dantrium).
- **Bethanechol (Urecholine),** a muscarinic agonist, is used for urinary retention.
- **Oxybutynin (Ditropan),** a muscarinic antagonist, is used for neurogenic bladder

Muscle relaxant/ Neuromuscular Blocking Agents cont.'

Depolarizing neuromuscular blocker: succinylcholine (Anectine)

Nondepolarizing neuromuscular blockers: pancuronium (Pavulon)

Other Medications:

Nondepolarizing neuromuscular blockers: atracurium (Tracrium), Vecuronium (Norcuron)

Expected Pharmacological Action

Neuromuscular blocking agents block acetylcholine (ACh) at the neuromuscular junction, resulting in muscle relaxation and hypotension. They do not cross the blood-brain barrier, so complete paralysis can be achieved without loss of consciousness or decreased pain sensation.

Neuromuscular Agents Cont…..

Therapeutic Uses

- Neuromuscular blocking agents are used as adjuncts to general anesthesia to promote muscle relaxation.
- These agents are used to control spontaneous respiratory movements in clients receiving mechanical ventilation.
- These agents are used as seizure control during electroconvulsive therapy.
- Neuromuscular blocking agents are used during endotracheal intubation and endoscopy

Side effects

- Respiratory arrest from paralyzed respiratory muscles
- Hypotension
- Low pseudo cholinesterase activity can lead to prolonged apnea
- Signs of malignant hyperthermia include muscle rigidity accompanied by increased temperature, reaching levels as high as 43° C (109.4° F).
- After 12 to 24 hr. postoperative, clients may experience muscle pain in the upper body and back.
- Hyperkalemia

Drug interaction

General anesthetics are often used concurrently in surgery.

- Dosage of tubocurarine should be reduced to prevent extreme neuromuscular blockade.

Aminoglycosides and tetracyclines can increase the effects of neuromuscular blockade.

- Take complete medication history of clients who are to receive neuromuscular blockade.

Neostigmine and other cholinesterase inhibitors increase the effects of depolarizing neuromuscular blockers, such as succinylcholine.

- Monitor clients during neuromuscular blockade reversal after surgery

LOCAL ANAESTHETICS

- local anesthetic bind reversibly to a specific receptor site within the pore of the sodium channels in nerves and block ion movement when applied locally to nerve tissues in appropriate concentration.
- Local anesthetic can act on any part of the nervous system, on every type of nerve fibers, reversibly blocking the action potentials responsible for nerve conduction.
- Thus a local anesthetic in contact with a nerve trunk can cause both sensory and motor paralysis in the area innervated.

Mechanism of action

- Local anesthetic block conduction by decreasing or preventing the large transient increase in the permeability of excitable membranes.
- This action is due to direct interaction with voltage gated sodium channels.
- As the anesthetic action progressively develops in the nerve , the threshold for electrical excitability increase. The rate of rise of the action potential also declines, impulse conduction slows, and nerve conduction eventually fails.

Local anesthetics

Drug	Duration of action
lidocaine	medium
Bupivacaine (Marcaine),levobupivacaine (chirocaine)	long
Ropivacaine (naropin)	long
Mepivacaine (carbocaine, isocaine)	medium
articaine	medium
Cocaine	medium
benzocaine	Surface use only
Tetracaine (pontocaine)	long

Neuromuscular agents

The action of non depolarizing muscle relaxant is antagonized, once muscle paralysis is no longer desired with an acetylcholinesterase inhibitor such as **neostigmine** or **edrophonium.**

Skeletal Muscle Relaxants

Succinylcholine

- Succinylcholine mimics ACh by binding with cholinergic receptors at the neuromuscular junction. This agent fills the cholinergic receptors, preventing ACh from binding with them, and causes sustained depolarization of the muscle, resulting in muscle paralysis.

Reversal agent: Pseudo cholinesterase enzyme

- **Pancuronium, atracurium, vecuronium**
- These agents block ACh from binding with cholinergic receptors at the motor end plate. Muscle paralysis occurs because of inhibited nerve depolarization and skeletal muscle contraction.

General Anesthetics

- General anesthetics depress the CNS sufficiently to permit surgery and other noxious or unpleasant procedures.
- Gas have a low therapeutic indices and are require great care in administration.
- The consideration of patients age, associated medical condition and medication use is important.
- The physiological state induced by general anesthesia include; **analgesia**, **amnesia, loss of consciousness**, inhibition of s**ensory** and **autonomic reflexes**, and **skeletal muscle relaxation.**

a)Parenteral anesthetics

Pharmacokinetic principle

- After a single intravenous bolus these drugs preferentially partition into the highly perfused and lipophilic tissues of the brain and the spinal cord where they produce anesthesia within a single circulation.
- Blood levels falls rapidly, resulting in drug redistribution out of the cns back into the blood.
- The anesthetics then perfuse into less perfused tissues such as muscle and viscera , and at a slower rate into the poorly perfused but very hydrophobic adipose tissue.

Parenteral Anesthetics

- **Thiopental** and **Propofol** are the two most commonly used parenteral agents.
- **thiopental** has a long established track record of **safety.**
- **Propofol** is advantageous for procedures where **rapid return** to a preoperative mental status is desirable.
- **Etomidate** usually is reserved for patients at risk for **hypotension** and /**myocardial ischemia**
- **Ketamine** is best suited for patients with **asthma**, **children** undergoing short ,painful procedures

Pharmacological characteristics of parenteral anesthetics (IV)

DRUG	INDUCTION AND RECOVERY	COMMENTS
etomidate	Rapid onset and moderate fast recovery	Provides cardiovascular stability, causes decreased steroidal genesis and involuntary muscle movement
ketamine	Moderate onset and recovery	Causes cardiovascular stimulation, increase cerebral blood flow and emergence reaction that impair recovery
midazolam	Slow onset and recovery; flumazenil reversal available	Provides cardiovascular stability and marked amnesia, used in balanced anesthesia and conscious sedation.
Propofol	Rapid onset and recovery	Used in induction and maintenance can cause hypotension ,has useful antiemetic action.
thiopental	Rapid onset and recovery (bolus dose) slow recovery following infusion.	Standard induction agent, causes cardiovascular depression, avoid in porphyria's
fentanyl	Slow onset and recovery. Naloxone reversal available	opioid used in balanced anesthesia and conscious sedation produces marked analgesia

Inhalation Anesthetics

- They have a low safety margin.
- The selection of inhalation anesthetic is often marching a patient pathophysiology with drug side effects.
- The inhalation anesthetics also vary widely in their physical properties, which govern the pharmacokinetics of the inhalation agents
- They produce a rapid induction of anesthesia and a rapid recovery following discontinuation.
- Examples are: **nitrous oxide, halothane,** desflurane, sevoflurane, enflurane, and methoxyflurane.

Side effect of Anesthetics

- Hemodynamic effect e.g. decrease in systemic arteria BP.
- respiratory effects; elimination of both ventilatory drive and reflex that maintain airway patency, gag reflex is lost, no cough stimulus, lower esophageal sphincter tone is reduced.
- Hypothermia, nausea and vomiting.

Other Emergence Postoperative effects

- Hypotension and tachycardia,
- myocardial ischemia,
- post anesthesia shivering, (give small dose of **meperidine** 12 mg lowers the shivering triggers temperature.
- Airway obstruction
- Respiratory suppression
- Hypoxemia may occur
- Negative pressure pulmonary edema may occur due to strong inspiratory efforts against a closed glottis
- pain control can be complicated
- These emergence phenomena can be greatly reduced when opioids are employed as part of the intraoperative regimen

CVS: DIURETICS

- Diuretics are drugs that increase the rate of urine flow; clinically useful diuretics also increase the rate of excretion of sodium and accompanying anion chloride.
- Most clinical application of diuretics aim to reduce extracellular fluid volume by decreasing total sodium chloride volume.
- diuretics alter excretion of sodium and also may modify handling of other cations(potassium, hydrogen and magnesium) anions (chloride, bicarbonate, hydrogen phosphate), and uric acid.

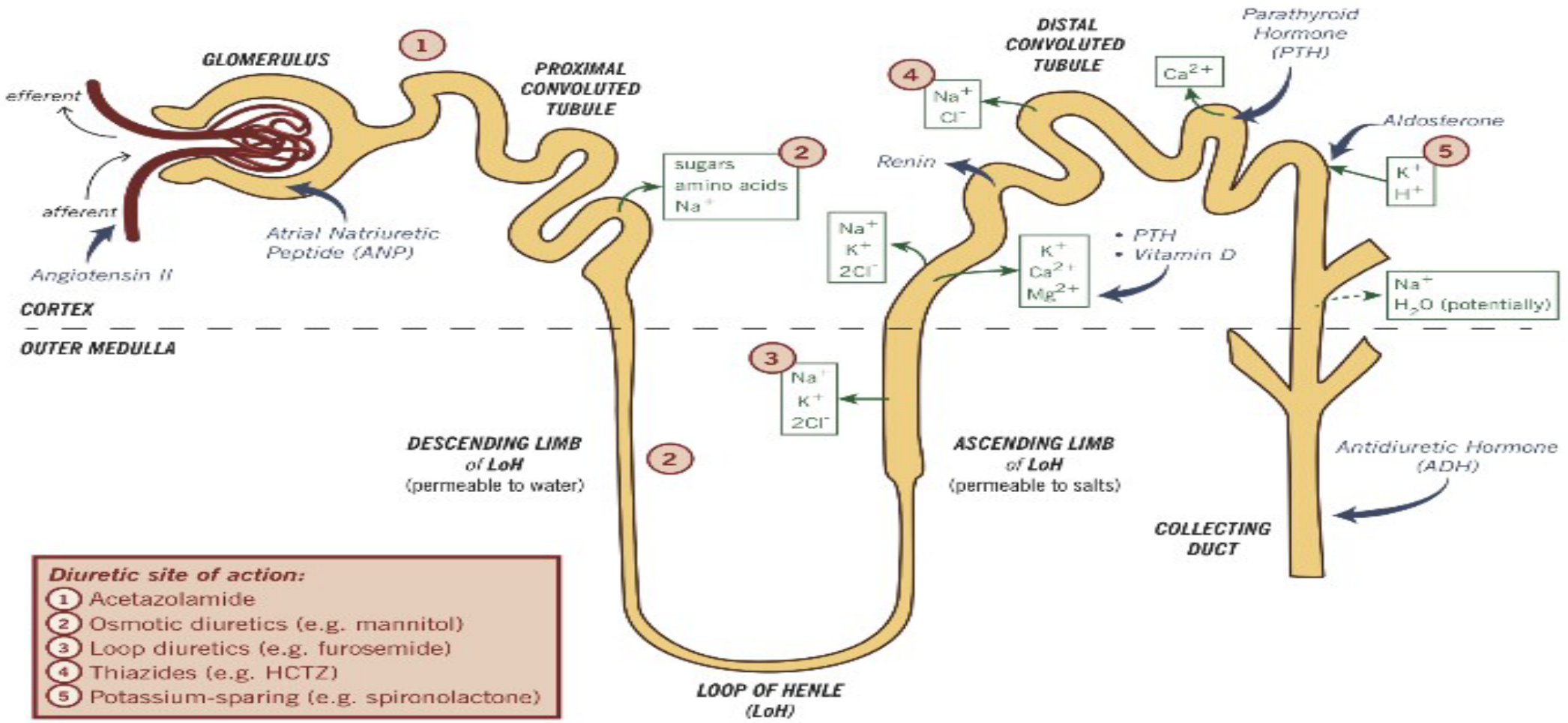
Clinical Pharmacology of Diuretics

- **Edematous** state :in heart failure, kidney disease and in renal failure.
- **Non edematous state :** in hypertension, nephrolithiasis hypercalcemia.

Classification of diuretics

- *Loop Diuretics* : furosemide
- *Thiazide Diuretics* : hydrochlorothiazide
- *Potassium Sparing diuretics* : spironolactone
- *Osmotic Diuretic* : mannitol
- *Carbonic Anhydrase Inhibitors* : acetazolamide (DIAMOX)

Hormones Acting on the Nephron / Diuretics and Their Site of Action



Diuretic site of action:

1. Acetazolamide
2. Osmotic diuretics (e.g. mannitol)
3. Loop diuretics (e.g. furosemide)
4. Thiazides (e.g. HCTZ)
5. Potassium-sparing (e.g. spironolactone)

a)High Ceiling Loop Diuretics

Furosemide (Lasix)

Other Medications:

- ❑Ethacrynic acid (Edecrin)
- ❑ Bumetanide (Bumex)
- ❑ Torsemide (Demadex)

Expected Pharmacological Action

- ❑High ceiling loop diuretics work in the **ascending limb of loop of Henle** to:
- ❑ Block reabsorption of sodium and chloride and to prevent reabsorption of water, Cause extensive diuresis even with severe renal impairment.

Therapeutic Uses of Furosemide (Lasix)

- High ceiling loop diuretics are used when there is an **emergent** need for rapid mobilization of fluid such as:
- Pulmonary edema caused by heart failure
- Conditions not responsive to other diuretics such as edema caused by **liver, cardiac, or kidney disease; hypertension**
- These medications may also be used to treat **hypercalcemia** related to kidney stone formation.
- Route of administration: **Oral, IV, IM.**

Side Effects

- Dehydration, hyponatremia, hypochloremia.
- Hypotension
- Ototoxicity (transient with furosemide and irreversible with ethacrynic acid)
- Hypokalemia (K+ less than 3.5 mEq/L
- Other adverse effects (hyperglycemia, hyperuricemia, and decrease in calcium and magnesium levels)
- **Contraindications/Precautions ;**Pregnancy Risk Category C , Avoid using these medications during pregnancy unless absolutely required. Use cautiously in clients who have diabetes and/or gout

Drug Interaction

- Digoxin (Lanoxin) toxicity can occur in the presence of hypokalemia.
- Concurrent use of antihypertensive can have additive hypotensive effect.
- Hyponatremia can lead to decrease in lithium carbonate excretion, which may lead to toxicity.
- NSAIDs reduce diuretic effect.

Precautions During Administration

- Obtain the client's baseline data to include orthostatic blood pressure, weight, electrolytes, and location and extent of edema.
- Weigh clients at the same time each day; usually upon awakening.
- Monitor the client's blood pressure and I&O.
- Avoid administering the medication late in the day to prevent nocturia. Usual dosing time is 0800 and 1400.
- Administer furosemide orally, IV bolus dose, or continuous IV infusion. Infuse IV doses at 20 mg/min or slower to avoid abrupt hypotension and hypovolemia.
- If potassium level drops below 3.5 mEq/L, clients should be placed on a potassium supplement.

Precautions During Administration Cont…

- If the medication is used for hypertension, teach clients to self-monitor blood pressure and weight by keeping a log.
- Advise clients to get up slowly to minimize postural hypotension. If faintness or dizziness occurs, instruct clients to sit or lie down.
- Teach clients to report significant weight loss, lightheadedness, dizziness, GI distress, and/ or general weakness to the provider.
- Encourage clients to consume foods high in potassium, such as avocados and strawberries.
- Instruct clients with diabetes to monitor for elevated blood glucose levels.
- Instruct clients to observe for signs of low magnesium levels such as muscle twitching and tremors.

b)Thiazide Diuretics

- Hydrochlorothiazide (Hydrodiuril)

Other Medications:

- Chlorothiazide (Diuril)
- Methyclothiazide (Enduron)

Thiazide-type diuretics:

- indapamide (Lozide, Lozol)
- chlorthalidone (Hygroton)
- metolazone (Zaroxolyn)

Mechanism of Action

Expected Pharmacological Action

- ❖ Thiazide diuretics work in the early distal convoluted tubule to:
- ❖ Block the reabsorption of sodium and chloride, and prevent the reabsorption of water at this site
- ❖ Promote diuresis when renal function is not impaired

Therapeutic Uses

- ❑ Thiazide diuretics are often the medication of first choice for essential hypertension.
- ❑ These medications may be used for edema of mild-to-moderate heart failure and liver and kidney disease.

Side/Adverse Effects

- Dehydration
- Hypokalemia (K+ less than 3.5 mEq/L)
- Hyperglycemia

Medication/Food Interactions

- Digoxin (Lanoxin) toxicity can occur in the presence of hypokalemia
- Antihypertensive have additive hypotensive effects. Monitor the client's blood pressure.
- Hyponatremia can lead to decrease in lithium (Eskalith) excretion, which may lead to toxicity.
- NSAIDs reduce diuretic effect

Precautions During Administration

- Chlorothiazide may be administered orally and IV, all others can only be given orally.
- Obtain the client's baseline data to include orthostatic blood pressure, weight, electrolytes, and location and extent of edema.
- Monitor the client's potassium levels
- Instruct clients to take the medication first thing in the morning; if twice-a-day dosing is prescribed, be sure the second dose is taken by 1400 to prevent nocturia.
- Encourage clients to consume foods high in potassium and maintain adequate fluid intake (1,500 mL per day, unless contraindicated).
- If GI upset occurs, clients should take the medication with or after meals. ●
- Alternate-day dosing can decrease electrolyte imbalance

c)Potassium-Sparing Diuretics

Spironolactone (Aldactone)

Other Medications:

t\Triamterene (Dyrenium), amiloride (Midamor)

Expected Pharmacological Action

Potassium-sparing diuretics block the action of aldosterone (sodium and water retention), which results in potassium retention and the secretion of sodium and water.

Therapeutic Uses

- Potassium-sparing diuretics are combined with other diuretics for potassium-sparing effects.
- Potassium-sparing diuretics are used for heart failure.
- In primary hyperaldosteronism, potassium-sparing diuretics block actions of aldosterone.

Route of administration: Oral

Side/Adverse Effects;

- Hyperkalemia (K+ greater than 5.0 mEq/L)
- Endocrine effects (impotence in male clients; irregularities of menstrual cycle in female clients).

Contraindications/Precaution

- Do not administer to clients who have hyperkalemia.
- Potassium-sparing diuretics are contraindicated in clients who have severe renal failure and anuria.

Medication/Food Interaction

- Concurrent use of ACE inhibitors increases the risk of hyperkalemia
- Concurrent use of potassium supplements increases the risk of hyperkalemia.

Precautions during Administration

- Obtain the client's baseline data.
- Monitor the client's potassium levels regularly.
- Can only be given orally.
- Teach clients to avoid salt substitutes that contain potassium.
- Teach clients to self-monitor blood pressure.
- Instruct clients to keep a log of blood pressure and weight.
- Warn clients that **triamterene** may turn urine a **bluish color.**

d)Osmotic Diuretics

✓Mannitol (Osmitrol)

Expected Pharmacological Action

✓ Osmotic diuretics reduce intracranial pressure and intraocular pressure by raising serum osmolality and drawing fluid back into the vascular and extravascular space.

Therapeutic Uses

✓ Osmotic diuretics prevent renal failure in specific situations, such as hypovolemic shock and severe hypotension.

✓These medications decrease intracranial pressure (ICP) caused by cerebral edema.

✓ These medications decrease intraocular pressure (IOP).

✓ Osmotic diuretics promote sodium retention and water excretion in clients with hyponatremia and fluid volume excess

Side/Adverse Effects

- ❑Renal failure
- ❑Heart failure, pulmonary edema
- ❑ Fluid and electrolyte imbalances

Contraindications/Precautions

- ❑Use extreme caution in clients with heart failure.

Drug Interactions

- Furosemide contributes to therapeutic effect by promoting renal excretion of fluid drawn into vasculature by osmotic diuretics.

Precautions during Administration

Administer mannitol by continuous IV infusion.

To prevent administering microscopic crystals, use a filter needle when drawing from the vial and a filter in the IV tubing.

Monitor daily weight, I & 0, and serum electrolytes.

Monitor for signs of dehydration, acute renal failure, and edema.

Use of furosemide may help prevent rebound fluid retention; this contributes to therapeutic effect.

Carbonic Anhydrase Inhibitors

- Blockade of carbonic anhydrase activity induces a sodium bicarbonate diuresis, which reduces body bicarbonate levels.
- These drugs include;
- Acetazolamide (DIAMOX)
- Dichlorphenamide (DARANIDE)
- Methazolamide (GLAUCTABS)
- Acetazolamide administration causes a reduction in aqueous humour and CSF fluid production

Acetazolamide cont.....

- The proximal tubule is the major site of action of carbonic anhydrase inhibitors.
- the collecting duct is the secondary site of action .

Clinical application

Glaucoma; because acetazolamide decreases the rate of aqueous humor production, a decline in IOP occurs.

The major indication of carbonate anhydrase inhibitor is **open angle glaucoma.**

It may also be given in **secondary glaucoma**

Preoperatively in acute angle glaucoma.

Treatment of epilepsy.

Altitude sickness familial periodic paralysis

Toxicity

- Hyper chloremic acidosis.
- Renal potassium loss.

Contraindication

Hepatic cirrhosis.

Antihypertensives

Cardiovascular pharmacology

- Antihypertensive drugs potential drug targets;
- CNS: decrease sympathetic tone
- Heart: decrease cardiac out put
- Veins: dilate; decrease preload
- arterioles: dilate; decrease preload
- Kidneys: increase diuresis; inhibit renin angiotensin aldosterone

Classification of Anti Hypertensives

Diuretics:

- ✓Thiazide and related agents (hydrochlorothiazide, chlorthalidone)
- ✓Loop diuretics (furosemide, bumetanide,, torsemide, ethacrynic)
- ✓Potassium sparing diuretics (amiloride, triamterene, spironolactone)

Angiotensin-converting enzyme (ACE) inhibitors (captopril, enalapril, lisinopril, quinapril, Ramipril, benazepril)

Angiotensin II receptor blockers (ARBS)

(losartan, candesartan, Irbesartan, valsartan, telmisartan, eprosartan)

Calcium channel blockers (CCB)

(verapamil, diltiazem, **nifedipine**, felodipine, nicardipine, isradipine, **amlodipine**),.

Classification of Antihypertensive Cont..

Vasodilators

- ✓Arterial (hydralazine, minoxidil, diazoxide fenoldopam)
- ✓Arterial and venous (nitroprusside)

Sympatholytic drugs

Alpha adrenergic blockers ; (prazosin, terazosin, doxazosin, phentolamine, phenoxybenzamine)

Beta adrenergic blockers ; (metoprolol, atenolol, etc)

Mixed adrenergic ; (labetalol, carvedilol)

Centrally acting alpha2 agonists (methyldopa, clonidine, guanabenz)

Adrenergic neuron blocking agents ;(guanethidine, reserpine)

Angiotensin-Converting Enzyme (ACE) Inhibitors

Captopril (Capoten)

- Other Medications: Enalapril (Vasotec), Enalaprilat (Vasotec IV), Fosinopril (Monopril), Lisinopril (Prinivil), Ramipril (Altace)

Mechanism of action

ACEIs prevents conversion of angiotensin I to angiotensin II which is a potent vasoconstrictor. this causes vasodilation, reduces peripheral resistance, and decreases secretion of aldosterone (thereby resulting in decrease sodium and water retention and extracellular volume).

Merits of ACEIs

- Safe for asthmatics, diabetics
- Absence of rebound hypertension upon abrupt withdrawal.
- Total absence of postural hypotension.
- maintains renal blood flow.
- devoid of electrolyte imbalance.

Therapeutic Uses

- Hypertension
- Heart failure
- Myocardial infarction (To decrease mortality and to decrease risk of heart failure and left ventricular dysfunction)
- Diabetic and nondiabetic nephropathy
- For clients at high risk for a cardiovascular event, Ramipril can be used to prevent MI, stroke, or death.

Side/Adverse Effects

- Cough related to inhibition of kinase II (alternative name for ACE) which results in increase in bradykinin
- First-dose orthostatic hypotension.
- Hyperkalemia
- Rash and dysgeusia (altered taste), primarily with captopril
- Angioedema.
- Neutropenia (rare but serious complication of captopril)

Contraindications/Precautions

- These medications are Pregnancy Risk Category D during the second and third trimester, related to fetal injury.
- renal stenosis when present bilaterally or in a single remaining kidney.
- history of angioedema following use of ACE inhibitor.
- Use cautiously in clients with renal impairment and
- collagen vascular disease because they are at greater risk for developing neutropenia. Closely monitor these clients for signs of infection.
- hypotension

Drug Interactions

- Diuretics can contribute to first-dose hypotension
- Antihypertensive medications may have an additive hypotensive effect.
- Potassium supplements and potassium-sparing diuretics increase the risk of hyperkalemia.
- ACE inhibitors can increase levels of lithium carbonate (Eskalith)
- Use of NSAIDs may decrease the antihypertensive effect of ACE inhibitors.

Precautions during Administration

- Administer ACE inhibitors orally except enalapril, which is the only ACE inhibitor for IV use.
- Advise clients that the medication may be prescribed as a single formulation or in combination with hydrochlorothiazide.
- Advise clients that blood pressure has to be monitored after the first dose for at least 2 hr. to detect hypotension.
- Instruct clients that captopril should be taken at least 1 hr. before meals. All other ACE inhibitors can be taken with or without food.
- Advise clients to notify the provider if **cough, rash, dysgeusia** (lack of taste), and/or **signs of infection** occur

Angiotensin II Receptor Blockers (ARBs)

Losartan (Cozaar)

- Other Medications: Valsartan (Diovan) , Irbesartan (Avapro) , Candesartan (Atacand) , Olmesartan (Benicar)

Expected Pharmacological Action

These medications block the action of angiotensin II in the body.

This results in:

- Vasodilation (mostly arteriole)
- Excretion of sodium and water, and retention of potassium (through effects on the kidney)

Therapeutic Uses

- Hypertension,
- Heart failure and prevention of mortality following MI,
- Stroke prevention ,
- Delay progression of diabetic nephropathy

Complications

The major difference between ARBs and ACE inhibitors is that cough and hyperkalemia are not side effects of ARBs

Side/Adverse Effects

- Angioedema

Contraindication

- Hypersensitivity
- Pregnancy
- renal stenosis when present bilaterally or in a single remaining kidney

Considerations

- monitor BP, HR, Weight, Edema, Blood Urea Nitrogen, Serum Creatinine.
- can be used in patients intolerant to aceis (due to cough)

CALCIUM CHANNEL BLOCKERS

- Nifedipine (Adalat, Procardia)
- Verapamil (Calan)
- Amlodipine (Norvasc)

Other Medications:

- Amlodipine (Norvasc)
- Felodipine (Plendil)
- Nicardipine (Cardene, Cleviprex)
- Diltiazem (Cardizem)

Mechanism of action of CCB

Mechanism of action

- Inhibits calcium influx in the smooth muscles and the myocardium.
- Blocking of calcium channels in blood vessels leads to vasodilation of peripheral arterioles and arteries/arterioles of the heart, slows down heart conduction and reduction of blood pressure.

NIFEDIPINE (ADALAT)

- give rise to coronary vasodilation.
- Enhances coronary blood flow.
- Reduces total periphery resistance, reduces systolic and diastolic pressure

Therapeutic use

- Chronic angina
- Congestive heart failure
- Acute myocardial infarction
- Peripheral vascular disorders

Adverse drug reaction

Palpitation, nausea, vomiting, flushing, headache, edema.

Amlodipine

- Serves as a long acting calcium channel blocker.

Therapeutic use

- Treatment of essential hypertension.
- Angina pectoris

Adverse drug reaction

Palpitation,epixtasis,cough,nocturia,musclecramps,breathless, importence, conjunctivitis

Verapamil

- Enhances coronary blood flow rate,vasodilation.
- Exerts anti arrhythmic action.
- Reduces peripheral resistance.

Therapeutic uses

- Supraventricular tachycardia.
- Acute coronary spasms
- Angina pectoris
- Hypertension with myocardial infarction

Adverse Reaction of Verapamil

- Dizziness, vertigo, constipation, hypotension, nausea, pedal edema

Advantages of calcium channel blockers

- ❖Exhibits rapid onset and longer duration of action hence administered once a day.
- ❖Do not exhibit cardiac depression.
- ❖Do not cause adverse effects on the fetus.
- ❖Cause no sedation.
- ❖Recommended for patients having **angina** and **asthma.**
- ❖Do not cause male impotence.
- ❖Mostly indicated for the elderly, pregnant and asthmatic.
- ❖safe with history of renal impairment.
- ❖Do not exhibit action on electrolyte balance.

Considerations

- Monitor BP, HR, rhythm,
- Control calcium supplement.
- Inform patient not to stop drug abruptly.
- Patient to report signs of adverse effects such as irregular heart beat, shortness of breath, oedema in the hands and feet, dizziness, constipation, nausea and hypotension.
- Discontinue in breast feeding because they are excreted in breast milk and have potential for adverse effects in neonates.

DIRECT ACTING VASODILATORS

HYDRALAZINE

Hydralazine (APRESOLINE) causes direct relaxation of the arterio smooth muscle secondary to a fall in the intracellular calcium. this is associated with powerful stimulation of the sympathetic nervous system, due to baroreceptor mediated reflexes.

Toxicity and Precaution

- These includes; headache, nausea, flushing, hypotension, palpitation, tachycardia, dizziness and angina pectoris.
- Myocardial ischemia (increased oxygen demand)
- Immunological reactions, drug induced lupus syndrome. this occurs after six months of treatment with hydralazine.
- symptoms include, arthralgia, arthritis and fever.
- The treatment can result in an illness that resembles serum sickness, hemolytic anaemia, vasculitis, and glomerulonephritis.

Therapeutic Uses

- Due to adverse effect profile, hydralazine is no longer a first line drug in the treatment of hypertension.
- Used in patients with CCF(in combination with nitrates for patients who cannot tolerate ACE inhibitors.
- Treatment of hypertension emergencies in pregnancy.
- (especially preeclampsia).
- The usual dose is twenty five to 100mgs twice a day
- He maximum recommended dose of hydralazine is 200mg/ day.

Contraindication

- Parenteral administration in coronary artery disease.
- Elderly patients

ALPHA ADRENERGIC BLOCKERS (SYMPATHOLYTICS)

- ✓Medication: prazosin (Minipress)
- ✓ doxazosin mesylate (Cardura)

Expected Pharmacological Action

- ✓It inhibits Alpha adrenergic receptor causing Venous and arterial dilation leading to reduction in total peripheral vascular resistance.
- ✓ Smooth muscle relaxation of the prostatic capsule and bladder neck

Therapeutic uses

- ✓ Primary hypertension.
- ✓Doxazosin mesylate (Cardura) may be used to decrease

Side/Adverse Effects

First-dose orthostatic hypotension

- Start treatment with low dosage of medication.
- First dose may be given at night.
- Monitor blood pressure for 2 hr. after the initiation of treatment.
- Instruct clients to avoid activities requiring mental alertness for the first 12 to 24 hr.
- Instruct clients to change positions slowly and to lie down if feeling dizzy, lightheaded, or faint

Contraindications/Precautions

- ✓ Pregnancy
- ✓clients with hypersensitivity to medication
- ✓Antihypertensive medications may have an additive hypotensive effect

Instruct clients to observe for signs of hypotension (dizziness, lightheadedness, faintness).

Instruct clients to lie down if these symptoms occur, and to change positions slowly.

- ✓NSAIDs and clonidine may decrease the antihypertensive effects of prazosin.

Advise clients to avoid OTC NSAIDs.

Contraindications/Precautions During Administration

- ✓Obtain baseline blood pressure and heart rate.
- ✓ Instruct clients that the medication can be taken with food.
- ✓ Recommend that clients take the initial dose at bedtime to decrease “first-dose” hypotensive effect.

CENTRALLY ACTING ALPHA2 AGONISTS

Clonidine (Catapres)

- guanfacine HCl (Tenex),
- methyldopa (Aldomet)

Expected Pharmacological Action

- These medications act within the CNS to decrease sympathetic outflow resulting in decreased stimulation of the adrenergic receptors (both alpha and beta receptors) of the heart and peripheral vascular system.
- Decrease in sympathetic outflow to the myocardium results in bradycardia and decreased cardiac output (CO).
- Decrease in sympathetic outflow to the peripheral vasculature results in vasodilation, which leads to decreased blood pressure.

Therapeutic Uses

Primary hypertension (administered alone, with a diuretic, or with another antihypertensive agent)

✓ Severe cancer pain (administered parenterally by epidural infusion)

Investigational use

✓ Migraine headache

✓Flushing from menopause

✓Management of ADHD and Tourette's syndrome

✓ Management of withdrawal symptoms from alcohol, tobacco, and opioids

Side/Adverse Effects

- ❖Drowsiness and sedation
- ❖Dry mouth
- ❖ Rebound hypertension

Contraindication

- ✓ Clonidine is Pregnancy Risk Category C.
- ✓ Avoid use during lactation.
- ✓ This medication is contraindicated for clients taking anticoagulant medications
- ✓ Avoid use of transdermal patch on affected skin in scleroderma and systemic lupus erythematosus (SLE).
- ✓ Use cautiously in clients with cerebrovascular disease, recent MI, diabetes mellitus, major depressive disorder, or chronic renal failure

Side/Adverse Effects cont…

- ✓Antihypertensive medications may have an additive hypotensive effect.
- ✓Concurrent use of prazosin (Minipress), MAOI s, and tricyclic antidepressants can counteract the antihypertensive effect of clonidine.
- ✓ Additive CNS depression can occur with concurrent use of other CNS depressants, such as alcohol.

Precautions During Administration

- Administer medication by **oral, epidural, and transdermal routes**.
- Medication is usually administered twice a day in divided doses. Take larger dose at bedtime to decrease the occurrence of daytime sleepiness.
- Transdermal patches are applied every seven days. Advise clients to apply patch on hairless, intact skin on torso or upper arm.

Methyldopa (ALDOMET)

- Acts through its metabolites (amethylnorepinephrine)which stimulates central alpha adrenergic receptors, thus increasing total peripheral resistance.
- It does **not** affect **glomerular filtration, cardiac output or heart rate.**

Therapeutic effects

Moderate to severe hypertension

Adverse effects

GIT upsets, sedation, depression, nasal stuffiness, myocarditis edema, orthostatic hypotension, diarrhea, dry mouth, erectile dysfunction, eosinophilia, hemolytic anemia, fever.

Contraindication

- ✓Hypersensitivity, activity liver disease, those who developed liver cirrhosis with previous treatment of methyldopa.

Caution;

- ✓Patients taking diuretics and antihypertensive.
- ✓Those taking levodopa because of potential for additive antihypertensive effects.

Consideration

- ✓patient to avoid hazardous task.
- ✓Lower dose in impaired renal disease.
- ✓Monitor liver functions.

Caution cont…..

- Monitor HB, RBCs for signs of anemia.
- Monitor weight, fluid input and out put.
- Signs of drug induced depression,
- Take BP in different patients position during dose adjustments, warn of signs and symptoms of adverse effects and toxicity
- Tolerance may develop 2to 3 weeks after start of treatment.
- Urine may darken on exposure to air(as drug is broken down to its metabolites)
- Dose increase should be made with the evening dose to minimize the effects of drowsiness.

BETA ADRENERGIC BLOCKERS (SYMPATHOLYTICS)

Cardioselective: Beta1

- Metoprolol (Lopressor)
- Atenolol (Tenormin)
- Metoprolol succinate (Toprol XL)
- Esmolol HCL (Brevibloc)

Nonselective: (Beta1 and Beta2)

- **Propranolol (Inderal)**
- Nadolol (Corgard)
- **Labetalol (Normodyne)**

Expected Pharmacological Action

They block beta- adrenergic receptors in the myocardium and in the electrical conduction system of the heart.

- ❖Decreased heart rate
- ❖Decreased myocardial contractility
- ❖Decreased rate of conduction through the AV node

Therapeutic Uses

hypertension , Angina, arrhythmias, heart failure and myocardial infarction.

Other uses may include: Treatment of hyperthyroidism, migraine headache, pheochromocytoma, and glaucoma

Adverse effects

- Bradycardia, fatigue, dizziness, nightmares, depression, memory loss, hallucination, impotence, cold extremities, elevated serum cholesterol.

Contraindication

severe hypotension, bradycardia, congestive heart failure, asthma, diabetics, critically abnormal lipid profile

Consideration

- Explain the rationale of therapy and importance of taking drugs as prescribed.
- Patient should not discontinue drugs abruptly because it can cause MI or angina

Consideration cont....

- ❖Advise clients to avoid sudden changes in position to prevent occurrence of orthostatic hypotension
- ❖Administer medications orally, usually once or twice a day.
- ❖ Administer the following medications by IV route: atenolol, metoprolol, labetalol, propranolol.
- ❖ Teach clients to self monitor heart rate and blood pressure at home on a daily basis.
- ❖Monitor weight & signs of hypovolemic shock especially in diabetic patients.
- ❖Glucagon is prescribed to reverse signs of overdose.
- ❖Dose are lowered in geriatrics due to delayed metabolism and enhanced side effects.

Medications for Hypertensive Crisis

Nitroprusside sodium (Nitropress)

Other Medications:

- ❖ Nitroglycerin (Nitrostat IV)
- ❖ Nicardipine (Cardene)
- ❖ Clevidipine (Cleviprex)
- ❖ Enalaprilat (Vasotec IV)
- ❖ Esmolol HCL (Brevibloc)

Mechanism of Action; Direct vasodilation of arteries and veins resulting in rapid reduction of blood pressure (decreased preload and afterload)

- ❖ **Therapeutic Uses;** Hypertensive emergencies

Side Effects

Excessive hypotension

- Administer medication slowly because rapid administration will cause blood pressure to go down rapidly.
- Monitor the client’s blood pressure and ECG.

Interactions

Nitroprusside should not be administered in the same infusion as any other medication.

Precautions during Administration

- Prepare medication by adding to diluent for IV infusion.
- Note color of solution. Solution may be light brown in color. Discard solution of any other color.
- Protect IV container and tubing from light.
- Discard medication after 24 hr.
- Monitor vital signs and ECG continuously

CARDIAC GLYCOSIDE

Two main types

- Cardenolides (digitalis, convallaria, oleandra)
- Bufadienolides (Helleborus, Poison Arrow Frog)

Mechanism of action

Cardiac glycoside slows down the heart rate and increase the force of contraction

Pharmacological Action

- Enhances myocardial contractility and is used in congestive cardiac failure.
- Enhances cardiac output, minimizes dilated cardiac size, blood volume and venous pressure.
- They modulate autonomic nervous system activity, and this contributes to their efficacy in management of heart failure.
- Diuretic effect, reduce oedema.
- It is usually given only when diuretics and ACEIs have failed.

Indications

- Congestive heart failure, heart failure with atrial fibrillation, or pts who remain symptomatic despite therapy with ACE inhibitors and b Adrenergic receptor antagonists
- Left ventricular failure.
- Atrial fibrillation.

Digoxin

It is the most commonly used digitalis

Forms

Tablets (Lanoxin)

Capsules (lanoxicaps)

Parenteral digoxin is available for intravenous administration and maintenance doses can be given intravenously when oral dosin is impractical.

Digoxin Cont.....

Expected Pharmacological Action

Positive inotropic effect

- ✓increased force of myocardial contraction Increased force and efficiency of myocardial contraction improves the heart's effectiveness as a pump,
- ✓improving stroke volume and cardiac output.
- ✓Increase perfusion of the kidneys which facilitates excretion of fluid by the kidneys

Negative chronotropic effect

- ✓decreased heart rate ,
- ✓ At therapeutic levels, digoxin slows the rate of SA node depolarization and the rate of impulses through the conduction system of the heart.
- ✓ A decreased heart rate gives the ventricles more time to fill with blood coming from the atria, which leads to increased SV and increased CO.

Digoxin cont.....

Therapeutic Uses

- Treatment of heart failure
- Dysrhythmias (atrial fibrillation)

Side/adverse effects

- Dysrhythmias (caused by interfering with the electrical conduction in the myocardium)
- Cardiotoxicity leading to bradycardia.
- GI effects include anorexia (usually the first sign), nausea, vomiting, and abdominal pain.
- Teach clients to monitor for these effects and report to the provider if they occur.
- CNS effects include fatigue, weakness, vision changes (diplopia, blurred vision, yellow-green or white halos around objects).

Digoxin cont…..

Contraindications/Precautions

- In Pregnancy
- clients with disturbances in ventricular rhythm, including ventricular fibrillation, ventricular tachycardia, and second- and third-degree heart block.
- Use cautiously in clients who have hypokalemia, partial AV block, advanced heart failure, and renal insufficiency.

Medication Interaction

- Thiazide diuretics, such as hydrochlorothiazide (HCTZ), and loop diuretics, such as furosemide (Lasix), may lead to hypokalemia, which increases the risk of developing dysrhythmias
- ACE inhibitors and ARBs increase the risk of hyperkalemia, which can lead to decreased therapeutic effects of digoxin.
- Sympathomimetic medications such as dopamine (Intropin) complement the inotropic action of digoxin and increase the rate and force of heart muscle contraction.
- Quinidine increases the risk of digoxin toxicity when used concurrently.
- Verapamil (Calan) increases plasma levels

DRUGS AFFECTING THE RESPIRATORY SYSTEM (Bronchodilators)

Overview

Asthma is a chronic inflammatory disorder of the airways. It is an intermittent and reversible airflow obstruction that affects the bronchioles. The obstruction occurs either by inflammation or airway hyper-responsiveness leading to bronchoconstriction.

- Medication management usually addresses both inflammation and bronchoconstriction
- These same medications may be used in symptomatic treatment of chronic obstructive pulmonary disease (COPD

Overview Cont....

- Advise clients to take the medication as prescribed. If a dose is missed, the next dose should **NOT** be doubled.
- Check pulse rate and rhythm before administration of digoxin and record. Notify the provider if heart rate is less than 60/min in an adult, less than 70/min in children, and less than 90/min in infants. Administer digoxin at the same time daily.
- Monitor digoxin levels periodically during treatment and maintain therapeutic levels between 0.5 to 2.0 ng/mL to prevent digoxin toxicity.
- Avoid taking OTC medications to prevent adverse and side effects and medication interactions.
- Instruct clients to observe symptoms of hypokalemia, such as muscle weakness, and to notify the provider if symptoms occur.
- Instruct clients to observe symptoms of digoxin toxicity (anorexia, fatigue, weakness), and to notify the provider if symptoms occur.

Management of Digoxin Toxicity

- Digoxin and potassium-sparing medication should be stopped immediately.
- Monitor K+ levels. For levels less than 3.5 mEq/L, administer potassium intravenously or by mouth. Do not give any further K+ if the level is greater than 5.0 mEq/L.
- Treat dysrhythmias with phenytoin (Dilantin) or lidocaine.
- Treat bradycardia with atropine.
- For excessive overdose, activated charcoal, cholestyramine, or Digibind can be used to bind digoxin and prevent absorption.

Bronchodilators Cont.....

Medications include:

Classification of Bronchodilator ;

- Beta2-adrenergic agonists short acting; salbutamol,
- Beta2-adrenergic agonists long acting; salmeterol and formoterol
- Methyl xanthine's e.g. theophylline
- Inhaled anticholinergics e.g. tiotropium
- Anti-inflammatory agents such as **glucocorticoids**, **mast cell stabilizers**, and **leukotriene modifiers**.

Beta2-Adrenergic Agonists

- Albuterol (Proventil, Ventolin)
- Formoterol (Foradil Aerolizer)
- Salmeterol (Serevent)
- Terbutaline (Brethine)
- Albuterol (Proventil, Ventolin)

Mechanism of Action

✓Beta2-adrenergic agonists act by selectively activating the beta2-receptors in the bronchial smooth muscle, resulting in bronchodilation. As a result of this: **Bronchospasm is relieved**, **Histamine release is inhibited**, **Ciliary motility is increased.**

Therapeutic uses

Medication	Route	Therapeutic uses
Albuterol (Proventil, Ventolin)	• Inhaled, short-acting Oral, long-acting	• Prevention of asthma attack (exercise-induced) • Treatment for ongoing asthma attack • Long-term control of asthma
Formoterol (Foradil Aerolizer) Salmeterol (Serevent)	• Inhaled, long-acting	• Long-term control of asthma
Terbutaline (Brethine)	Oral, long-acting	• Long-term control of asthma

Side Effects

- Inhaled agents (short and long acting) have minimal adverse effects.
- Oral agents can cause **tachycardia** and **angina** because of activation of alpha1 receptors in the heart.
- Tremors caused by activation of beta2 receptors in skeletal muscle.

Contraindications/Precautions

- Beta2-adrenergic agonists are Pregnancy Risk Category C.
- These agents are contraindicated in clients with tachydysrhythmia.
- Use cautiously in clients who have diabetes, hyperthyroidism, heart disease, hypertension, and angina.

Drug Interaction

- Use of beta-adrenergic blockers (propranolol) can negate effects of both medications.
- MAOIs and tricyclic antidepressants can increase the risk of tachycardia and angina.

Precautions

Instruct clients to follow manufacturer's instructions for use of device: metered-dose inhaler (MDI), dry-powder inhaler(DPI), and nebulizer.

When a client is prescribed an inhaled beta2-agonist and an inhaled glucocorticoid, advise the client to inhale the beta2-agonist before inhaling the glucocorticoid.

The beta2-agonist promotes bronchodilation and enhances absorption of the glucocorticoid.

Advise clients not to exceed prescribed dosages.

Ensure that clients know the appropriate dosage schedule (if the medication is to be taken on a fixed or a when-necessary schedule).

Precautions Cont…

- Formoterol and salmeterol are both long-acting beta2-agonist inhalers. These inhalers are used every 12 hr. for long-term control and are not to be used to abort an asthma attack. A short-acting beta2-agonist should be used if clients need to treat an acute attack.
- Advise clients to observe for signs of an impending asthma attack and to keep a log of the frequency and intensity of attacks.
- Instruct clients to notify the provider if there is an increase in the frequency and intensity of asthma attacks.

METHYLXANTHINES

Theophylline (Theolair, Theo-24)

Expected Pharmacological Action

Theophylline causes relaxation of bronchial smooth muscle, resulting in bronchodilation.

Therapeutic Uses

Oral theophylline is used for long-term control of chronic asthma.

Route of administration: oral or IV (emergency use only)

Side/Adverse Effects

Mild toxicity reaction may include GI distress and restlessness.

- More severe reactions can occur with higher therapeutic levels and can include dysrhythmias and seizures.

Contraindications/Precautions

- In Pregnancy
- Use cautiously in clients who have heart disease, hypertension, liver and renal dysfunction, and diabetes.
- Use cautiously in children and older adults.

INHALED ANTICHOLINERGICS

- Ipratropium (Atrovent)
- Tiotropium (Spiriva)

Expected Pharmacological Action

- These medications block muscarinic receptors of the bronchi, resulting in bronchodilation.

Therapeutic Uses

- These medications are used to relieve bronchospasm associated with chronic obstructive pulmonary disease (COPD)
- These medications are used for **allergen-induced** and **exercise-induced asthma.**

Route of administration: inhalation

SIDE/ADVERSE EFFECTS

Local anticholinergic effects (dry mouth, hoarseness)

Advise clients to sip fluids and suck on hard candies to control dry mouth.

Contraindications/Precautions

- ❖ Inhaled anticholinergics are Pregnancy Risk Category B.
- ❖ These agents are contraindicated in clients who have an allergy to peanuts because the medication preparations may contain soy lecithin.
- ❖ Use cautiously in clients who have narrow-angle glaucoma and benign prostatic hypertrophy (due to anticholinergic effects).

Drug Interactions Interactions

- Caffeine increases CNS and cardiac adverse effects of theophylline.
- Caffeine can also increase theophylline levels.
- Advise clients to avoid consuming caffeinated beverages (coffee, caffeinated colas).
- Phenobarbital and phenytoin decrease theophylline levels.
- Cimetidine (Tagamet), ciprofloxacin (Cipro), and other fluoroquinolone antibiotics increase theophylline level.

GLUCOCORTICOIDS

Inhalation: beclomethasone dipropionate (QVAR)

Oral: prednisone (Deltasone)

Inhalation:

- ❖Budesonide (Pulmicort Flexhaler)
- ❖ Fluticasone propionate and salmeterol (Advair)
- ❖Fluticasone propionate (Flovent)
- ❖ Triamcinolone acetonide (Azmacort)

Systemic

- Oral Prednisolone E 30 to 40mg for initial to 7 days,
- IV/IM dexamethasone
- IV Hydrocortisone sodium succinate (Solu-Cortef) (
- IV Methylprednisolone sodium succinate (Solu-Medrol)

Expected Pharmacological Action

- These medications prevent **inflammation**, **suppress airway mucus production**, and promote responsiveness of beta2 receptors in the bronchial tree.
- The use of glucocorticoids does not provide immediate effects, but rather promotes decreased frequency and severity of exacerbations and acute attacks.

Therapeutic Uses

Therapeutic Uses

- Short-term IV agents are used for status asthmaticus.
- Inhaled agents are used for long-term prophylaxis of asthma.
- Short-term oral therapy is used to treat symptoms following an acute asthma attack.
- Long-term oral therapy is used to treat chronic asthma.
- Replacement therapy is used for primary adrenocortical insufficiency.
- **Promote lung maturity** and **decrease respiratory distress** in fetuses at risk for preterm birth

Side/Adverse Effects

Beclomethasone dipropionate

Difficulty speaking, hoarseness, and candidiasis

- ❖ Advise clients to use a spacer with MDI.
- ❖ Advise clients to rinse mouth or gargle with water or salt water after use.
- ❖ Advise clients to monitor for redness, sores, or white patches and to report to provider if they occur.
- ❖ Candidiasis may be treated with nystatin oral suspension.

Prednisolone When Used for More Than 10 days

- Suppression of adrenal gland function, such as a decrease in the ability of the adrenal cortex to produce glucocorticoids: Can occur with inhaled agents and oral agents

Taper the client's dose.

- Bone loss (can occur with inhaled agents and oral agents)
- Myopathy as evidenced by muscle weakness
- Hyperglycemia and glycosuria
- Myopathy as evidenced by muscle weakness a
- Peptic ulcer disease
- Infection
- Disturbances of fluid and electrolytes (fluid retention as evidenced by weight gain, and edema and hypokalemia as evidenced by muscle weakness)

Contraindications/Precautions of PDL

- Pregnancy risk category C
- Contraindicated in clients who have received a live virus vaccine
- Contraindicated in clients with systemic fungal infections
- Use cautiously in children, and in clients who have diabetes, hypertension, peptic ulcer disease, and/or renal dysfunction.
- Use cautiously in clients taking NSAIDs.

Medication/Food Interactions

- Concurrent use of potassium-depleting diuretics increases the risk of hypokalemia.
- Concurrent use of NSAIDs increases the risk of GI ulceration. Concurrent use of glucocorticoids and hypoglycemic agents (oral and insulin) will counteract the effects.

Precautions During Administration

- Instruct clients to use glucocorticoid inhalers on a regular, fixed schedule for long-term therapy of asthma.
- Glucocorticoids are not to be used to treat an acute attack.
- Administer using an MDI device, DPI, or nebulizer.
- When a client is prescribed an inhaled beta2-agonist and an inhaled glucocorticoid, advise the client to inhale the beta2-agonist before inhaling the glucocorticoid. The beta2-agonist promotes bronchodilation and enhances absorption of the glucocorticoid.
- Oral glucocorticoids are used short-term, 3 to 10 days following an acute asthma attack.
- If client is on long-term oral therapy, additional dosages of oral glucocorticoids are required in times of stress (infection, trauma).
- Clients who discontinue oral glucocorticoid medications or switch from oral to inhaled agents require additional doses of glucocorticoids during periods of stress.

MASTCELL STABILIZERS ANTI INFLATORY DRUGS (cromolyn sodium (Intal)

Others are: nedocromil sodium (Tilade)

Expected Pharmacological Action

- ❖ Anti-inflammatory action
- ❖ These medications stabilize mast cells, which inhibits the release of histamine and other inflammatory mediators.
- ❖ These medications suppress inflammatory cells (eosinophils, macrophages).

Complications Safest of all asthma medications, Safe to use for children

Therapeutic Uses

- Management of chronic asthma
- Prophylaxis of exercise-induced asthma
- Prevention of allergen-induced attack
- Allergic rhinitis by intranasal route
- Route of administration: inhalation

Contraindications/Precautions

- These agents are Pregnancy Risk Category B.
- Fluorocarbons in aerosols make this medication contraindicated for clients who have coronary artery disease, dysrhythmias, and status asthmaticus.
- Use cautiously in clients with liver and kidney impairment.

LEUKOTRIENE MODIFIERS

leukotriene receptor antagonist ;

- Montelukast (Singulair), Zileuton (Zyflo),Zafirlukast (Accolate)

Expected Pharmacological Action

Leukotriene modifiers prevent the effects of leukotrienes, thereby suppressing inflammation, bronchoconstriction, airway edema, and mucus production.

Therapeutic Uses

Leukotriene modifiers are used for long-term therapy of asthma in adults and children 15 years and older and to prevent exercise-induced bronchospasm.

Route of administration: oral

Contraindications/Precautions

- Use cautiously in clients with liver dysfunction

Medication/Food Interactions

- ❖Zileuton and zafirlukast inhibit metabolism of warfarin (Coumadin), leading to increased warfarin levels.
- ❖Zileuton and Zafirlukast inhibit metabolism of theophylline, leading to increased theophylline levels.

Precautions during Administration

- ❖ Advise clients to take zileuton as prescribed. Zileuton can be given with or without food.
- ❖ Advise clients that zafirlukast should not be given with food, and to administer it 1 hr. before or 2 hr. after meals.
- ❖ Advise clients to take Montelukast once daily at bedtime.

GIT DRUGS(PEPTIC ULCER DISEASE)

Acid peptic disease includes:

- peptic ulcers (gastric ulcer, duodenal ulcer , NSAIDS induced ulcers)
- gasro oesophageal reflux disease,
- hypersecretory states like Zollinger Ellison Syndrome (ulcerogenic tumour of the islets of Langerhans.

Principles of therapy

The aim of therapy is to;

- ❖ relieve symptoms,
- ❖ induced ulcer healing and cure in the long run
- ❖ Decreased risk of complications
- ❖ Stopping reoccurrence

Classification Of Agents Used in Treatment of Peptic Ulcer

Inhibition Of Acid Secretion

- H2 receptor agonist e.g. cimetidine, ranitidine, famotidine roxatidine.
- Proton pump inhibitors e.g. omeprazole, pantoprazole, esomeprazole, lansoprazole.
- Anticholinergics e.g. pirenzepine.
- Prostaglandin analogue e.g. misoprostol.

Neutralization of gastric acids

- Sodium bicarbonate systemic
- Non systemic: magnesium hydroxide, aluminium hydroxide, magnesium trisilicate.

Mucosal protective agents e.g. sucralfate, colloidal bismuth.

•**Anti helicobacter pylori drugs (ANTIBIOTICS)** e.g. Clarithromycin, Ampicillin, Metronidazole, Tetracycline, Tinidazole

Anti H. pylori drugs

- ❖ Amoxicillin (Amoxil)
- ❖Bismuth (Pepto-Bismol)
- ❖ Clarithromycin (Biaxin)
- ❖Metronidazole (Flagyl)
- ❖ Tetracycline

Expected Pharmacological Action

- Eradication of H. pylori bacteria
- Therapy should include: Combination of 2 or 3 antibiotics for 14 days

Two weeks Regimen

- Tetracycline 500mg QID and metronidazole 200mg BID and Bismuth sub salylicylate.
- Amoxicillin 100mg BID and clarithromycin 500mg BID+ Lansoprazole 30mgs BID.
- Clarithromycin 500mg TDS +Omeprazole.

ONE WEEK REGIMEN

Clarithromycin 250mg BID + Metronidazole 400mgs + Omeprazole 20mgs BID.

Amoxicillin 500mg Bid + Clarithromycin 250mg Bid+ Omeprazole 20mg

Histamine2 -Receptor Antagonists

- Ranitidine hydrochloride (Zantac)
- Cimetidine (Tagamet)
- Nizatidine (Axid)
- Famotidine (Pepcid)

Expected Pharmacological Action

Histamine2-receptor antagonists suppress the secretion of gastric acid by selectively blocking H2 receptors in parietal cells lining the stomach.

Therapeutic Uses

- Gastric and peptic ulcers,
- Gastroesophageal reflux disease (GERD),
- Hypersecretory conditions, such as Zollinger-Ellison syndrome.
- Histamine2-receptor antagonists are used in conjunction with antibiotics to treat ulcers caused by H. pylori.

Side/Adverse Effects

- Cimetidine may block androgen receptors, resulting in decreased libido and impotence.
- Cimetidine may cause CNS effects (lethargy, depression, confusion)
- Ranitidine, nizatidine, and famotidine have few adverse effects and interactions.

Contraindications/Precautions

- ❖ These medications are Pregnancy Risk Category B
- ❖ Use in older adults can cause antiadrenergic effects (e.g., impotence) and CNS effects (e.g., confusion).
- ❖ H2-receptor antagonists decrease gastric acidity, which promotes bacterial colonization of the stomach and the respiratory tract. Use cautiously in clients who are at a high risk for pneumonia, such as clients with chronic obstructive pulmonary disease (COPD).

Medication/Food Interactions

- ✓ Cimetidine can inhibit medication metabolizing enzymes and thus increase the levels of warfarin, phenytoin (Dilantin), theophylline, and lidocaine.
- ✓Concurrent use of antacids can decrease absorption of histamine2 -receptor antagonists.

Proton Pump Inhibitor

- omeprazole (Prilosec)
- Pantoprazole (Protonix)
- Lansoprazole (Prevacid)
- Rabeprazole sodium (AcipHex)
- Esomeprazole (Nexium)

Expected Pharmacological Action

- Proton pump inhibitors reduce gastric acid secretion by irreversibly inhibiting the enzyme that produces gastric acid.
- Proton pump inhibitors reduce basal and stimulated acid production.

Therapeutic uses

- ❖Gastric and peptic ulcers,
- ❖GERD,
- ❖h\Hypersecretory conditions such as Zollinger-Ellison syndrome.

Complications

- ❑Insignificant side effects and adverse effects with short-term treatment
- ❑ Low incidence of headache, diarrhea, and nausea/vomiting

Contraindications/Precautions

- These medications are Pregnancy Risk Category C.
- Use cautiously with children and women who are breastfeeding.
- Contraindicated for clients hypersensitive to medication
- These medications increase the risk for pneumonia. Omeprazole decreases gastric acid pH, which promotes bacterial colonization of the stomach and the respiratory tract. Use cautiously in clients at high risk for pneumonia, such as clients with COPD.
- Long-term use of proton pump inhibitors increases the risk of gastric cancer and osteoporosis.

Drug Interactions

- Digoxin (Lanoxin) levels may be increased when used concurrently with omeprazole.
- Monitor digoxin levels carefully if prescribed concurrently.
- Absorption of ketoconazole (formerly Nizoral), itraconazole (Sporanox), and atazanavir (Reyataz) is extremely decreased when taken concurrently with proton pump inhibitors.

Precautions During Administration

- Do not crush, chew, or break sustained-release capsules.
- Clients may sprinkle the contents of the capsule over food to facilitate swallowing.
- Clients should take omeprazole once a day prior to eating in the morning.
- Encourage clients to avoid alcohol and irritating medications such as NSAIDs.

Precautions During Administration cont…

- Active ulcers should be treated for 4 to 6 weeks.
- *Pantoprazole (Protonix)* can be administered to clients intravenously. In addition to low incidence of headache and diarrhea, there may be irritation at the injection site leading to thrombophlebitis. Monitor the client's IV site for signs of inflammation (redness, swelling, local pain) and change the IV site if indicated.
- Teach clients to notify the provider for any sign of obvious or occult GI bleeding such as coffee-ground emesis.

ANTICHOLINERGICS

Piperazine :

- It is a selective M1 receptor blocker
- Produces less effects.
- Reduces acid secretion by 40 to fifty percent
- Has a small therapeutic window

Prostaglandins Analogue

- They have o cytoprotective role by inhibiting acid secretion by increasing mucus and bicarbonate secretion.
- Inhibit gastrin secretion and increase mucosal blood flow.

Misoprostol

- A synthetic pge1 analogue and inhibits acid output.
- ulcer heal in 4 to six weeks but relieving pain

Therapeutic Use

prevent ulceration and bleeding induced by NSAIDS

MUCOSAL PROTECTANT

Sucralfate (Carafate)

Expected Pharmacological Action

The acidic environment of the stomach and duodenum changes sucralfate into a thick substance that adheres to an ulcer. This protects the ulcer from further injury that may be caused by acid and pepsin.

This viscous substance can stick to the ulcer for up to 6 hr.

Therapeutic Uses

- promotes healing of duodenal and gastric ulcers
- Poorly absorbed systemically, not used frequently due to a large doses.
- Should not be used with antacids, H2 Antagonist, PPIs as it is dependent on gastric PH.

Colloidal Bismuth Compounds

- Promote healing of duodenal and gastric ulcers.
- Act by binding to an ulcer, denaturing the protein and creating a physical barrier.
- Inhibition of pepsin, activation of mucous production, increase of prostaglandins.
- It is effective in healing of duodenal and gastric ulcers.
- Effective in non ulcer gastritis, caused by H.pylori

Considerations

- Take before meals and at bed time for 4 to 8 weeks.
- Poor acceptance due to blackening of tongue, dentures and stool
- inconvenience of dosing used as a regimen of multiple therapy for H.Pylori not used alone.

LAXATIVES

This are drugs tha promote deafacation

- laxatives; mild action
- Purgative; strong action
- Classification

Bulk Forming Purgatives

- Magnesium sulphate, magnesium hydroxide, sodium phosphate, lactulose, sodium tartrate, osmotic cathartic.
- Vegetable fibres, bran
- Hydrophillic colloids, methyl cellulose

Irritants and stimulants

- Diphenylmethanes; phenolphthalein, Bisacodyl
- Anthraquinone derivatives; senna, cascara
- Fixed oil; castor oil
- Stool softeners; docusate, mineral oil, glycerin suppositories

Mechanism of action of laxatives

- Laxatives cause retention of fluid in colonic contents increasing bulk and softness of stool and its transit.
- They may decrease absorption of water and electrolyte by acting on intestinal mucosa.
- They may enhance intestinal motility reducing absorption of water.

Bulk Forming Purgatives

Osmotic or saline cathartics

- ✓They are poorly absorbed hold water through osmosis.
- ✓In addition the ions stimulate secretion and motility.
- ✓Main used salts are; magnesium sulphate, sodium sulphate, magnesium hydroxide, sodium potassium tartrate.
- ✓Sodium salts contraindicated in congestive heart failure.

Considerations

- Cause after constipation therefore not used routinely
- Preferred for pre-operative care before colonoscopy and in poisoning.

Lactulose

- A synthetic disaccharide containing fructose and galactose absorbed in the GIT.
- Produces soft stools within 1-3 days
- Side effects; abnominal cramps, flatulence,
- Contraindicated in patients requiring galactose free diet.

Vegetable fibres

- Dietary fibres derived from whole grains, vegetables and fruits. They contains the indigestible portion of cell wall.
- Dietary fibre act by binding water and ions in the intestine softens stool and promotes peristables. Also increases faecel mass.

Vegetable fibres

Indications

- Prevention and treatment of functional constipation.
- Used for symptomatic relief of mild diarrhea

Adverse effects

Flatulance

Intestinal obstruction, oesophageal obstruction may occur.

Contraidication

Stenosis

Ulceration

Irritant and stimulant purgatives

- They promote accumulation of water and electrolytes in the lumen.
- Enhance intestinal motility
- Increased water secretion is through activation of cAMP and synthesis of prostaglandins
- Phenolpthalein and bisacodly are widely used.
- Castor oil is hydrolysed to glycerol and ricinoleic acid which stimulates peristalsis. Effect in the small intestines causes rapid complete evacuation.
- Side effects include; Cramping, dehydration.
- Regular use bordestroys mucosa.
- Should be avoided in pregnant women, can intiate labour.

Stool softeners

Docusates

- Used as an emulsifying, wetting and dispersing agent.
- soften stool with 1-3days

Liquid paraffin

- It's a mineral oil.
- Pharmacologically inert and acts as lubricants and softens stool.

Adverse effects of liquid paraffin

- Leakage of oil past anal sphincter
- Affect absorption of fat soluble vitamins.

Glcerin

- Used as a suppository, produces effects within 30mins.

Indication of laxatives

- Constipation not responding to non- pharmacological measures: fibre rich diet, regular exercise, regular bowel movements, (bulk laxatives are the 1st choice).
- Before and after surgery to produce soft stool in patients with haemorrhoids and fissures.

Contraindications

Undiagnosed abnominal pain

Appendicitis

Intestinal obstruction

Should be avoided during later stages of preganancy.

Anti- Diarrhoeal Agents

- Diarrhoea is marked by frequent passage of unformed or liquid stools.

Treatment of diarrhoea

- ❖ Fluid and electrolyte replacement
- ❖ Nutritional management
- ❖ Drug therapy

Drug Therapy

Anti-diarrhea drugs include;

- ❑ Antimotility drugs
- ❑ Antisecretory drugs
- ❑ Adsorbents
- ❑ Antibacterial agents

Atimotility drugs

E.g loperamide, diphenoxylate

Loperamide

- Acts mainly on GIT receptor.
- Acts quickly and has a longer duration of action
- Decreases GIT motility and is excreted unchanged indicated for non infective diarrhea, mild travellors diarrhea.

Adverse effects

- Skin rash , abdominal cramps with excessive use paralytic ileus
- Contraindication; below 4years, infective diarrhea, ulcerative colitis

Antisecretory drugs

Racecadotril

- Enkephalinase inhibitor that increases endogenous enkephalin level and reduce intestinal hyper tension of water and electrolytes.
- Used for systematic treatment of diarrhea.
- Has no side effects like bloating and after constipation.
- Should not be used in pregnancy, lactation and children.

Adsorbents

- Include kaolin, pectin, methylcellulose , magnesium aluminium silicate.
- They act by absorbing microorganisms and/ toxins by altering normal flora or by protecting the mucosa of the intestines.
- Their efficacy is doubtful

Antimicrobial agents

- Cholera; tetracyclines, norfloxacin/ciprofloxacin
- Infections with camphylobacter; erythromycin and flouroquinolones
- Amoebiasis or giardiasis; metronidazole, diloxanide furoate, ornidazole
- Shigella spcs, ciprofloxacin, norfloxacin or cotrimoxazole.

Miscellaneous

- Contain viable lactic acid bacilli.
- Improve intestinal microflora
- Known as probiotics
- Useful in rotavirus diarrhoea and anti biotic induced diarrhoea

D.ANTI EMETICS

- Vomitting is reflex action that results in forceful evacuation of gatric contents.
- Conditions pregnancy, ulcers, motion sickness, chemotherapy.

Anti emetics

Applied to suppress or prevent vomiting.

Classification

Anti muscarinic: scopolamine (hyoscine), dicyclomine

H1 antagonist: promethazine, doxylamine,

Prokinetic drugs; metoclopramide, domperidone, cisapride, mosapride.

Neuroleptics; phenothiazines, chlorpromazine

Adjuvant antiemetics; dexamethasone, benzodiazepines

1. Prokinetic drugs

a. **Metroclopramide**

- Effective for all types of vomiting, post- operatively, radiation, chemotherapy.
- Less effective in motion sickness.
- Blocks dopamine receptors, enters CNS

Side effects: extrapyramidal effects, dystonia, dyskinesia.

Indications;

- Anti emetic
- Dyspesia
- facilitate lactation

Prokinetic drugs Cont….

b, Domperidone

- Peripheral D2 receptor agonist .
- Causes less extra pyramidal effects, doesnot cross the blood brain barrier.
- Lower efficacy than metoclopramide

Uses; levodopa or bromocriptine induced vomiting.

Side effects; increased prolactin, galactorrhoea, dry mouth, rashes. Headache.

2. Anti muscarinic

Scopolamine (hyoscine)

- Alkaloid related to atropine
- Most effective in prophylaxis of motion sickness
- Antimuscarinic action blocks afferent pathways for vomiting reflex.
- Has short duration of action
- Produces anticholinergic effects; blurred vision, dry mouth, sedation.
- Not effective with vomiting of other aetiologies.

3. Neuroleptics

- Phenothiazines: chlorpromazine
- potent anti emetics in vomiting due to drug toxicity, chemotherapy.
- They act by blocking the D2 receptors in the medulla oblongata chemoreceptor trigger zone.
- Not effective in motion sickness
- Dosage is lower than antipsychotics

Side effects;

Sedation, extrapyramidal effects; dyskinesia, dystonia

4. H1 Antagonist

- Doxylamie useful in motion sickness
- Modest effect on chemotherapy
- Reduce extra pyramidal effects of D2 receptor antagonist.
- Are antagonist therefore avoided in pregnancy.

Adjuvant Antiemetics

Corticosteroids

dexamethasone, methylprednisolone, used to control chemotherapy vomiting.

- ❖Act by blocking prostaglandins.
- ❖Cause insomnia and hyperglycemia

Cannabinoids

tetrahydrocannabinol

- active principle of marijuana
- Reduce chemotherapy emesis.
- For patients intolerant or refractory to others antiemetics

Side effects; hallucinations. Disorientation, vertigo, sedation

HEMATOLOGIC DRUGS – ANTI COAGULANTS

- Anti coagulant refers to any substance which inhibits normal blood clotting, lowers coagulability of blood.
- The anti coagulant interfere with normal coagulation process by interfering with the clotting cascade and thrombin formation.
- These agents are used to inhibit clot formation but they do not dissolve existing clots.

Classification of Anticoagulants

- **Parenteral anticoagulants:**

Heparin

- **Low molecular weight heparin;** enoxaparin, dalteparine, nadroparin, arteparin.
- Semisynthetic heparinoid; heparin sulphate, dextran sulphate, ancrod, danaparoid.
- Others; lepirudin, bivalirudin, argatroban

- **Oral anticoagulant;** warfarin, acenocoumarin, dicoumarol
- **Fibrinolytic; streptokinase urokinase, alteplase**

HEPARIN

mechanism of action: heparin acts prophylactically to prevent the formation of clots in the vasculate.it activates **anti thrombin III** which inhibits thrombin and clotting factor IX, X, XI, XII, consequently conversion of fibrinogen to fibrin does not occur and the formation of a fibrin clot is prevented

Therapeutic Uses

Heparin sodium, LMWH, fondaparinux sodium

- In conditions necessitating prompt anticoagulant activity (evolving stroke, pulmonary embolism, massive deep venous thrombosis)
- As an adjunct for clients having open heart surgery or renal dialysis
- As low-dose therapy for prophylaxis against postoperative

Administration

- These medications cannot be absorbed by the intestinal tract and must be given by subcutaneous injection or IV infusion.
- Heparin sodium: Subcutaneously every 12 hr., continuous or intermittent IV infusion
- Enoxaparin, dalteparin sodium, tinzaparin: Subcutaneously every 12 hr. for 2 to 8 days
- Fondaparinux sodium: Subcutaneously every 12 hr. for 5 to 9 day.

Side/Adverse Effects

- Hemorrhage secondary to heparin overdose
- thrombocytopenia,
- Hypersensitivity reactions (chills, fever, urticaria)
- Administer a small test dose prior to the administration of heparin. Toxicity/overdose
- Administer **protamine sulfate**, which binds with heparin and forms a heparin-protamine complex that has no anticoagulant properties.
- Protamine sulfate should be administered slowly intravenously, no faster than 20 mg/min or 50 mg in 10 min.

Enoxaparin

- **Hemorrhage** Monitor vital signs • Advise clients to observe for signs and symptoms of bleeding, such as increased heart rate, decreased blood pressure, bruising, petechiae, hematomas, black tarry stools. • Monitor platelet count. Instruct client to avoid aspirin.
- **Neurologic damage** from hematoma formed during spinal or epidural anesthesia
- **Thrombocytopenia**, as evidenced by low platelet count , Monitor platelets. Discontinue medication for platelet count less than 100,000/mm3 .
- **Toxicity/overdose;** Administer **protamine sulfate**

- **Contraindications/Precautions**
- Parenteral anticoagulants are contraindicated in clients with low platelet counts (thrombocytopenia) or uncontrollable bleeding.
- These medications should not be used during or following surgeries of the eye(s), brain, or spinal cord; lumbar puncture; or regional anesthesia.
- clients who have **hemophilia**, increased capillary permeability, dissecting **aneurysm**, **peptic ulcer disease**, **severe hypertension, hepatic** or **renal disease**, or **threatened abortion**

Medication/Food Interactions

- Anti-platelet agents such as aspirin, NSAIDs, and other anticoagulants may increase risk for bleeding..

ORAL ANTI COAGULANTS

- These are the most commonly used oral anti coagulants;
- Warfarin,
- Dicoumarol,
- Acenocoumarol

Mechanism of action

Vitamin K antagonist; these agents inhibit the liver synthesis of vitamin K clotting factor II,VII, IX, X.

Advantages over heparin

- Bioavailability is almost 100 percent.
- Low volume distribution,
- Long half life.

Pharmacokinetics

- Produces delayed action,
- possibility of genetic resistance

Clinical indication

- Treatment deep venous thrombosis.
- Pulmonary embolism
- Prevent blood clotting in patients with thrombophlebitis, pulmonary embolism and embolism from arterial fibrillation.

Contraindication /precaution

- Not given to pregnant women because it crosses the placenta barrier, it is teratogenic, and can cause an a abortion.
- Not given to patients with bleeding disorders e.g. hemophilia, peptic ulcer, sever renal/ liver disease and eclampsia.

Monitoring

- Monitor prothrombin time usually done before administering the dose.
- The PT SHOULD BE 1.5-2.5 times the reference value to be therapeutic
- If it is below the recommended range warfarin should be increased.
- If it above the recommended range warfarin should be decreased.

Adverse effects of warfarin

- Hematologic effects: increased bleeding, thrombocytopenia
- Anorexia, nausea, vomiting, diarrhoea and dermatitis.
- Hemorrhage
- Interference with bone formation in early pregnancy

Drug interaction

Potentiation activity

- Inhibition of metabolism: chloramphenicol, ciprofloxacin, cotrimoxazole, cimetidine.
- Displacement from plasma protein; ethacrynic acid.
- Platelet function inhibition; NSAIDs (Aspirin)

retarded activity

- inhibition of absorption; Sucralfate
- Enzyme induction; barbiturates, carbamazepine, rifampicin

Acenocoumarol

- take 2-3 DAYS.

Indication

- Arterial fibrillation,
- pulmonary embolism,
- prophylaxis following insertion of heart valve.

Adverse drug reaction

Alopecia, diarrhoea, hepatic dysfunction, pancreatitis vomiting

Precautions during Administration of warfarin

- Administration is usually oral, once daily.
- Obtain the client's baseline vital signs.
- Monitor PT levels (therapeutic level 18 to 24 sec) and INR levels (therapeutic levels 2 to 3). INR levels are the most accurate. Hold dose and notify the provider if these levels exceed therapeutic ranges.
- Obtain baseline and monitor CBC, platelet count, and Hct levels.
- Instruct clients that anticoagulant effects may take 8 to 12 hr and full therapeutic effect is not achieved for 3 to 5 days. For clients in the hospital setting, explain the need for continued heparin infusion when starting oral warfarin.
-

Precautions during Administration of warfarin

- Advise clients that anticoagulation effects can persist for up to 5 days following discontinuation of medication because of long half-life.
- Advise clients to avoid alcohol and over-the-counter and non-prescription medications to prevent adverse effects and medication interactions, such as risk of bleeding.
- Advise clients to employ nonmedication measures to avoid development of thrombi, including avoiding sitting for prolonged periods of time, not wearing constricting clothing, and elevating and moving legs when sitting.
- Advise clients to wear a medical alert bracelet indicating warfarin use.

Precautions during administration of warfarin

- Be prepared to administer vitamin K for warfarin overdose.
- Teach clients to self-monitor PT and INR at home as appropriate.
- Advise clients to record dosage, route, and time of warfarin administration on a daily basis.
- Plan for frequent PT monitoring for clients who are prescribed medications that interact with warfarin. The client is at greatest risk for harm when the interacting medication is being deleted or added. Frequent PT monitoring will allow for dosage adjustments as necessary.
- Advise clients to notify the provider regarding warfarin use.
- Advise clients to use a soft-bristle toothbrush to prevent gum bleeding

Thrombolytic /Fibrinolytic Medications

Two phenomena which causes hemostasis include,

- Coagulation of blood .
- Formation of a thrombus

Formation of a thrombus is restricted through:

1. **Fibrin inhibition:** anti thrombin III, Ant plasmin, Antitrypsin, Macroglobulin
2. **Fibrinolysis:** tissue plasminogen activator and CF XII activate fibrin bound plasminogen to active plasmin, restrict formation of a thrombus.

Mechanism of action of Fibrinolytic

Thrombolytic/fibrinolytic medications dissolve clots that have already formed. Clots are dissolved by conversion of plasminogen to plasmin, which destroys fibrinogen and other clotting factors. The result is clot disintegration.

The commonly used fibrinolytic include:

- Streptokinase (Streptase)
- Urokinase
- Alteplase (Activase, tPA),
- Anistreplase
- Reteplase (Retavase)

Streptokinase

Mechanism of action:

- streptokinase is a semi synthetic that acts systematically to dissolve the blood clot by activating plasminogen to plasmin.

Clinical indication

- Acute myocardial infarction
- Deep vein thrombosis (DVT)
- Massive pulmonary emboli
- thrombo embolic stroke (alteplase)
- Peripheral arterial thrombosis
- To open clotted iv catheters

Adverse reaction

- Allergic reaction (urticaria, itching, flushing, bronchospasms); possible severe anaphylactic reaction.
- Serious risk of bleeding from different sites (within brain, needle puncture sites, wounds)
- Hypotension
- Arrhythmias

Contraindications/Precautions

- Any prior intracranial hemorrhage (hemorrhagic stroke)
- Active internal bleeding
- History of significant closed head or facial trauma in the past 3 months
- Acute pericarditis
- Brain tumors
- Use cautiously in clients who have severe hypertension, a recent episode of ischemic stroke (6 months prior to start of treatment), or a recent major surgery (2 to 4 weeks prior to start of treatment).

Urokinase

- ❖Isolated from human renal cells from tissue cultures.
- ❖Helps in direct conversion of plasminogen to plasmin.

Therapeutic uses

- ❑Myocardial infarction.
- ❑Venous thrombosis.
- ❑Pulmonary embolism.

Adverse reaction

- ❖Fever.
- ❖Hemorrhage.

Alteplase

Mechanism of action

- Recombinant tissue plasminogen activator (t-PA)
- helps in Critical activation of plasminogen bound in fibrin clot. Reduces the risk of systemic bleeding to an appreciable extent.
- Half life 4-8 minutes
- More efficacious than others

Therapeutic use

Lysis of occlusive coronary artery thrombi associated with myocardial infarction.

Deep venous thrombosis.

Ischemic cerebrovascular disease

Adverse reaction

- Nausea
- Fever
- Rash, pruritic
- Mild hypertension
- Localized bleeding

Precautions during Administration of thrombolytic agents

- Use of thrombolytic agents must take place within 4 to 6 hr. of onset of symptoms
- monitor in a setting that provides for close supervision and continuous monitoring during and after administration of the medication.
- Obtain baseline platelet counts, hemoglobin (Hgb), hematocrit (Hct), a PTT, PT, INR, and fibrinogen levels, and monitor periodically.
- Obtain baseline vital signs (heart rate, blood pressure) and monitor frequently per protocol.
-

Precautions during Administration of thrombolytic agents cont….

- Special care includes continuous monitoring of hemodynamic status to assess for therapeutic and adverse effects of thrombolytic (relief of chest pain, signs of bleeding). Follow facility protocol.
- Provide for client safety per facility protocol.
- Ensure adequate IV access for administration of emergency medications and availability of emergency equipment.
- Do not mix any medications in IV with thrombolytic agents.

Precautions during administration cont.....

- Minimize bruising or bleeding by limiting venipunctures and subcutaneous/intramuscular injections.
- Discontinue thrombolytic therapy if life-threatening bleeding occurs. Treat blood loss with whole blood, packed red blood cells, and/or fresh frozen plasma. IV aminocaproic acid (Amicar) should be available for administration in the event of excessive fibrinolysis.
- Following thrombolytic therapy, administer heparin or aspirin as prescribed to decrease the risk of rethrombosis.
- Following thrombolytic therapy, administer beta blockers as prescribed to decrease myocardial oxygen consumption and to reduce the incidence and severity of reperfusion arrhythmias.
- Administer H2 antagonists, such as ranitidine (Zantac), or proton pump inhibitors, such as omeprazole (Prilosec), as prescribed to prevent GI bleeding.

Anti Platelets Drugs

- These are agents that decrease the formation of platelet plug by decreasing their responsiveness to various stimuli that would cause them to risk and combine together on a vessel wall.

This include;

- Acetyl salicylic acid (aspirin)
- Thienopyridine analogues
  - Ticlopidine,
  - Clopidogrel
- Glycoprotein receptor antagonist:
  - Abciximab
  - Eptifibatide and Tirofiban

Mechanism of action of platelet inhibitors

- These agents inhibit the aggregation of platelets in the clotting process by **blocking receptor sites on the platelets membrane,** preventing platelet to platelet interaction, there by prolonging the bleeding time.

Acetyl salicylic acid (aspirin)

Universally accepted anti platelet drug.

Mechanism of action

- Irreversibly causes inhibition of cyclooxygenase **(COX)** that leads to formation of thromboxane A2 and prostacyclin.
- TXA2 is the key platelet activator inhibition of platelets action.

Therapeutic Uses

- ❖Primary prevention of acute myocardial infarction
- ❖ Prevention of reinfarction in clients following an acute myocardial infarction
- ❖ Prevention of stroke
- ❖ Acute coronary syndromes (abciximab, tirofiban, eptifibatide)
- ❖Intermittent claudication (cilostazol, pentoxifylline, dipyridamole)

Route of administration

- ✓Aspirin: Oral
- ✓ Abciximab: IV
- ✓ Clopidogrel: Oral
- ✓ Pentoxifylline: Oral

Side/Adverse Effects

- Aspirin GI effects (nausea, vomiting, dyspepsia) Advise clients to use enteric-coated tablets and to take aspirin with food. Concurrent use of a proton pump inhibitor, such as omeprazole (Prilosec), may be appropriate.
- Hemorrhagic stroke
- Prolonged bleeding time, gastric bleed, thrombocytopenia
- Tinnitus, hearing loss

Precautions during Administration

- Advise clients that prevention of strokes, myocardial infarctions, and reinfarction can be accomplished with low-dose aspirin (81 mg).
- Aspirin 325 mg should be taken during initial acute episode of myocardial infarction

Thienopyridine analogues

Clopidogre and ticlopidine

- Clopidogre and ticlopidine reduces platelets aggregation by inhibiting the **ADP pathway of platelets.**
- These drugs achieved their antiplatelet effects by irreversibly blocking the ADP receptor on platelets.
- unlike aspirin, these drugs have no effects on prostaglandin metabolism.
- Important for aspirin intolerant
- Use of clopidogre or ticlopidine to prevent thrombosis is now considered standard practice in patients undergoing placement of **coronary stent.**
- **Clopidogrel** plus **aspirin** is used for long term treatment of severe cases of coronary syndromes.
- Rashes caused by ticlopidine.

Hemostatic Agents/ coagulants

❖Haemostatic agents help to stop bleeding at the local site.thus enhancing and promoting coagulation and formation of network fibrin around the wound.

These drugs are :

Aminocaproic acid and **tranexamic**

- These are fibrin stabilizers that maintain or stabilize the clot in the bleeding vessels.

Protamine sulfate

❖This agent antagonizes the anticoagulant effects of heparin.

❖It is derived from fish testis and is high in arginine content.

❖The positive charge interacts with the negative charge of heparin to form a stable inactive complex.

Drugs for Various Bleeding Conditions

- Epistasis – **adrenaline**
- Overdose of fibrinolytic, bleeding post surgery – **aminocaproic acid**
- Menorrhagia, metrorrhagia – **adrenochrome, ethamesylate.**
- PPH – **carboprost**

Vitamin K

Is a fat soluble vitamin occurs in two forms :

vitamin K1 (phytonadione):leafy vegetables

Vitamin k2 (menadione): GIT through microbes.

Bile salts are required for absorption of vitamin K from the intestines.

VIT .K cont.

Deficiency occurs due to two conditions

- Prolonged gut sterilization. VIT. K2
- Obstructive jaundice. VIT. K1, K2.

Phytonadione

may be given orally, IM, IV

if given orally give with bile salts.

Menadione sodium bisulphate

Oral, IM ,IV, or SC

does not require bile salts

Takes longer duration

Vitamin K is given to antagonize oral anticoagulants.

The response to vitamin K is slow, requiring about 24 hours thus, if immediate hemostasis or bleeding control is required, fresh frozen plasma should be ordered.

Therapeutic uses

- Vitamin K deficiency.
- Treatment of hemorrhagic disease of the newborn.
- newborn and premature to cover the reduced intestinal synthesis.
- Prolonged anti microbial therapeutic activity.
- Obstructive jaundice.
- malabsorption

Hematinic

A hematinic is a nutrient required in the formation of blood cells the main hematinic are **iron , B12** and **Folate.** deficiency can lead **to anemia**

Iron and iron salts

- Iron deficiency is the most common nutritional anaemia in humans
- It result from inadequate **iron intake**, **malabsorption**, **blood loss**, or **an increased requirement** as with pregnancy.
- When severe it results in microcytic hypochromic anemia.

Ferrous sulphate

Pharmacokinetics

Iron is given orally as a ferrous salt 50 -100MG is administered daily for the treatment of anemia .

Iron is absorbed readily in presence of gastric acid.

Ferrous Sulphate Cont…..

- It is given before meals though many patients cannot tolerate it due to its irritating effects.
- After sometime the patient shows improved appetite, increased erythrocyte cell count and decreased microcytic hypochromic anaemia .
- At lest six months of therapy is necessary to restore iron levels to storage site.
- It can be given parenterally as iron dextran or iron sucrose that is by slow im or iv.

Unwanted Effects

- Oral can cause GIT discomfort
- Liquid form for infants can stain teeth.
- Allergic reactions are possible with chills, urticaria, sweating , fever and even anaphylaxis after parenteral administration.
- Patients pass black or dark stool this in harmless results of unabsorbed iron.

Folic Acid

Expected Pharmacological Action

- Folic acid is essential in the production of DNA and erythropoiesis (RBC, WBC, and platelets).

Therapeutic Uses

- Treatment of megaloblastic (macrocytic) anemia secondary to folic acid deficiency
- Prevention of neural tube defects during pregnancy; therefore it is needed in all women of child-bearing age who may become pregnant.
- Treatment of malabsorption syndrome such as sprue

Contraindications/Precautions .

Indiscriminate use of folic acid is inappropriate because of the risk of masking signs of vitamin B12 deficiency.

Medication/Food Interactions

- Decreased folate levels with concurrent use of sulfonamides, sulfasalazine, or methotrexate.

Precautions during Administration

- ❑ Assess clients for signs and symptoms of megaloblastic anemia (pallor, easy fatigability, palpitations, paresthesia of hands or feet).
- ❑ Obtain the client's baseline folic acid levels, RBC and reticulocyte counts, Hgb, and Hct levels. Monitor periodically.
- ❑ Advise clients with folic acid deficiency to concurrently increase intake of food sources of folic acid, such as green leafy vegetables and liver. Monitor clients for risk factors indicating that folic acid therapy may be needed, such as heavy alcohol use and child-bearing age.

Insulin, oral hypoglycemic agents

Overview

- Diabetes mellitus is a chronic illness that results from an absolute or relative deficiency of insulin.
- Various insulins are available to manage diabetes. These medications differ in their onset, peak, and duration.
- Oral hypoglycemic agents work in various ways to increase available insulin or modify carbohydrate metabolism.
- Newer injectable medication are used to supplement insulin or oral agents to manage glucose control.

Diabetes Mellitus and Effects of Insulin

- DM consists of agroup of disorders characterized hyperglycemia, altered metabolism of lipids, carbohydrates and proteins and increased complications from vascular diseases.
- Most patients can be classified clinically as having either type1 or type 2 DM.
- The criteria for the diagnosis of DM include symptoms (e.g. polyuria, polydipsia, and unexplained weight loss)and a random plasma glucose concentration of greater than 200ml/dl) 11.1mmol.
- A fasting plasma glucose of greater than (126ml/dl) 7mmol
- there two types of DM . **DM TYPE 1** and **DM TYPE 2**

Insulin Therapy

- Insulin polypeptide hormone is the mainstay for treatment
- Of all types of diabetes.
- Insulin may be administered **IM , IV, SC**.
- long term treatment relies on subcutaneous injections of the hormone.

Expected Pharmacological Action

- ✓ Promotes cellular uptake of glucose (decreases glucose levels)
- ✓ Converts glucose into glycogen
- ✓Moves potassium into cells (along with glucose)

Therapeutic Uses

- Insulin is used for glycemic control of diabetes mellitus (**type 1, type 2, gestational**) to prevent complications.
- Clients with type 2 diabetes mellitus may require insulin when:
- Oral hypoglycemic, diet, and exercise are unable to control blood glucose levels.

✓ Severe renal or liver disease is present.

✓ Painful neuropathy is present.

✓Undergoing surgery or diagnostic tests.

✓Experiencing severe stress such as infection and trauma.

✓Undergoing emergency treatment of diabetes ketoacidosis (DKA) and hyperosmolar hyperglycemic nonketotic syndrome (HHNS).

✓ Requiring treatment of hyperkalemia.

Classification of insulin

classified according to duration of action

classification	Generic (trade name)	Onset	Peak	duration
Rapid acting	Lispro insulin (Humalog), Insulin aspart (NovoLog) , Insulin glulisine (Apidra)	Less than 15 min	Less than 15 min 0.5 to 1 hr.	3 to 4 hr.
Short acting	• Regular insulin (Novolin R)	0.5 to 1 hr.	2 to 3 hr.	5 to 7 hr.
Intermediate acting	neutral protamine Hagedorn(NPH) insulin (Humulin N) , lente insulin	1 to 2 hr.	4 to 12 hr.	18 to 24 hr.
Long acting	Ultra lente, Insulin glargine (Luntus)	1 hr.	None	10.4 to 24 hr.

Premixed insulins

- 70% NPH and 30% Regular (Humulin 70/30) – mixture of intermediate acting and short-acting insulin
- 75% insulin lispro protamine and 25% insulin lispro (Humalog 75/25) – mixture of intermediate acting and rapid-acting insulin Complications

Side/Adverse Effects

Risk for hypoglycemia (too much insulin)

- Monitor clients for signs of hypoglycemia. If abrupt onset, client will experience sympathetic nervous system (SNS) symptoms **(tachycardia, palpitations, diaphoresis, shakiness).** If gradual onset, client will experience parasympathetic (**PNS)** symptoms (**headache, tremors, weakness).**
- Administer glucose. For conscious clients, administer a snack of 15 g of carbohydrate (4 oz. orange juice, 2 oz. grape juice, 8 oz. milk, glucose tablets per manufacturer's suggestion to equal 15 g).

- If the client is not fully conscious, do not risk aspiration. Administer glucose parenterally such as IV glucose, or SC/IM glucagon.
- Encourage clients to wear a medical alert bracelet.

Lipohypertrophy

- atrophy of the sub cutaneous fat at the site of insulin injection is probably an immune response to insulin.
- It may occur with human insulin if patients inject themselves repeatedly in the same site
- Instruct clients to systematically rotate injection sites and to allow 1 inch between injection sites.

Insulin Allergy Resistant

- Identify the underlying cause.
- If allergic reaction to porcine insulin human insulin should be used.
- Antihistamines may provide relieve in patients with cutaneous reaction.
- Glucocorticoids are used in patients with resistant to insulin or more severe systemic reactions

Drug interaction

- Drug interaction is often caused by ethanol, adrenergic receptor antagonist, and salicylates.
- Adrenergic receptor antagonist pose a risk of hypoglycemia due to inhibition of catecholamine effects on gluconeogenesis and glycogenolysis.
- These agents may also mask he autonomic symptoms associated with hypoglycemia.
- Salicylates enhance cell sensitivity to glucose and potentiate insulin secretion and also have a weak insulin – like action in the periphery.
- Epinephrine, glucocorticoid, atypical antipsychotic drugs such as clozapine and olanzapine, and ARVS (protease inhibitors) have direct effects on peripheral tissues that counter the effect of insulin.
- Phenytoin, clonidine, ca2+channel blockers cause hyperglycemia by inhibiting insulin secretion directly or in directly via depletion of K+ (diuretics)

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Oral hypoglycemic Classification

Medications	Expected pharmacological action
Sulfonylureas • 1st generation – tolbutamide (Orinase), chlorpropamide (Diabinese) • 2nd generation – glipizide (Glucotrol, Glucotrol XL) ,glyburide (DiaBeta, Micronase , glibenclamide) glimepiride (Amaryl)	Results in insulin release from the pancreas
Meglitinides repaglinide (Prandin) nateglinide (Starlix)	Results in insulin release from the pancreas
Biguanides metformin HCl (Glucophage)	• Reduces the production of glucose within the liver through suppression of gluconeogenesis • Increases muscles' glucose uptake and use
Thiazolidinedione's (Glitazones) , rosiglitazone (Avandia) , pioglitazone (Actos)	• Increases cellular response to insulin by decreasing insulin resistance • Results in increased glucose uptake and decreased glucose production
Alpha glucosidase inhibitors acarbose (Precose) , miglitol (Glyset)	• Slows carbohydrate absorption and digestion
Gliptins • Sitagliptin (Januvia	• Augments naturally occurring incretin hormones, which promote release of insulin and decrease secretion of glucagon

Therapeutic Uses

- All classifications of oral hypoglycemic agents control blood glucose levels in clients with type 2 diabetes mellitus and are used in conjunction with diet and exercise lifestyle changes.

Metformin HCl is used to treat polycystic ovary syndrome (PCOS).

Side/Adverse Effects

Glipizide And Repaglinide

- Hypoglycemia

Metformin

- Gastrointestinal effects (anorexia, nausea, vomiting, which frequently results in weight loss of 3 to 4 kg [6 to 8 lb])
- Vitamin B12 and folic acid deficiency caused by altered absorption
- Lactic acidosis (hyperventilation, myalgia, sluggishness, somnolence) – 50% mortality rate

Rosiglitazone

- Fluid Rosiglitazone retention
- Elevations in low density lipoproteins (LDL) cholesterol
- Hepatotoxicity .

Side/ Adverse Effects

Acarbose

- Intestinal effects (abdominal distention and cramping, hyperactive bowel sounds, diarrhea, excessive gas).
- Risk for anemia due to the decrease of iron absorption
- Hepatoxicity with long-term use

Sitagliptin

- generally well tolerated

Contraindications/Precautions

- Pregnancy Risk Category C: Glipizide, repaglinide, rosiglitazone
- Pregnancy Risk Category B: Metformin HCl (Glucophage), acarbose (Precose), sitagliptin (Januvia)
- These oral agents are generally avoided in pregnancy and lactation, but the provider may decide to prescribe them.
- Use cautiously in clients with renal failure, hepatic dysfunction, or heart failure because of the risk of medication accumulation and resulting hypoglycemia. Severity of disease may indicate contraindication.
- Contraindicated in the treatment of diabetic ketoacidosis (DKA) Metformin HCl is contraindicated for clients with severe infection, shock, and any hypoxic condition.
- Acarbose is contraindicated for clients with gastrointestinal disorders, such as inflammatory disease, ulceration, or obstruction.