PHARMACOLOGY KRCHN/KECHN-30 HOURS

**BROAD OBJECTIVES**-1.To acquire knowledge, skills &attitude in understanding importance of pharmacology. 2. Administer drugs safely in mx of patients to promote health and prevent illness.

**Specific objectives**

-describe drug administration-routes/dosages,rights.

-Sources/uses of drugs.

-describe pharmacodynamics-MOA,receptors

-pharmacokinetics(absorption,distribution ,metabolism/elimination)

-role of a nurse in drug administration/safety factors

-patient teachings on drug compliance/adherence on discharge.

-prescription symbols

-describe various drugs.

**Content**

-Introduction-pk/PD,Drug mx-supply,storage,drug administration,stock control,drug records-(s11/12,antibioticregister),drug history,controlled drug act,PPA.

**- Antimicrobials**-**antibiotics**/AntiTBs,**antifungals**,**antiprotozoas**-antimalarials,antihelminthics,**antivirals**-ARVS

-Cardiovascular system- antihypertensives,digitalis,antiangina,**antiarrythmics**;

-Circulatory system-Coagulants,anticoagulants,antianemics ,antiplateletes,**cholesterol lowering agents**.

-GIT-antiulcers/Antihistamines,laxatives/purgatives/,antispasmodics-muscle relaxants

-Endocrine system-steroids,insulin,OHA,antithyroid/hyperthyroidism drugs,

-Immune system-Anticancer/cytotoxic drugs

-Respiratory system;bronchodilators,Histamine(H1)inhibitors(antihistamines) Expectorants/cough suppressors

-CNS- Analgesics/antipyretics,anticonvulsants,Opiod/Narcotic analgesics,(anxiolytics,barbiturates), hypnotics,sedatives,**antipsychotics/antidepressants**,GA/LA,Anticholinergics.

**Study guide**-drug name-generic/trade,classification,MOA,dosage,Ind,CI,S/E,Adverse effects&nurses responsibilities.

**Review A&P,Microbiology**

**References**

Drug index

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**Definition of terminologies**

 **PHARMACOLOGY-**study of drugs (actions) on living organs/tissues.or science of study of drugs in all their aspects. Body of information utilizing drugs in Dx,Rx&prevention of dses or ilness.

**Branches**

**Pharmacy-manufucturing&dispensing of drugs or medicine's**

**Clinical pharma**-drug effects on human beings.

**Pharmacodynamics-**study of drug mechanism of action e.g receptor,specificity,agonists and antagonists,potency

**Pharmacokinetics-**study of drug effects in the body or the body deals with drugs to include;absorption,distribution,metabolism&excretion/clearance/elimination**.**

**Toxicology-**study of toxic effects of drugs. Eg teratogenic Carcinogenic Mutagenic

**Pharmacoeconomics-**deals with health economics relating to drug usage and its costs.

**Pharmacovigilance**-monitoring and reporting any drug adverse reactions and drug poor quality.

**Pharmacognosy**-science of identification

**Drug-**chemical used in the diagnosis,treatment or prevention of infections.

**Dose-**the amount of drug at a given time or quantity of the drug used or administered to get desired effect without getting unwanted effects.

**Indication –**significant use of drugs or reasons or conditions/diseases drugs are given to.

**Contraindications-**any condition that makes aparticular line of treatment impracticable or undesired.

**Side effects-**occurs as a normal secondary effect of medication eg metallic taste,headache,N&V.

**Adverse effects**-undesired effect of the drug affecting normal body functioning eg fluid&electrolyte imbalance.ototoxicity,BM suppression-anemia.

**Drug interaction-**one drug modifies response to another differently eg ASA/Heparin,rifampicin/coc.aminoglycoside/furosemide,tetracyclines/antiacids

**Idioscransy- unique individual reaction to a drug.**

**SIGNIFICANCE OF PHARMACOLOGY IN NURSING**

**-**Correct administration of drugs both inpatient&outpatient.

-Prescribing drugs

-Drug Mx-ordering,receiving,stroring,packaging&dispensing drugs.

**USES OF DRUGS**

**-cure diseases** like chemotherapy/antibiotics **-alleviate symptoms** ie antacids/NSAIDS**,Replace deficies-**insulin,iron,thyroxine,**To intervene in normal body functions**-contraceptives,to prevent or delay end stage consequences of degeneratve diseases/aging.

**Sources of drugs**

**Plants-such as roors,leaves,bark,stem,seeds and flowers.**

Plants contain active constituents that include;

Alkaloids- a basic nitrogenous compound of plant origin which produces salt when combined with acid and is physiologically active in plant and animal.

Glycoside-non nitrogenous, colourless crystalline solids that splits up into sugar and non-sugar parts.They don’t form salts. Some are poisonous.

Oils-Volatile oil.

Gums and mucilage

Carbohydrates and related compounds

Seeds-reserpine from rauwolfia vomitora,digitalis-foxglove,opium-poopy plant.

**Animals –**parts of animals like hormone insulin from pancreas if RX of DM and some insects are sources of drugs.heparin-leech, thyroxin- sheep thyroid gland, cod liver-vit A&D,ant p gland-gonadotropins-infertility.urine from pg woman contains-HCG-Rx of infertility.

**Minerals-**clay, activated charcoal, iron-Rx anemia,mercury-syphillis,Zinc-diarhoea/eczema,iodine-Goitre,gold-R/A,sulphur,al,mg-antacid/laxative,Na-fluid&electrolyte imbalance.Ca-osteoporosis/rickets,etc.

**Laboratory or synthetic-**produced artificially by combining 2 or more compounds or elements. May be partially or totally synthesized. The structural alteration of the natural substance by the addition of a pure chemical substance leads to the production of a partially (semi) synthetic substance.apomorphine,diacetyl morphine,ethinyl estradiol,homatropine,ampicillin,methyl testosterone.

**Microorganisms-**actinomycetes and aspergillate have been used to produce antibiotics-tetracylines,streptomycin,CAF, and antifungals

**Abbreviations in side effects.**

CNS- Central ner

vous system. U&E-Urea and Electrolyte

ENT-Ear Nose and Throat. Hemat -Haemotologic

RESP or RS –respiratory loc-Local

CVS –cardivascular system metab- metabolic

GI- gastrointestinal MS-musculoskeletal

GU-genitourinary neuro-Neurologic

Derm-dermatologic misc-miscellaneous

Endo-endocrinologic

F&E-Fluid and electrolyte

**DRUG PRESCRIPTION SYMBOLS**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **abbreviation** | **Meaning** | **abbreviation** | **Meaning** |  **Abbreviation** | **meaning** |
| **AC** | Before meals | **Pc**  | After meals  | **Tid /tds** | Three times daily |
| **Bid or BD** | TWICE daily | **p.o** | By mouth/per oral | **Top**  | topical |
| **Cap** | Capsule | **Prn** | S needed/when necessary | **Tsp** | Teaspoonful=5ml |
| **G** | Grams | **Q** | Every | **Hs**  | At bed time |
| **Gr**  | Grains | **Qd** | Every day | **Transderm**  | On skin or topical |
| **Gutt** | Drops | **Qh**  | Every hour | **Patch** | On the skin |
| **Im**  | Intramuscular | **Qid** | 4times aday | **Iv**  | intraveneously |
| **In**  | Inches | **Qod** | Every other day | **Id**  | intradermal |
| **Inhaln** | Inhalation | **Qwk** | Every week | **Nocte**  | At night |
| **Kg**  | Kilograms | **Q2h** | Every 2 hours | **Pt**  | patient |
| **Bwt**  | Body weight | **Q3h** | Every 3 hours | **Mx**  | management |
| **Ht**  | Height | **Q4h** | Every 4 hours |  |  |
| **Hrs**  | Hours  | **Am** | Every morning |  |  |
| **L**  | Litres | **Sc**  | Subcutaneous |  |  |
| **Mg**  | Miligrams | **Sl**  | Sublingual |  |  |
| **Mcg** | Micrograms | **STAT** | Immediately |  |  |
| **Ml**  | Mililitres | **SUPP** | Suppository |  |  |
| **Oint**  |  Ointment  | **Tab**  | Tablet |  |  |
| **O/s**  | Out of stock | **Tbs** | Tablespoon |  |  |

**FOOD AND DRUG ADMINISTRATION**

**PREGNANCY CATEGORIES**

Category A-NO fetal risk in the 1,2,3 trimesters.probably remote.

Category B-Risks to fetus in animals is seen.No or insufficient data in pregnancy.

Category C-adverse effects shown in animals.Insufficient data in pregnancy.benefits of medication outweigh possible risks.

Category D-Human fetal risk has been demonstrated.

Category X- Human fetal risk has been clearly demonstrated. Possible risk to fetus outweighs potential benefits to the pregnant woman. Avoid using in pts who are pregnant or who become pregnant**.**

**Routes of Administration**

**A.Local-Skin Topicals-**applied on Skin Surface eg Ointments/creams.

 -**ocular Drops/ointment**s-eye eg TEO,GEED

 **-Inhalation-**Drug to the resp system-salbutamol inhaler**.**The most rapid effect and action

 -**Transdermal**-topical application of drug on the skin using adhesive so that is slowly absorbed.

**B.Systemic**

**1.Enteral-a.Oral**-administered vial mouth.

preps include

 -Table-coated/non coated.

 -capsule-gelantine&easily digested in stomach or intestine.

 -powder-

 -Mixture-liquids dissolved or diffused in water or other solvent

 -Emulsion

 -Linctus-liquid containing sweet syrup substance and for its soothing effects on coughs.]

 **Aids to taking oral drugs**

**-**Ensure pt is sitted up easy swallowing –prepare adequate fluid for taking it.-liquid preparation may be given via an oral syringes.-unpleasant taste drugs swallow it with flavoured drink

 **b.Rectum/vagina**-suppositories/pessaries eg clotrimazole pessaries-table,suppositories-glycerin.

 **c.Sublingual**-below the tongue eg sublingual adalat

**2.Parenteral or injection** directly into the tissue**-IV-vein**

 **-IM-90 degrees muscular tissue**

 **-ID-15 degrees dermis BCG**

 **-SC-45 degrees**

 **-intrathecal(IT)-cns in subarachnoid space-BBB.**

 **-Intra-articular**

**Aids in administering injections**

**-**sterile equipment must be used&strict aseptic technique observed.-cleansing of the skin with antiseptic solution eg spirit,alcohol.

**Safety factors in drug administration**

**-**Don’t leave drug trolley unattended.

-Don’t give drugs from memory-refer to prescription sheet.

-Don’t give a drug prepared by anyone else.

-Don’t return used dose to a stock bottle.

-unused drugs may be returned to the pharmacy,checked and used for another patient.

**Patient education**

**-**The name &purpose of the drug, stressing its positive effects.

-frequency&timing of administration according to home routine including advice-required medication.

-method of administration with explanation with required accessories other than orals.

-Proposed length of Rx short or longterm.

-Importance of not stopping or starting drugs without advice and where to obtain the advice.

-How to obtain further supplies and safely dispose of unwanted drugs.

-Adverse effects to be reported&any changes to be made.

-Drugs prescribed for others should not be shared despite similar problem.

-Keep off drugs from moisture.-Different drugs should not be put in the same container as errors may occur&also drugs may interact chemically.- All drugs should be kept out of reach off children preferably locked in cupboard.

**Rules of drug administration**

-read pt’s name from prescription sheet.

 –Read prescription ,checking validity&time of last administration

.-Read name of drug from label when removing container from shelf.

-check container label for;name,strength or drug dose,route of administration&expiry date.

-measure correct dose after shaking the bottle

.-Recheck label before returning container to the shelf

.-Verify pt identity by details of prescription sheet

.-Ensure pt is in fit state to receive the drug.

-Give dose&ensure swallowed.

-Record administration if taken or not.

**Drug nomenclature-naming of drugs**

1. **Chemical name**-describes atomic/chemical&molecular structure eg dental local anaesthetic called acetamide &compound name is diethylamino-N-2,6 dimethyl phenyl-monohcl (C14H22N2OHCLH20).ASA-acetylsalicylic acid,N/S-NaCl,H202-hydogen peroxide,
2. **Generic name**-common name of the drug or drug name under which it is sold.eg Lidocaine HCL.
3. **Trade name**-manufacturer’s name or brand name.eg augpen,amoxiclav,rapiclav

**Assignment**-write short notes on;-drug storage-stock control-drug records-drug history-controlled drug act-pharmacy&poisons act.

**The number of drops that equal 1ml as specified on the package of IV tubing.Most common are 10,12,15 or 20 drops/ml.To calculate the flow rate,the nurse must know the volume of fluid to be infused and the specific time for the infusion.**

**Methods used in indicating flow rate**

**Milimitres per hour**

Hourly rates can be calculated by dividing the total infusion volume by the infusion time in hours.

Total infusion volume(mls) divided by total infusion time(hrs)=mls/hr.

**Drops per minute=**total infusion volume(Mls) times drop factor divided by total time of infusion in minutes eg 1000mls in 8HRS Drip factor of 20 drops/mil.

**1000times 20 divided by 8times 60**

**The nurse regulates the drops per minute by tightening or releasing the iv tubing clamp and counting the drops for 15secs,then multiple the no.by 4.**

**Factors influencing flow rates**

The position of the forearm

The position and patency of the tubing

The height of infusion bottle

Positive infiltration of fluid leakage

**Principals of drug administration-**Rt pt, dose, drug form, route,time &duly recorded.

**Pharmacokinetics**-how the body deals with drugs.

Pharmacokinetic characteristics of drug molecules concern the processes of absorption, distribution,

metabolism, and excretion/elimination.

**Absorption**-transfer of the drug from external(drug within cell) to internal environment(blood stream) of the body.

Its through;passive diffusion –less energy required.-facilitated transport-proteins&active diffusion-ATP energy.

Factors affecting it-**pt body factors**-ph,presence of other substances-alcohol,GI motility,functional integrity of absorptive surface,diseases-liver,vascularity&area of absorptive surface.

 Drug factors-lipid water solubility,molecular size,dosage forms,formulation,concentration,

Bioavailability-drug has reached the circulation&available to all the tissues.

**Distribution-**Drug targets specific organs like Lasix- kidney ,digoxin-heart. **Body**-vascularity,transport mechanisms,bariers-blood,placental,plasma binding proteins,volume of distribution, **drug**-degree of ionization,duration of action,therapeutic effects,toxic effects.

**Metabolism-**Absorption occurs at GIT then to blood system to the liver where it occurs.(1st pass metabolism).**Half life** (t1/2)-drugs duration in the body.Time taken for the plasma conc.of the drug to decline to one half of its value.**bioavailabilty**-drug in circulation(absorbed&transported by body to site of action/tissues eg ASA 600MG.

Age ,gender,genetic-drug removal inability,

**Elimination/excretion/clearance**-rate at which the body get rid of drugs as fast as possible by binding to enzymes via-lungs,kidneys or gut.lipid solubility,ionization,urine flow and PH,state of the kidneys,DI,renal perfusion,plasma drug conce,biological factors.

**Factors modifying efficacy (elicit max effectiveness)&choice of drugs in pts**

-Pt age/size-elderly&young less dosages.

-genetic factor-interperson variation some break down drug rapidly while others slowly.

-Nutritional factors like malnutrition modifies drugs due loss of body mass hence less proteins prolonging drug action.

Ethnicity-propronolol less effective inlowering BP in blacks than whites.

-intercurrent illness.

-DIs

-Psychological factors

**Pharmacodynamics-**How drugs (chemicals) exert their effects OR MOA of drugs.

Helps in designing of new drugs to treat disease.

To find out optimal route of admn,dose&frequency of dosing to maintain effective body concentrations.

**Receptors-**proteins occurring on the surface of cell or inside it whereby they receive chemical signals.

**Properties of drugs.**

**1.Receptor specificity**-recognize specific configurations&bind to them selelectively.eg adrenaline receptors-alpha&beta adrenoceptors.

Functions-binds the bodys own chemical messengers-**hormones&neurotransmitters. eg Histamine(H1-mast cell,**

**H2-stomach),cholinergic(muscarinic bronchioles,Nicotinic-muscles),Adrenergic(beta1-heart,beta2-bronchioles) –**convert binding environment into a signal that cell can recognize &respond to it.

 -Ligand is any substance that binds to a protein receptor.

**2.Affinity**-ability of a given drug to bind to its receptor by direct chemical interactions-ectrostatic,hydrophobic within the binding site of a receptor. recognize&bind certain chemicals tightly.

**3.Efficancy-**effectiveness of the drug in terms of drug of therapeutic effect produced by it.

**4.Potency**-concentration of active drug in preparation.

**How drugs work or elicit reaction**

**Agonists**-ability of drug to bind to receptors to produce response.eg morphine,pethidine

**Partial agonists**-ability to stimulate&block at a receptor.eg tramadol

**Antagonists**-block agonists by blocking the binding effect of a drug at a receptor.(antidote)

Guidelines for safe Narcotic administration&control

.store in lockable cabinet

.Nurse I/C to be custodian of keys

.proper handing over of drugs during change of shifts

.Report discrepancies immediately

.Special inventory used for recording dispensed drugs

.Record should have;pt name,date,time of admn,drug name,dosage,&signature of dispenser

.2 nurses should be present during drug admn&destruction of expired drugs

**Antibiotics-antibacterials**

**GEN.MOA**

-**Bactericidal**-kill bacteria rapidly eg aminoglycosides alter bacterial component at 30s ribosomal subunit.

 - **Bacteriostatic-**prevent bacteria from replicating hence allow body defence mechanisms to destroy infecting organism ie don’t kill eg sulphonamides,tetracyclines,CAF.

**Factors to consider while choosing antibiotic or principles of antimicrobial therapy**

**Patient factors**

-Possible complicating or contradicting factors/patient condition eg pregnancy-

tetracyclines&aminoglycoside,hepatic/renal failure-absorption &elimination considerations.

-Cost as some antibiotics like cephalosporins are expensive as compared to penicillins.

-Drug history on current /previous drugs, adverse and hypersensitivity reactions like rash.

-Susceptibility- patient intrinsic ability to combat infection-ISS,malnutrition.

**Organism factors**

-Infecting organism-nature of disease like streptococcal sore throat identified by culture results.

-resistance to some antibiotics due to repeated exposure occurs by;

=**Cell Membrane permeability** to drugs is reduced eg tetracylines&antiTbs,

=**alteration in bacterial structure or component** at 3os ribosomal subunit in org eg aminoglycoside

=**drug destruction** by organisms to drugs like penicillin by forming betalactamases (penicillinase) enzymes& inhibit certain acids **(PABA)** during their respiration which is broken down within organism for energy.

**Drug factors**

-Ability of antibiotic to penetrate infection site eg mengitis-the drug should cross the blood brain barrier into the CSF-CAF(chloramphenicol),cephalosporins

-Route of administration-some drugs are ineffective orally except parenterally(absorption) –aminogoglycosides.

-Correct antibiotic to eradicate infection or drug sensitivity eg penicillins&cephalosporins are more sensitive due to beta lactam ring.

-Adverse reaction/drug interactions leading to ,eg ototoxicity,Bone Marrow depression or reduced efficacy eg -rifampicin&oral contraceptives.

BACTERIAL RESISTANCE TO ANTIBIOTICS

If an antibiotic is prevented from carrying out its function or is not active against a particular organism, that organism will survive and that’s is termed as being **resistant**

Several waysin which organisms become resistant to antibiotic:-

1. **Production of enzymes**

Some produce enzymes which destroy the active drug e.g. staphylococci resistant to penicillin produces β-lactomase or penicillinase enzyme. This attacks the β-lactam ring of the penicillin drug converting it to penicillin acid which makes the drug harmless.

Some gram negative organism may be resistant to chloramiphenic acetile transferase.

1. **Inhibition of certain acids**

Most microorganisms produce certain acids (PABA) during their respiration. PABA is broken down within organism for energy. Some antibiotics like sulphonamides and bacitracin will block their pathway. If organism produce large quantities of the acid, they become resistant.

1. **Altered structure**

Some organisms develop an altered structural target for the drug e.g. dimensional resistance to aminoglycosides is associated with the loss or alteration of a specific protein on the 30S subunit of the bacterial ribosomes which serves as a binding site in susceptible organism.

Erythromycin resistant organisms have an altered protein on the bacterial ribosome.

1. **Cellular metabolism**

Some antibiotics bind themselves into the ribosome causing death. Upon binding to the ribosome, they cause some misleading genetic information. When certain cells fail to bind with the antibiotic, the process of protein synthesis continues and the cell survives

TRANSMISSION OF DRUG RESISTANCE

RNA and DNA are the genetic material of an organism and can be transferred from one bacteria cell to the other. The factors involved in the transfer are referred to as ***R-factor.*** R-factors are chromosomal e.i. if a resistant transfers its R-factor to a similar or susceptible organism will become resistant.

3 methods of transmitting resistance are:-

1. **Transformation** – occurs when a bacteria cell raptures and cells taken up by another organism. If the organism was resistant, then the recipient cell becomes resistant also.
2. **Transduction** – occurs when a resistant bacteria is attacked by a bacteriophage (bacteria attacked by virus) it will transfer the R-factors to the new cell.
3. **Conjugation** – this is mating a direct contact between two bacteria cells therefore if one is resistant to a certain drug it passes the R-factor to the 2nd cell.

**Preventive measures to antibiotic resistance**

-Correct use of antibiotics by use of culture/sensitivity results

-Train and re-train prescribers

-Follow policies in hospitals-drug adherence,

-Restrict sale of drugs

**Beta lactam antibiotics**

 **==CEPHALOSPORINS==**

**-they are structurally similar to penicillins**

1st generation-orals-Cephalexin,cefazolin,cefadroxil,cepharadine,cephapirin

2nd generation-some orals/parenterals-Cefuroxime,cefaclor,cefotetan,cefrozil,cefodixime,cefmetazole

3rd generation-parenterals-Cefotaxime,ceftriaxone,ceftazidime,cefpodoxime-oral

4th generation-cefepime

**MOA**-Binds to the bacterial cell wall membrane causing cell death.

-they are bactericidal

**INDs**-Skin&skin structure infections eg burn wounds.

 -pneumonia,OM,UTIs,bone&joint infections,septicaemia(endocarditis),meningitis,intrabdominal infections,peri-op.prophylaxis

**CIs**-hypersensitivity to cephalosporins/penicillins,

 -renal failure

 -lactation

**S/Effects**-seizures,Diahrroeah,pseudomembranous colitis,N&V,cramps,hepatic dysfunction,rashes,urticaria,bleeding disorders,blood dyscrasias,pain at IM site,phlebitis at IV site,allergic reactions like anaphylaxis.

DRUG INTERRACTIONS

-increased nephrotoxicity with aminoglycosides

-disulfiram-like reactions may occur if alcohol is taken within 72 hrs after cephalosporin administration

==AMINOGLYCOSIDES==

=these includes;amikacin,gentamicin,neomycin,netilmicin,spectinomycin,streptomycin and tobramycin.

=MOA-they interfere with protein synthesis in the bacteria and are bactericidal.

-they have a wide range of anti-bacterial activity with streptomycin being the main drug against mycobacterium tuberculosis.

 =PROPERTIES OF AMINOGLYCOSIDES

-they are all given parenterally for systemic effect or topically.

-they are all excreted renally and toxicity occurs in renal failure

-they are all ototoxic (they impair hearing/balance)

-there is a very small difference in their antibacterial

spectrum.

=gentamicin is widely used in treating severe infections by staphylococci and various gram negative organisms.

-it is usually given parenterally three times a day and elimination is through the kidneys

-close monitoring of blood levels is necessary to avoid ototoxicity.it should not exceed 10mg/litre.prolonged use should be avoided

-it should be avoided during pregnancy as it is ototoxic to the foetus.

=spectinomycin is reserved for treatment of gonorroeah that has become resistant to penicillins.

=neomycin is bactericidal against a wide range of gram +ve and gram –ve micro-organisms and also against m.tuberculosis.

-but it is very poorly absorbed from the GIT,but is also not given parenterally due to high toxicity.it is mainly given orally pre-operatively to sterilize the GIT,and as eye and ear drops and as topical antibiotic powder.

=streptomycin is derived from one of the actinomyces group of the fungi.it is only given by IM injection.

-it is currently reserved for treating drug resistant tuberculosis,but may be combined with doxycycline to treat brucellosis

-it is usually combined with another antibiotic to prevent emergence of resistance.

=tobramycin may be given by inhalation to kill pseudomonas aeruginosa in cystic fibrosis patients.

==TETRACYCLINES==

=They are bacteriostatic.they inhibit protein synthesis in susceptible bacteria thus preventing cell replication

=examples are:doxycycline,minocycline,oxytetracycline,demeclocycline and tetracycline

=INDICATIONS

-used in treatment of psittacosis,ornithosis and lymphogranuloma venerum caused by mycobacterium pneumonia

-as adjunct to amoebicides in acute intestinal amoebiasis.

-treatment of acne

-treatment of complicated urethral,endocervical or rectal infections caused by chlamydia trachomatis

-treatment of ocular infections caused by susceptible organisms

-prophylaxis of opthalmia neonatorum due to n.gonorrhea and c.trachomatis.

=CONTRAINDICATIONS

-allergy to any tetracycline or tartrazine

-pregnancy-toxic to fetus

-lactation-causes damage to the teeth of infants.

-use cautiously in hepato/renal dysfunction,presence of ocular viral infections,mycobacterial or fungal infections

=ADVERSE EFFECTS

-phototoxic reactions,rashes and exfoliative dermatitis

-discoloration and inadequate calcification of teeth in the newborn if used during pregnancy or lactation

-glossitis and dysphagia may also result

-fatty liver or hepatic failure

-hemolytic anaemia or other hematologic disorders

-hypersensitivity reactions ranging from urticaria to anaphylaxis and intracranial hypertension

=DRUG INTERRACTIONS

-decreased absorption if taken with calcium/magnesium salts(antacids),aluminium/zinc salts(anti-diahrroeals),iron salts(hematinics.

-also reduced absorption if taken with food,dairy products and charcoal.

-there is increased digoxin toxicity

-there is decreased effectiveness of oral contraceptives

-decreased activity of penicillins.

=TEACHING POINTS

-take the drugs on an empty stomach,1 hour before or 2-3 hrs after meals with a full glass of water

-donot take the drugs with food,dairy products,iron preparations or antacids.

-if on oral contraceptives,use additional methods while on tetracyclines.

-to give eye drops or ointments;lie down,or tilt head up,drop antibiotic on lower eyelid then apply gentle pressure on the inner corner of the eye for drops or close the eye and roll the eye in all directions for ointments.

==MACROLIDES==

=They can be bacteriostatic or bacteriocidal in susceptible bacteria.

=they bind to the cell membranes at the 50s ribosomal units of the bacteria and causes bacterial cell death.

=examples includes;azithromycin,clarithromycin,dirithromycin and erythromycin.

=INDICATIONS

=treatment of infections caused by sensitive strains of:s.pneumoniae,mycoplasma pneumonia,listeria monocytogenes &legionella pneumophilia

=these can cause diseases such as;URTI”S,LTI”S,skin and soft tissue infections,PID caused by n.gonorrhoea,intestinal amoebiasis

=it is also used in treatment of infections caused by chlamydia trachomatis in pregnancy and for the new born where tetracycline is contraindicated.

=it is used in management of syphilis caused by treponema pallidum in penicillin allergic individuals.

=generally they are used to treat most infections that are susceptible to penicillin as a replacement in penicillin allergic patients.

=CONTRAINDICATIONS.

-allergy to any macrolide antibiotic.

-use cautiously in hepatic dysfunction and in lactating mothers since they may modify normal flora of a nursing mother.

=ADVERSE EFFECTS

-may cause reversible hearing loss

-edema,urticarial,dermatitis may also occur

-can also cause;abdominal crambing,anorexia,diahrroeah,vomiting,pseudomembranous colitis and hepatotoxicity

-hypersensitive individuals may develop a rash or even anaphylaxis

=DRUG INTERRACTION

-may interact with the following drugs to increase their serum levels;digoxin,oral anticoagulants,theophyllines,carbamazepine& corticosteroids

=TEACHING POINTS

-Ideally take the drug 1 hr before meals or 2-3 hrs after.however if there is reported stomach upsets,the drug may be taken with meals

-ensure the drug is taken round the clock and that the patient finishes full course of the therapy

-tell patient to report any severe watery diahrroeah,severe vomitting or nausea,dark urine,yellowing of the skin or eyes and loss of hearing as this may require change of antibiotic.

 ==FLUOROQUINOLONES==

=They are bactericidal antibiotics

=they interfere DNA replication in certain susceptible gram negative bacteria leading to cell death.

=Examples includes:ciprofloxacin,levofloxacin,norfloxacin,ofloxacin,sparfloxacin,moxifloxacin etc.

=INDICATIONS

-Treatment of infections caused by gram negative bacteria like;E.coli,proteus vulgaris,p.mirabilis.pseudomonas aeruginosa. and some gram +ves like;staph aureus,staph epidermidis and group D streptococci.

=CONTRAINDICATIONS

-allergy to any fluoroquinolone

-pregnancy or lactation

-use cautiously with renal dysfunction and seizures

=ADVERSE EFFECTS

-headache,dizziness,insomnia,fatigue and depression in the CNS

-nausea,vomiting and diahrroea

-fever,rash and photosensitivity

=There is decreased therapeutic effects if taken with antacids and ferrous sulphate.

=TEACHING POINTS

-take oral drugs on empty stomach one hour before meals or two hours after

-if an antacid is needed,donot take within two hrs of fluoroquinolone dose.

-drink plenty of fluids

-observe for possible side effects.

 ==SULPHONAMIDES==

=They are bacteriostatic.

=they competitively antagonise para-amino benzoic acid(PABA) an essential component of folic acid synthesis in susceptible gram –ve and +ve bacteria.

=Examples are;balzalazide,sulfadiazine,sulfalazine,sulfisoxazole,sulfamethoxazole(sulfamethoxazole 400mg+trimethoprim 80mg=septrin)

=INDICATIONS

-Treatment of ulcerative colitis,otitis media,inclusion conjunctivitis,meningitis,toxoplasmosis,trachoma and UTIs.

-management of rheumatoid arthritis,collagenous colitis,crohns disease

-prophylaxis in PLWHA against PCP and CM.

=CONTRAINDICATIONS

-allergy to sulphonamides,sulfonylureas,thiazides

-pregnancy(teratogenic)

-lactation-can cause kernicterus,diaohrea&rashes in baby

-use cautiously in impaired renal or hepatic function,g-6-pd deficiency and in porphyria.

=ADVERSE EFFECTS

-headache,peripheral neuropathy,mental depression and other CNS manifestations

-photosensitivity,cyanosis,petechiae and alopecia

-nausea,emesis,abd pains,diahrroea,pancreatitis,impaired folic acid absorption and hepatocellular necrosis

-crystalluria,hematuria,proteinuria,nephrotic syndrome with oliguria and anuria

-oligospermia and infertility

-agranulocytosis and aplastic anemia and other hematologic disorders

-steven Johnson syndrome,exfoliative dermatitis and anaphylactic reactions

=DRUG INTERRACTIONS

-increased risk of hypoglycemia if concurrently taken with tolbutamide,tolazamide,glibizide,glyburide or chlorpropamide

-increased risk of folate deficiency if patient is on folic acid supplements.

=TEACHING POINTS

-take drugs with food or meals to reduce GIT upsets

-drink eight glasses of water a day

-discontinue drug immediately if hypersensitivity reaction occurs

-offer support and encouragement to deal with side effects of drug therapy including changes in sexual function.

 **==PENICILLINS==**

**a) benzylpenicillins(injectables)**-benzylpenicillin sodium/CP/, Procaine benzyl penicillin(PPF)

Benzathine penicillin/panadur/2.4MU

 **MOA**-Binds to bacterial cell wall causing cell death.Active against;streptococci,pneumococci,H.influenzae,E.coli,Proteus mirabiliss,N.meningitidis,shigella,salmonella,Moraxella catarrhalis.

**INDs-**skin&skin structure infections,OM,sinusitis,RTIs,Genital UTIs,meningitis&septicaemia.

**CIs**-hypersensitivity to penicillins,hepatorenal failure.

**S/Effects**-seizures,D,N&V,hepatic dysfunction,rashes,urticarial,blood dyscrasias,allergic reactions like anaphylaxis.

**b)** **Penicillinase resistant penicillins(narrow spectrum) (antistaphylococcal penicillins)**-oxacillin,flucloxacillin,dicloxacillin,methicillin,nafcillin).

**MOA-**Bind to bacterial cell wall leading to cell death.active against;gram+ive anaerobic cocci,S.aureaus&S.epidermidis.

**INDs**-RTIs-sinusitis,skini&skin structure infections,Bone&joint infections, UTI,endocarditis, septicaemia, meningitis.

**CIs-**Hypersensitivity to penicillins/cephalosporins.

**S/Effects**-seizures,D,N&V,hepatic dysfunction,rashes,urticarial,blood dyscrasias,allergic reactions like anaphylaxis.

**c)** **Aminobenzyl penicillins** (broad spectrum)-ampicillin,amoxicillin,

**d)** phenoxy-penicillins(oral)-pen.v

**e)** **Beta-lactam/beta lactamase inhibitors(broad spectrum**)-augumentin/enhancing-amoxyl 500mg+Clavulanate or clavulunic acid-125mg synergic.fluxavate(amoxyl+ampicillin).

**MOA**-Binds to bacterial cell wall causing cell death.

Active against; streptococci, pneumococci, H.influenzae, E.coli,Proteus mirabiliss,N.meningitidis,shigella,salmonella,Moraxella catarrhalis.

**INDs-**skin&skin structure infections,OM,sinusitis,RTIs,Genital UTIs,meningitis&septicaemia.

**CIs**-hypersensitivity to penicillins,hepatorenal failure.

**S/Effects**-seizures,D,N&V,hepatic dysfunction,rashes,urticarial,blood dyscrasias,allergic reactions like anaphylaxis.

1. **Extended spectrum-ureido penicillins. (antipseudomonal) penicillins**-azlocillin,piperacillin,ticarcillin.

**MOA-**Binds to bacterial cell wall membrane causing cell death. Inhibits beta lactamase an enzyme destroying penicillin.active against gram negative aerobic pathogens&some anaerobic bacterias.

**INDs**- skin&skin structure infections,bone&joint infections,RTIs,Genital UTIs,septicaemia &intra abdominal infections.

**CIs**-hypersensitivity to penicillins&cephalosporins.

S/Effects-seizures in high dose,confusion,lethargy,arrhythmias,CHF,diarrhea,drug induced hepatitis,nausea,hematuria,intestinal nephrites,rashes,urticarial,hypokalemia,hypernatremia,bleeding,blood dyscrasias,pain at IM site,phlebitis at IV site,metabolic alkalosis,hypersensitivity reactions.

=ADVERSE REACTIONS TO PENICILLINS

-can be very painful when given IM and may occasionally cause abscesses

-sensitization rashes may occur after systemic administration.these may be urticarial or erythematous

-rarely,penicillins may cause an acute anaphylactic reaction which may be fatal.

 **==Chlorampenical (CAF)==**

**-broad specrum antibiotic**

**-MOA-**Binds to 50s of bacterial ribosome&bacterial protein synthesis bacteriostatic.

**-Indications**

-meningitis-crosses BBB into CSF,Salmonelliasis,URTI/LRTI,eye&ear infections.

**Contra Indications**

**-**aplastic anemia due to BM depression,renal/hepatic failure,pg,hypersensitivity,newborns/children<2yrs,leucopenia&thrombocytopenia,lactation.

**Side effects**

-anemia due to BM depression, hypersensitivity,reduced WBCs,reduced platelets,grey syndrome.

**Macrolides-**erythromycin 500mg QID 5-7/7,Roxithromycin,clarithromycin 500mg BD 5-10/7,Azithromycin-500mg OD 3/7

**MOA**-Inhibits protein synthesis at the level of the 50s bacterial ribosome.(bacteriostatic). Active against;Gram+ive bacteria;S.aureas,pnemoniae,pyogenes,Gram-ive bacteria-H.influenzae,Moraxella catarrhalis,Neisseria gonorrhea.Others-mycoplasma,legionella,chlamydia trachomatis,Borrelia.

**INDs-URTIs-**streptococcal pharyngitis&tonsillitis,LRTIs-bronchitis&pneumonia,skin&skin structure infections,UTIs to include;Non-gonococcal urethritis,cervicitis,gonorrhea,chancroid.prevention of disseminated mycobacterium complex(MAC) infection in patients with advanced HIV infection.

Prevention of bacterial endocarditis.Eradication of H.Pylori in combination with other drugs(clarithromycin)

 **==Lincosamides==**

-clindamycin 300mg BD 1/12,lincomycin,vancomycin

**MOA-**inhibits protein synthesis in susceptible bacteria at the level of 50s ribosome. Active against;gram+ive aerobic cocci,anaerobic bacteria,bacterial vaginosis&p.carinii,toxoplasma gondii.

**INDS-**complicated bowel/bone surgery infected with anaerobic organisms.

**CIs-**hypersensitivity, hepatorenal failure.

**S/effects**-hypersensitivity,D,N&V.

**DNA Topoisomerases**

**Fluoroquinolones-norfloxacin,**ofloxacin,levofloxacin,moxifloxacin,sparfloxacin,gemifloxacin,nalidix acid-125-500mg OD 3/7 Uncomplicated UTIs in children.

**MOA-**Inhibit bacterial DNA synthesis hence causing death of susceptible bacteria.Gram +ive –staphylococci aureus/epidermides,strep pneumonia,Gram-ive –E.Coli,klebsiella,enterobacter,salmonella,shigella,proteus vulgaris,pseudomonoas aeruginosa,serratia,hemophillus,mycobacterium TB.

**INDs-**UTIs&Gynaecologic infections-gonorrhea,prostatitis,RTIs-sinusitis.

-skin&skin structure infections,bone&joint infections,infectious diarrhea,intraabd infections,peri-op prophylaxis before transurethral procedures,hospital acquired pneumonia.

**CIs**-hypersensitivity,pregnancy,children <18years.

S/Effects-seizures,dizzinesss,drowsiness,headache,insomnia,acute psychoses,agitation,confusion,hallucinations,increased ICP,light headedness,tremors.arrythmias,vasodilation,phepatotoxicity,abd pain,diarrhea,nausea,altered taste,interstitial cystitis,vaginitis,photosensitivity,phototoxicity,hyperglycaemia/hypoglycaemia,local phlebitis at IV site,tendinitis,tendon rupture,hypersensitivity reaction-anaphylaxis.

**Folic acid synthesis-**

**Sulphonamides**-septrin (sulfamethoxazole 400mg+trimethroprim 80mg),sulfasalazine or silver sulfadiazine,sp

**MOA-**PABA inhibitor by interfering with follic acid synthesis.(Bacteriostatic).

**INDs**-Rx of UTIs,URTIs,toxoplasmosis&malaria in combination with other anti-infectives.prophylaxis PLWHA-PCP,diarrhoeal diseases,skin infections.

CIs-hypersensitivity,glucose-6 phosphate dehydrogenase deficiency,pregnancy or lactation of infants(<2mons).

**S/Effects**-ataxia,confusion,dizziness,drowsiness,mental depression,psychosis,restlessness,nausea,anorexia,drug induced hepatitis,unpleasant metallic taste,vomiting.crystalluria.rashes,exfoliative dermatitis,photosensitivity,agranulocytosis,aplastic aneamia,leukopenia,eosinophilia,thrombocytopenia,peripheral neuropathy&hypersensitity reactions,hypoglycemia,hyperglycaemia,hyperkalemia,hypocalcaemia,nephrotoxicity.

**DNA damage-Metronidazole-anaerobic**

**Urinary cleansers**-**Nitrofurans**-nitrofurantoin

MOA-Bacteriostatic

Ind-Uncomplicated UTI in pregnancy.

CI-hypersensitivity hepatorenal failure.

S/Es-metallic taste or altered taste,D,N&V,abd pains,Anorexia,rashes(hypersensitivity),dizziness,headache,drowsiness,photosensitivity,hypoglycaemia.

 **==Antituberculous==**

=streptomycin,rifampicin,isoniazid,pyrazinamide&ethambutol

**Ind**-TB,Leprosy,IPT in PLWHA

 =**CIs**-Hypersensitivity,Hepatorenal failure.

**=AntiTBs** for MDR-capreomycin ,kanamycin amikacin,pyrazinamide

,levofloxacin,cycloserine,Moxifloxacin,Augumentin

**Aims of TB Rx**

-cure patients &prevent suffering&death fromTB.

-Prevent long term complications of TB.

-Prevent relapse of the disease

-Prevent spread or transmission of TB infection.

-prevent devt of drug resistant TB.

**Basic principles of TB treatment**

-Never use single drugs.

-Always use drugs in combinations-FDCs

-Drug dosage based weight.

-Drug intake should be DOT.

-Ensure the entire 6 month rx course is taken.

**Regimen**

Intensive phase-2SRHZE Continuation phase-4RH

 children 2RHZ 4RH

Merits of FDCs

-Reduced risk of resistance/Relapse–Fewer medication errors –fewer prescription errors,increases compliance,reduces cost.**NB-Genexpert is used to detect RH resistance**.

**Basic approaches to prevent drug resistant TB**

-Implementation of good DOTS program.

-Good history taking to choose proper regimen.

-Use of recommended standard Rx regimens.

-Use of FDCs.

-Advocate for free treatment for all TB cases.

-Strict supervision of treatment (DOT) for rifampicin based regimens.

-Improve TB cure in private sector.

**Side effects**

Rifampicin-Red urine,jaundice due to elevated liver enzymes-ALT,AST.Reduces effectiveness of oral hormonal contraceptives by increasing ostrogen breakdown.

Isoniazid-neuropathy or neuritis antidote-pyridoxine(Vit B6) 50mg

Ethambutol-optic nerve damage-blindness.

Pyrazinamide-liver damage,photophobia&gout attack,swelling of eyelids.

Streptomycin-tinnitus,vertigo,deafness

MDR drugs-capreomycin,cycloserine,amikacin,levofloxacillin,clarithromycin,pyrazinamide.

**Nurses responsibility**

-modify lifestyle-smoking,alcoholism,khat chewing.

-drug adherence/compliance (DOT)

-Take drugs after meals.

-advice on side effects like red urine/neuropathy increases adherence.

-Take drugs same time.

-b/diet rich in proteins,energy,fats&vitamins.

-Progress monitoring like sputum/wt.

**ANTI-LEPROTIC**

**Dapsone**

**INDs-all types of lerprosy,toxoplasmosis,mycetoma&malarial prophylaxis esp in PLWHA allergic to septrin.**

 **==Antifungals==**

**-**Rx of fungal infections.

**General actions-**kill(fungicidal) or stop growth of cells (fungistatic) susceptible by affecting the permeability of the fungal CM or protein synthesis within the fungal cell itself.

**1.Local** **topicals**

Nystatin ,Clotrimazole cream,Miconazole gel,Ticonazole

**INDs-**Oral candidiasis,skin fungal infections.

**2.Vaginal-** Clotrimazole pessaries,miconazole,butoconazole,ticonazole.

**MOA**-damages fungal CM allowing leakage of cellular contents.

**INDs-**Rx of vulvovaginal candidiasis.

**CIs**-hypersensitivity ,lactation &1St trimester pregnancy

**S/Effects**-headche,irritations,vulvovaginal burning,hypersensitivity reactions,body pain.

**3.Systemic**- ketoconazole,Intraconazole,Fluconazole,Griseofulvin,Amphotericin B,Flucytosine

**INDs-**Tineal infections-capitis,pedis,versicolor.

**CIs-**hypersensitivity,severe liver disease.

**S/Effects**-dizziness,headache,D,N&V,gastric distress,flatulence,hearing loss,photosensitivity,rashes,leukopenia,hypersensitivity reactions.

 **==Anti-protozoals==**

 **==ANTIHELMINTICS==**

**=antihelmintics are used to reduce or eradicate the number of helmintic parasites in the intestinal tract or tissues of the body.**

**=most antihelmintics are active against specific parasites thus parasites must be identified before treatment is started.**

**A)==ALBENDAZOLE**

**-it is a broad spectrum antihelmintic**

**-it is used for pinworm infection,ascariasis,trichuriasis,strongiloidiasis and infection with both hookworm species**

**-albendazole is also the drug of choice in hydatid disease and cystercicosis**

**=mode of action**

**-albendazole blocks glucose uptake by larval and adult stages of susceptible parasites,depleting their glycogen stores and decreasing formation of ATPs.as a result the parasite is immobilized,detaches from the lumen and dies.**

**-the drug has larvicidal effects in necatoriasis,and ovicidal affects in ascariasis,ancylostomiasis and trichuriasis.**

**-the drug is teratogenic and embryotoxic in some animal species and therefore contraindicated in the first trimester of pregnancy.**

**=clinical uses**

**-ascariasis,trichuriasis,hookworm and pinworm infections**

**-strongyloidosis:400mg twice daily for 3 days (with meals)**

**-hydatid disease:800mg/kg in divided doses,for 3 months**

**-neurocysticercosis:15mg/kg for 8 days**

**-can be given 400mg stat for prophylaxis.**

**-other infections:-at a dosage of between 200-400mg twice daily.**

**-albendazole is a drug of choice in treatment of cutaneous larval migrans(give daily 3-5 days) and in intestinal capillariasis(10 day course)**

**=adverse reactions**

**-mild and transient epigastric distress,diahrroea,headache,nausea and dizziness**

**-in 3months treatment courses,it causes jaundice,nausea,vomiting,abd pain,alopecia,rash or pruritus.**

**B)==DIETHYLCARBAMAZINE CITRATE**

**-diethylcarbamazine is a drug of choice in treatment of filariasis,loiasis and tropical eosinophilia.**

**=mode of action**

**-diethylcarbamazine immobilizes microfilariae and alters their surface structure;making them more susceptible to destruction by host’s defense mechanisms.**

**-the mode of action by diethylcarbamazine against adult worms is uknown.**

**=clinical uses.**

**-wochereria bancrofti (loa loa) :-diethylcarbamazine is the drug of choice for treatment of infections with these parasites given its high therapeutic efficacy and lack of serious toxicity.**

 **-microfilariae of all species are rapidly killed,adults are more slowly killed thus requiring several courses of treatment**

**-onchocerca volvulus :-diethylcarbamazine temporarily kills microfilariae but are poorly effective against adult worms.**

 **-if diethylcarbamazine is used against onchocerciasis,suramin(a toxic drug) must be added to the regimen to kill the adult worms.**

**=Adverse reactions**

**-reactions induced by the drug itself are mild and transient and includes;headache,malaise,anorexia and weakness.**

**-reactions induced by the dying parasites as a result of release of foreign proteins are more severe in sensitized patients.**

**-reactions in onchocerciasis affects the skin and eyes in most patients.vision can be permanently damaged as a result of dying microfilariae in optic discs and retina.**

**-reaction with w.bancrofti and loa loa includes fever,papular rash,headache,cough,chest and muscle pains.**

**c)==IVERMECTIN.**

**=ivermectin is the drug of choice in the treatment of individual or mass infections of onchocerciasis and strongylodiasis.**

**-the drug is rapidly absorped and has wide tissue distribution**

**-it apparently enters the eye slowly and to a limited extent.**

**-excretion of the drug and its metabolites is almost exclusively through the feaces.**

**=Mode of action.**

**-ivermectin paralyses nematodes and athropods by intensifying GABA mediated transmission of signals in peripheral nerves.**

**-in onchocerciasis,ivermectin is microfilaricidal and affects embryogenesis**

**-the mode of action of ivermectin in microfilariae is uncertain.**

**=Clinical uses**

**-onchocerciasis,bancroftian filariasis,strongyloidiasis,scabies and cutaneous larva migrans.**

**=Adverse reactions**

**-the adverse effects of ivermectin are the mazotti reaction which starts on the first day after a single oral dose and peaks on the second day.**

**-the reaction is due to the killing of microfilariae loads**

**-the mazotti reaction includes; fever,headache,dizziness,somnolence,weakness,rash,increased pruritis,diahrrea,joint and muscle pains,hypotension,tachycardia,lymphadenitis and lynphagitis and peripheral edema.**

**-mazotti reaction diminishes with repeated dosing but steroids may be necessary for several days.**

**C)==MEBENDAZOLE.**

**=mebendazole has a broad spectrum of antihelmintic activity and a low incidence of adverse effects.**

**=it is poorly absorbed after oral administration,is rapidly metabolized and excreted mostly in the urine either unchanged or as decarboxylated metabolites.**

**=Mode of action.**

**-mebendazole inhibits microtubule synthesis in nematodes,thus irreversibly impairing glucose uptake.as a result intestinal parasites are immobilized or die slowly.**

**=Clinical uses.**

**=the drug can be taken before or after meals.the tablet should be chewed before swallowing.**

**-pinworm infection:-give 100mgs once,then repeat after 2 and 4 weeks.**

**-ascaris lumbricoides,trichuris trichuria and hookworm infection:-100mg bd for 3 days.or 500mgs stat.**

**-hydatid disease;mebendazole is the alternative.**

**-taeniasis:-in taenia solium infection mebendazole has theoretic advantage over niclosamide in that proglottids are expelled intact.**

**-strongyloidiasis.**

**E)==METRIFONATE.**

**=Metrifonate is a safe alternative drug in the treatment of schistosoma haematobium infections**

**=metrifonate,an organophosphate compound is rapidly absorbed after oral administration.**

**=clearance happens to be through non-enzymatic transformation into its active metabolites(dichlorvos).metrifonate and active metabolites are well distributed in tissues and are completely eliminated in 24-48 hrs.**

**=Aderse reactions.**

**-mild and transient cholinergic symptoms including;nausea and vomiting,diahrrea,abdominal pain,bronchospasm,headache,sweating,fatigue,weakness,dizziness and vertigo.**

**F)==LEVAMIZOLE (KETRAX)**

**=levamizole hydrochloride is highly effective in eradicating ascaris and moderately effective against both species of hookworms’**

**=dosing:-150mg od for 3 days.**

**=side effects**

**-nausea,vomiting,diahrrea due to increased gastric motility and metallic taste.**

**G)==NICLOSAMIDE.**

**=it is a treatment of choice for most tapeworm infections.**

**=it appears to be minimally absorbed from the gastrointestinal tract;neither the drug nor its metabolite has been recovered from blood or urine.**

**=Clinical uses.**

**=niclosamide should be given in the morning on an empty stomach.the tablets should be chewed thoroughly and then swallowed with a glass of water.**

**=effective against;**

**-T.saginata,T.solium and diphyllobotrium latum.**

**-hyrenolepis nana:niclosamide is effective against adult parasites in intestinal lumen.**

**-intestinal fluke infections:niclosamide can be used as alternative.**

**=Adverse reactions**

**-it causes nausea,vomiting and abdominal discormfort.**

**H)==OXAMINIQUINE.**

**=oxaminiquine is used for the treatment of s.mansoni infections.it is effective against both mature and immature stages of s.mansoni parasites.**

**-it has been used extensively for mass treatment.**

**-oxaminiquine is rapidly absorbed orally.**

**=Clinical uses**

**-oxaminiquine is safe and effective in all stages of s.mansoni disease including advanced hepatosplenomegally.**

**-it is better tolerated if given with food although food delays absorption.**

**-in mixed infection of s.mansoni and s.haematobium,oxaminiquine has been used successfully in combination with metrifonate.**

**=Adverse reactions.**

**-central nervous system symptoms are most common.**

**-nausea,vomiting,diahrea,colic,pruritis and urticarial also occurs.**

**I)==PIPERAZINE.**

**=piperazine salts are alternative drugs in management of ascariasis**

**=piperazine is rapidly absorbed from the GIT and maximum plasma levels achieved 2-4 hrs later.**

**=most of the drug is excreted unchanged in urine after 2-6 hrs.**

**=Mode of action.**

**-piperazine causes paralysis of ascaris by blocking acetylcholine at the myoneural junction.**

**-the paralysed roundworms are unable to retain their position in the host and are expelled live by normal peristalsis.**

**=Clinical use**

**-to treat ascariasis’**

**=Adverse reactions**

**-piperazine causes;nausea,vomiting,diahrea,abdominal pain,dizziness and headache.**

**J)==SURAMIN.**

**=suramin is an alternative drug for the eradication of adult parasites of onchocerca volvulus**

**=it is the drug of choice in the treatment of the hemolymphatic stage of African trypanosomiasis due to trypanosome brucei gambiense and trypanosome brucei rhodesiense.**

**=suramin is non-specific inhibitor of many enzymes.toxic reactions are frequent and sometimes severe.**

**=examples are;nausea,vomiting,urticarial,fever,anemia,nephrotoxicity,peripheral neuropathy,jaundice and exfolliative dermatitis.**

**=the drug should be given only under expert guidance.**

**==OTHERS==**

**Pyrantel pamoate**-vermifugen 10mg/kg stat or 3 doses-expel worms from the bowel.

**IND-**Round,hook,pin

**S/effects**- D,N&V,Hypoglycaemia,allergy

**Praziquantel**

**-IND-**schisomiasis-liver,lung&intestinal flukes&tapeworm.

==AMOEBICIDES==

**3.Metronidazole,secnidazole,Tinidazole,ornidazole,Aminosidine(Gabbrol),Entamizole or Dyradem(Metronidazole/diloxanide)**

MOA-disrupts DNA&protein synthesis in susceptible organisms.

INDs-Bactericidal (anaerobes),trichomonacidal,amebicidal,giardiasis

CIs-1st trimester pg,lactation,hypersensitivity

S/E-metallic taste,D,N&V,anorexia,abd pains,hypersensitivity reactions,dizzines,vertigoperipheral neuropathy,convulsions,leukopenia,dark urine,headache,&tiredness.

==LOCAL ANAESTHETICS==

=Cocaine is the only naturally occurring local anaesthetic and was the first one to be used’

=procaine was the first synthetic derivative of cocaine to be used in 1904 before lidocaine was developed during the second world war

=Mechanism of action

-local anaesthetics produce anaesthesia by inhibiting excitation of nerve endings,or by blocking conduction in peripheral nerves by reversibly binding to,and inactivating sodium channels.

-by blocking sodium channels,no action potential can be generated and therefore no sensation will be felt in the area supplied by the nerve.

=Types of local anaesthetics

-there are two broad types;

 (i) amino amides

 (ii) amino esters

1. ==Amino Amides==

 =they have an amide link between the intermediate chain and aromatic end of their structures.

=examples includes;lidocaine,mepivacaine,prilocaine,bupivacaine& etidocaine

=lidocaine is by far the most commonly used’

=they are metabolized in the liver and are very stable in solution

1. ==Amino Esters==

=they have an ester link between the intermediate chain and the aromatic end of their structure.

=they are metabolized in plasma by pseudocholinesterase enzymes

=they are more likely to cause allergic reactions than amino amides’

=examples includes;cocaine,procaine,teracaine,chloroprocaine and benzocaine.

==NOTE==

-local anaesthetics exists in ionized and non-ionized forms.anaesthetic with greater non-ionized form have a faster onset of action,since the non-ionized form is able to diffuse across the nerve membranes and block sodium channels’

-all local anaesthetics except cocaine causes vasoldilation and therefore adrenaline is usually included in local anaesthetic solutions to counteract this.

-bicarbonate is also usually added to local anaesthetic solutions to make them less acidic and lessen patient discormfort during administration.

=ADVERSE REACTIONS.

=adverse reactions may occur as a result of overdose of the drug or from accidental direct intravascular injection of the drug.

=tissue toxicity usually occurs in the cns (neurotoxicity) and in cardiovascular system (myotoxicity)

 **==CARDIOVASCULAR SYSTEM==**

**=antihypertensives,digitalis,antiangina**

**==Antihypertensive Drugs==**

**Rationale for use:**

=Minimize complications; stroke,heart failure,renal diseases, peripheral vascular disease, and

Coronary artery disease

=Prolong life by coping mechanisms like modify life styles.

**Strategies**

**=they act by targeting;**

**-Sympathetic vagal tone (heart rate &cardiac output)**-Beta&alpha adrenergic blockers,central acting drugs.

**-Body fluid volume** - Diuretics, ACE inhibitors,

**-Peripheral resistance**-sympathoplegics,calcium channel blockers,diuretics &direct vasodilarors.

**Antihypertensive Drugs**

**=Centrally acting –**Methyldopa (Aldomet),&clonidine

=CLONIDINE

**MOA**=Blocks presynaptic and adrenoceptors inhibiting synthesis of norepinephrine &epinephrine lowering heart rate and blood volume.

**IND=**Mild-moderate HTN,Reduce left ventricular hypertrophy,PET-Pgcy related HTN.

**S/Effects**=sedation,dizziness,low libido,edema,anxiety,nightmares,vivid dreams,thrombocytopenia,drowsiness,dryness of the mouth,headache,diarhoea,hypoprolactinemia,N&V,orthostatic HTN,stuffy nose, bradycardia.

=ALPHA METHYLDOPA

Pro-drug converted to alphamethyl-noradrenaline, which activates presynaptic alpha2 adrenoceptors in the

medulla vasomotor centre, mainly lowers PVR.it also inhibits renin secretion. Used in mild-to-moderate HTN.

Decreases left ventricular (LV) hypertrophy.

**Adverse effects**: sedation, dizziness, decreased libido, edema, positive Coombs' (hemolysis).

Safe in renal dysfunction and in pregnancy.

**=Direct Acting(Vasodilators)** ;Hydralazine(apresoline)-inj, Nitroprusside ,Minoxidil-oral

MOA-Reduce PVR by arteriolar dilatation or direct vasodilation of blood vessels

.INDs-mod-severe HTN,CHF,severe aortic insufficiency&after valve replacement.

**CIs**-high output CHF,RHD,idiopathic SLE(systemic lupus erythematosus),Severe tachycardia,rheumatoid arthritis,hypersensitivity,hypotension.

 **S/effects**-headche,flushing,sweating,fluid retention(oedema), tachycardia, hypotension, palpitations,angina&hirsutism.

**=Diuretics=**

 **–**inhibit Na&water reabsorption hence excretion.1st choice in Rx mild-moderate HTN.

1. **Loop diuretics-**frusemide or furosemide(Lasix)-20-100mg,Torsemide-20-200mg,bumetanide.

**MOA-**inhibits reabsorption of NA+CL ions in proximal&distal convoluted tubules and at loop of Henle thereby lowering blood volume.

**INDs**-oedema , CHF,oliguria due to renal failure,mild-moderate HTN,barbiturate poisoning,breast engorgement in failed b/feeding,hepatorenal failure.

**CIs**-hypersensitivity,early pg,anuria.

**s/effects-**hypokalemia,hypomagnesia,hyponatremia,hyperglycaemia,tinnitus&deafness,headache,orthostatic hypotension,fatigue.

**DI-**aminoglycosides,anticoagulants,digitalis,thiazides, and NSAIDS.

 **2.Thiazides**-Hydrochlorthiazide-50mg,Bendroflumethiazide-5mg,chlorthalidone-50mg

 ,chlorthiazide-50mg.

**MOA-**inhibits reabsorption of NACL ions in the cortical thick ascending limb of loop Henle&distal tubules lowering BV.

IND-essential HTN,Oedema,Nephrogenic DI,Breast engorgement due to no b/feeding,hypercalciuria

**CIs**-Severe renal failure,hepatic failure,pg-fetal toxicity,hypokalemia,hypomagnesia,hyponatremia,hyperglycaemia-decreases glucose tolerance.

**S/effects-** hypokalemia,hypomagnesia,hyponatremia,fatique,orthostatic hypotension,allergic rashes,defeaness,tinnitus.

 **3. Potassium sparing diuretics-**spironolactone(aldactone)-100mg OD,Eplerenone,Amiloride

**MOA-**antagonist of aldosterone.Acts by competitively binding of receptors at aldosterone dependent Na,k exchange site in the distal convoluted renal tubule hence increased levels of Na&water to be excreted while potassium retained.

**INDs-**essential HTN, Hyperaldosteronism,adjunct therapy in oedema ass with CHF,nephrotic syndrome,hepatic cirrhosis,Rx of hypokalemia,hirsutism,PMS short term ,Rx of acne vulgaris,precocious puberty.

**CIs**-Allergy,hyperkalemia,lactation,hepatorenal impairment,addisons disease.

**s/effects-**dizziness,headache,drowsiness,ataxia,fatique,confusion,dry mouth,diarrhea,thirst,hyperkalemia,hyponatremia,gynaecomastia,deepening of voice,impotence,irregular menses,post menopausal bleeding,amenorhoea

 **4. Osmotic diuretics-mannitol,urea**

**MOA-**act at proximal convoluted tubule&oppose action of ADH.

**IND-**cerebral oedema,elevated ICP in head injury,prophylaxis&Rx of oliguric phase of acute renal failure,elevated IOP,prophylaxis of hemolysis during transurethral prostatic resection or transurethral surgical prostatectomy.

 **CI**-CCF,pulmonary oedema.

**S/effects**-expansion in blood volume,chills or fever,chest pain,fast heartbeat,difficulty in micturation,pulmonary congestion,renal failure,oedema of lower limbs,thrombophlebitis at injection site.

 **5. Carbonic anhydrase inhibitors-**acetazolamide(Diamox),methazolamide

**MOA**-Enzyme inhibitor-(carbonic anhydrase) by reversibly catalyzing reaction of hydration of co2&carbonic acid or blocks caHCO3 reabsorption and causes diuresis.

-reduces aqueous humour secretion on the eye hence lowering IOP(intra ocular pressure)

**Ind-**chronic simple(open angle) glaucoma,secondary glaucoma,acute glaucoma,drug induced oedema,hypercalcemia,DI,HTN,Nephrotic syndrome,Rxin acute mountain sickness,Adjuvant in treatment of epilepsy&Rx of metabolic&respiratory alkalosis.

**CIs-**Hypersensitivity,severe renal/hepatic impairment,adrenocorticoid insufficiency,severe pulmonary obstruction,hypokalemia,hyponatremia.

**S/Eefects-**drowsiness,rashes,crystalluria,Bone marrow depression,loss of appetite,flaccid paralysis,glycosuria,hepatic impairment,fever,allergic reaction,impotence/sexual dysfunction

Dry mouth,sedation, sexual dysfunction,

**=Calcium Channel Antagonists or Blockers (CCAs)**

**short acting**-nifedipine,nicardipine,diltiazen.

**Long acting**-felodipine,amlodipine Verapamil-angina&cardiac arrhythmias.

**MOA**-Inhibits influx of calcium ions into the cardiac cells slowing conductivity and contractility of the heart.

**IND**-angina pectoris,mild-mod HTN.

**CI-**renal&hepatic impairment,pregnancy&lactation.Hypersensitivity.

**S/effects**- postural hypotension,incontinence,flushing,N&V,headache,oedema,fatigue, dizziness,erythema multiforms,muscle cramps,myalgia&sensitivity reaction.

**=ACE Inhibitors-**Low levels of BP,blood volume&Na ions causes production of renin by the juxtaglomerular cells in the kidneys which then converts angiotensinogen produced by the liver&lungs to angiotensin I. ACE (angiotensin converting enzyme) produced in the lungs converts AG I to AG II-a Potent vasoconstrictor raising

BP.Renin also Stimulates aldosterone secretion from adrenal glands which increases H20&Na reabsorption in the kidneys thus increasing BV&BP.

**Drugs**-captopril-5mg, Enalapril-5mg, Lisinopril, Ramipril.

**MOA**-prevents conversion of AGI-AGII hence reducing or inhibiting vasoconstriction.

**IND-**Mild-moderate HTN,CHF,diabetic nephropathy in IDDM by reducing proteinuria,after myocardial infarction.

**CIs-** Low Bp**,** Renal failure, pregnancy, porphyria, hypersensitivity. Gout

**S/Effects-**persistent dry cough by blocking kinases in the lungs that breakdown bradykinin which accumulates &irritates bronchioles,voice changes,chest pain,taste disturbances,,bronchospasms,blood dyscrasias,tachycardia,anaphylactic reactions-rash,hepatorenal impairment,hypotension,sleep disturbances,flushing&impotence.hypercalemia in pts with renal disease or taking K+Sparing diuretics

**=Angiotensin Receptor blockers(ARBs)/Angitensin II Antagonists-sartan** drugs-Losartan -50mg OD,candesartan-16-32mg OD,Valsartan-80mg OD,Telmisartan-40mg OD (**LOCAVATE)**

**MOA-**Block effects of AG II by inhibiting vasoconstriction & aldosterone secretion.

**IND**-HTN,prevention of diabetic nephropathy(Renal damage) in DM.

**CIs-**Renal failure,pregnancy,hypotension,hypersensitivity,Gout.

**S/effects-**rebound HTN,Alkalosis,hypokalemia,

hypotension,hyperkalemia,jaundice,angioedema,metallic taste,dizziness,headache,pharyngitis,rhinitis.

cough(dry),A-angioedema,P-proteinuria,T-taste changes,H-hypotension,fetotoxicity,Rashes,increased K+levels,L-low AGII&Aldosterone levels.

**Nurses responsibility**

**-**Monitor BP regularly,

-Modify lifestyle-smoking,lcohol&miraa chewing.

-Low fat/ salt diet

-Drug compliance,

-H/educate on s/effects increases compliance.

-comply with MOPC for follow up.

-Reduce wt if obese by exercise.

-Administer drugs using 6 rights

**=BetaBlockers-**Reduce cardiac outputby lowering heart rate.

**(i)Cardio-selective beta blockers-**Atenolol,Esmolol,metoprolol,Acebutolol.

**(ii)Non-selective beta blockers-(b1-heart&b2-bronchioles receptors)-**Propranolol,nadolol,Timolol,pindolol.

(iii) **Combined alpha&beta blockers-**Labetolol

**(iv)Combined beta1blocker&beta2 stimula**nt-carvedilol,celiprolol.

**MOA**- reduce cardiac output hence lowering BP.Blocks activity of alpha,beta1(slow HR)&beta2(blood vessels) receptors hence vasodilation &subsequent lowering Bp.Also block Ca2+ions to the cardiac cells&blood vessels.

**IND**-migraine prevention,Angina,MI,mild-moderate HTN,Cardiac arrhythmias,CHF-Cervedilol.

**CIs-**Hx of asthma (bronchospasm),cardiogenic shock due heart failure exacerbation,phaeochromocytoma,bradycardia,metabolic acidosis,hypoglycaemia,hypotension.

**S/Effects-**renal damage,allergic reactions,bradycardia,chestpain, dizziness, dyspnea,oedema,hypotension,wtincrease,syncope,syncope,fever,hematuria,hepatic injury.

**Nurses role**

-emphasize on drug compliance

-modify lifestyle

-exercise if obese

-regular Bp monitoring

- Advise on side effects.

- and diet low in fats&salts.

**Antidote of overdose-Glucagon**

**=SYMPATHOPLEGICS**

**-/Sympathetic Blocking drugs or agents/Alpha blockers**

**=Short acting-Prazosin,**

**=Long acting; Doxazosin,Terazosin .**

**MOA**-Reduce Sympathetic tone hence block vasoconstrictive effects on blood vessels leading to vasodilation.

**INDs**-Moderate to severe HTN,benign prostate hypertrophy-improves urine flow,

**CIs-**Hypotension,hypersensitivity,1st trimester pg

**S/E**-postural hypotension,urinary incontinence in women.

**=Digitallis/cardiac glycosides-**drugs used for heart failure

Digoxin-0.125-0.75mg.

Digitoxin

**Aims of Rx**

Increase efficiency&output of the heart

Reduce congestion&oedema

Remove factors causing heart failure.

**MOA**-increases intracellular ca2+ ions by allowing entry to the myocardial cells during depolarization via Na+/k+ATPase pumping mechanism.

**This has 3 effects**;

-**positive inotropic** action by increasing myocardial contractility subsequently increasing renal perfusion (direct effect)

 -**Negative chronotropic**-slows heart rate by increasing activity of vagus nerve (indirect effect).

 - **Negative dromotropic**-slows conduction velocity at AV node&bundle of His (indirect effect).

**IND**-CHF, atrial flutter (atria conducting at higher speed-240-300/min),

 -Atrial fibrillation-atria contractions of 450/min.

 -Cardiogenic shock,supraventricular arrhythmias-slows conduction at AV node&bundle of HIS.

**CIs-**Ventricular fibrillation,ventricular tachycardia,beriberi heart disease,allergic reactions, complete heart block.

**s/effects-**anorexia,N&V,visual disturbances,gynaecomastia,bradycardia.

**Nurses role-**

Correct dose,ensure.

take pulse regularly when administering the drug if <60b/min withhold drug.,

monitor for toxicity signs-coloured urine&confusion in elderly,

modify lifestyle,low salt/fat diet.

**Antiangina –**cardiac ischaemia **(assignment)**

Nitroglycerin

 **=ANTI-MALARIALS=**

**=there are four types of plasmodia that causes malaria;p.vivax,p.falciparum,p.ovale and p.malariae.**

**=humans are infected with sporozoites from an infected mosquito,on entering the bloodstream they migrate to the liver before going thru a 3 phase life cycle:1.pre-erythrocytic stage**

 **2.erythrocytic stage**

 **3.development of sexual forms**

**=drugs are therefore designed to eradicate them at the various stages,and against the various species.**

 **==plasmodium parasite life cycle==**

**-the mosquito becomes infected by taking human blood infected with parasites in gametocyte stage(sexual form)**

**-the sporozoites that develop in the mosquito are then inoculated into humans at its next feeding.**

**-in the pre-erythrocytic stage,the sporozoites multiply in the liver to form tissue schizonts.**

**-then the parasites escapes from the liver into bloodstream as merozoites**

**-merozoites invade red blood cells,multiply in them to form blood schizonts and finally rupture the cells to release a new crop of merozoites,that will then invade new red blood cells.this cycle may be repeated many times.(erythrocytic stage)**

**-some schizonts develop into gametocytes which are then released into circulation where they may be taken in by another mosquito.(sexual stage)**

**-p.falciparum and p.malariae have only one cycle of liver cell invasion and multiplication,thus liver infection ceases spontaneously in less than four weeks.then multiplication is continued in the red blood cells.**

**-so treatment that eliminates these species from the red blood cells four or more weeks after inoculation of the sporozoites will cure these infections.**

**-in p.vivax and p.ovale infections however,sporozoites also induce in the hepatic cells formation of hypnozoites(dormant form) which will cause subsequent relapses of the infection.**

**-therefore,treatment that eradicates parasites from both the red blood cells and the liver is required to cure these infections.**

**=CLINICAL CLASSIFICATIONS-ANTIMALARIALS**

**i)true causal prophylactics**

**-destroys the sporozoites before they enter the host’s reticuloendothelial cells.**

**-they are currently not available**

**ii)causal prophylactics**

**-these drugs prevent the maturation of,or destroys the sporozoites within the infected hepatic cells and thus prevent erythrocytic invasion**

**-they are also known as primary tissue schizonticides**

**=examples are :primaquine,pyrimethamine and proguanil which are effective against p.falciparum**

**iii)suppressives**

**-these drugs inhibits erythrocytic schizogony and prevent the rapture of the infected erythrocytes**

**-this leads to relief of fever and chills but does not eradicate the parasites**

**=examples includes:**

**(a)Rapidly acting;quinine,4-aminoquinolones,mefloquine,artemisinin&atovaquone**

**(a)slowly acting;proguanil,pyrimethamine,sulfadoxine&tetracycline**

**-treatment with suppressives can cure p.falciparum but relapse can occur in p.vivax which has hypnozoites**

**iv)Radical curatives**

**-these drugs eradicates both erythrocytic and secondary exoerythrocytic schizogony so that relapse does not occur.**

**-they are used for radical cure of p.vivax malaria**

**=examples are;primaquine and proguanil**

**v)gametocytocidal drugs**

**-the suppressives like chloroquine,quinine and artesunate are effective against gametocytes of all species except p.falciparum**

**-primaquine however is effective against gametocytes of all species**

**-proguanil and pyrimethamine are known as sporonticidal drugs:they donnot kill gametocytes but prevent their development in the mosquito.**

**=CHEMICAL CLASSIFICATION-ANTIMALARIALS**

**i)Cinchona alkaloids;quinine,quinidine**

**ii)quinolone derivatives:**

**a)4-aminoquinolones;chloroquine,amodiaquine,**

**pyronaridine**

**b)8-aminoquinolones;primaquine,tafenoquine,**

**bulaquine.**

**c)quinolone methanol;mefloquine.**

**iii)phenantrine methanols;halofantrine,lumefantrine**

**iv)antifolates**

**(a)biguanides;proguanil**

**(b)diaminopyrimidines;pyrimethamine**

**(c)sulfonamides;sulfadoxine**

**v)artemisinin compounds; =artesunate,artheter,artemeter**

**vi)antimicrobials;doxycycline,clindamycin,tetracycline,atovaquone.**

==QUININE==

=Is an alkaloid derived from the bark of the cinchona tree.it is the drug of choice for cerebral malaria and chloroquine resistant p.falciparum.

 =Pharmacological action

=it is useful only as a suppressive but is gametocidal to all species except p.falciparum

=it has been termed as a general protoplasmic poison;it depresses various enzymatic processes,reduces cilliary activity and inhibits phagocytosis and the growth of fibroblasts in the plasmodia.

=it has no action against sporozoites,the pre-erythrocytic stage and hypnozoites.

 =Adverse reactions

=local irritant action-pain,edema,reactive fibrosis

=is very bitter and can cause nausea,vomiting &epigastric pain

=depresses the myocardium leading to bradycardia,hypotension,cardiac arrest

=cinchonism with prolonged use-tinnitus,nausea,visual impairment,headache etc

=idiosyncrasy-flushing,angioneurotic oedema,or asthmatic attack

=black water fever-acute intravascular hemolysis,hemoglobinuria,fever and acute renal failure(p.falciparum)

=hypoglycemia-by releasing insulin from the pancrease

 =pharmacokinetics

=administered orally,it is almost completely and rapidly absorbed from the small intestines;it’s plasma levels peaks at 1-3 hrs.

=it crosses the placental barrier

=it is metabolized in the liver and has a half-life of about 10hrs.

=it is prolonged in acute stage of falciparum infection because of hepatic impairment

=about 5% appears in urine unchanged.

 =dose

=tablets:quinine hydrochloride or sulfate-300-600mgs

=quinine sulfate injection iv or im-300-600 mgs.

==4- AMINOQUINOLONES==

 =CHLOROQUINE&AMODIAQUINE=

=MOA

=Malarial parasites digest haemoglobin in their lysosomes to utilize amino acids.the released heme is toxic to the plasmodia, but is converted by parasitic polymerase to non-toxic hemozoin.amodiaquin just like chloroquine,binds to released heme ,thus preventing polymerization. This results in oxidative damage to organelles of the parasites,causing death.

=PHARMACOLOGICAL ACTIONS

=As a suppressive it is superior to quinine.

= It kills the erythrocytic forms of p.vivax and p.falciparum.is also effective against gametocytes of p.vivax,p.ovale and p.malariae.

=however it has no effect against the sporozoites,the pre-erythrocytic stage and the hypnozoites.

=Resistance has developed against chloroquine by p.falciparum due to an efflux mechanism whereby the parasite pumps the drug out of its cell.this resistance affects all the 4-aminoquinolones.

=other antiparasitc actions includes,effective in giardiasis,taeniasis and extra-intestinal amoebiasis

=it also has some anti-inflamatory,antihistaminic and local anaesthetic effects.

=however it is a direct cardiac depressant and may cause hypotension.

=it is widely distributed in the body and therefore a loading dose is necessary to initiate therapy

=ADVERSE REACTIONS

=It is a relatively safe drug

=however it can cause nausea and vomiting when used as an antimalarial.

=when used for prolonged periods as in management of RA,it can cause more severe effects like;skin rashes,angioneuritic edema,photosensitivity,exfoliative dermatitis and bleaching of hair.

=visual impairments,acute psychotic episodes,seizures and cardiac arrest can also occur.

=DOSE

=loading dose of 1gm then 500mgs daily for 2 days.

 ==8-AMINOQUINOLONES==

=PRIMAQUINE

=They are effective against the persistent tissue forms(hypnozoites) of p.vivax and gametocytes and hepatic schizonts of all the plasmodia species.

=it kills a proportion of gametocytes in blood and renders the rest incapable of further maturation in the mosquito

=it is ineffective against schizonts of p.falciparum and therefore cannot be given as a suppressant but is given in conjunction with a 4-aminoquinolone for radical cure of p.vivax infection.

=ADVERSE REACTIONS

=At the recommended dosage,toxicity is uncommon ,but may include;

=epigastric distress and abdominal cramps-take with or after meals

=may cause mild anaemia and leucopenia,cyanosis and agranulocytosis.

=it can cause intravascular hemolysis in patients with G6PD deficiency

=it is usually given 15mgs(2tabs) daily for 14 days togather with chloroquin for 3 days.

=proguanil potentiates its toxicity

 ==QUINOLINE METHANOL==

=MEFLOQUINE=

=MOA is similar to chloroquin

=it is effective against the erythrocytic stage.

=it is highly effective as a single dose against p.falciparum including chloroquin and MDR strains.

=can be given 12 hrs after quinine,but quinine cannot be given after because mefloquine has a long half life and both are cardio-toxic.

=has no effect on hypnozoites

=is tightly protein bound and has a very long half life of about 20 days.

=it is excreted in feces

=ADVERSE REACTIONS

=GI disturbances-D,N&V,abdominal pain

=affective disorders,anxiety and hallucination

=bradycardia and sinus arrhythmia

=it is teratogenic in the first trimester,and pregnancy should be avoided for atleast 3 months after mefloquin Rx.

=DOSE:

=750mgs(3tabs) single dose or may be repeated 6hrs later.

==PHENANTRENE METHANOLS==

=HALOFANTRENE

=It is a blood schizonticide

=very effective against chloroquine resistant p.falciparum

=MOA is similar to the other quinolones

=it has a half life of 1-2 days

=it is give in three doses of 500mgs 6hrs apart.

=LUMEFANTRINE=is structurally similar to quinine and is usually given in conjunction with arthemeter

 ==BIGUANIDES==

=PROGUANIL

=Proguanil is a prodrug.it is converted into its active form cycloguanil in the body.

=they bind to enzyme dihydrofolate reductase; which is responsible for conversion of folic acid to folinic acid.defficiency of folinic acid prevents completion of schizogony.

=since sulfonamides prevents conversion of PABA into folic acid,they synergise with the antimalarial effects of proguanil.

=it is an effective schizonticide against both p.vivax&falciparum

=prevents the development of gametes encysted in the gut wall of the mosquito and is useful in sporonticidal prophylaxis

=ADVERSE REACTIONS ; are rare but may include;gastrointestinal disturbances,stomatitis,and mouth ulcers.reduction in leucocytes megaloblastic anemia may also result.

=MALARONE is a combination of proguanil 100mg with atovaquone 250mg. used to treat MDR falciparum malaria

 ==DIAMINOPYRIMIDINES==

=PYRIMETHAMINES=

=It is selectively toxic to the malarial parasites by selectively binding to its dihydrofolate reductase.it is more potent than proguanil.

=its antimalarial activity is enhanced by combination with sulfonamides(eg fansidar)

=Pharmacokinetics

= it is slowly but completely absorbed from the small intestines then is extensively metabolized and then slowly excreted by the kidneys.

=a single dose of 25mg persists in plasma and is slowly excreted in urine for more than 14 days.

=Adverse reactions

=it is a relatively safe drug even in pregnancy

=may cause GI disturbances,ataxia and megaloblastic anemia which responds to folic acid

=Therapeutic use

=antimalarial in combinations:

-Pyrimethamine 25mgs+sulfadoxine 500mgs(fansidar)

-pyrimethamine 25mgs +sulfadimethopyrazine 500mgs(metakelfin)

=a combination of pyrimethamine 12.5mgs and dapsone 100mgs(maloprim) is used as a prophylactic for p.falciparum.

=Toxoplasmosis mgx: use pyrimethamine 25mgs BD then 25 mgs OD for one month togather with sulfadiazine 4gms daily.

=SULFONAMIDES

=have a different mechanism of action

=they are effective against the asexual forms of the parasites but their action is slow requiring thei combination with pyrimethamine

=sulfadoxine have a long half life of 200hrs.and is used in combination with pyrimethamine.

 ==ARTEMISININ COMPOUNDS==

=ARTEMISININ=

=This is obtained from the Chinese plant ;Artemisia annuta.which has been used in china for over 2000 years to treat fever.

=artemisinin is lipophilic and is poorly soluble in wter.other derrivatives include artether and artemeter which are both lipid soluble and artesunate which is water soluble.

=Mechanism of action

=Artemisinin compounds covalently bind to parasitic proteins.intraparasitic heme iron catalyses cleavage of endoperoxide bridge in artemisinin.The resultant free radicals damage parasitic proteins.

=They act mainly as blood schizonticides against all malarial parasites including those resistant to chloroquin.

=Pharmacokinetics

=Orally they are well absorbed and are metabolized into their active form;dihydro-artemisinin.

=half life of artesunate is short-23 mins while that of artemether is about 45 mins.this is a major disadvantage.

=Adverse reactions

=nausea,vomiting,abdominal pain,anorexia and leucopenia.

=higher doses mayproduce bradycardia and distortion of the cardiac cycle.

=they are contraindicated in pregnancy,lactation and in immuno-compromised individuals.

=Preparations and dosage

(i)=artesunate 50mg tabs(falcigo)

=artesunate IM injection contains 60mgs.give 120 mgs on day one, followed by 60mgs 12 hrs later then 60mgs daily for the next four days.

(ii)=artether(E-mal).is a synthetic ethyl derivative of artemisinin.dose is 150mgs IM OD for 3 consecutive days.

(iii)=artemether(paluther).is available as an injection containing 80mgs/ml in arachis oil.dose is 80mgs first day then 80mgs od for 5 days.

(iv)=they are also available as suppositories

 ==ANTIMICROBIALS==

=DOXICYCLINE

=has a slow but potent action against blood schizonts and the primary exo-erythrocytic forms of p.falciparum including those resistant to chloroquin and proguanil.

=it is used in combination in rssitant cases.

=ATOVAQUONE

=This is a highly lipophilic hydroxynapthoquinone compound which has potent action against ;p.jiroveci,plasmodia and T.gondii.

=it acts by selectively interfering with mitochondrial electron transport in susceptible parasites.

=its absorption is slow and incomplete, but may be increased threefold by fatty food.

=its plasma t1/2 is 2-3 days and is excreted mostly unchanged in feaces

=they are never used alone due to risk of resistance developing.

=Adverse reactions

=includes fever,vomiting,anorexia,headache,diahrrea,dose related maculopapular rash,anemia and neutropenia.

=Therapeutic uses

=proguanil potentiates antimalarial activity of atovaquone.atovaquone+proguanil(malarone) is useful as a prophylactic against p.falciparum and ind in treating MDR malaria

=it is more effective than mefloquine.for prophylaxis dose is 1 tablet daily taken with food,for treatment of MDR malaria it is 4 tabs as a single dose for 3 days.

= in p.jiroveci pneumonia associated with AIDS dose is 750mgs tds for 21 days.

=it is also used in treatment of txoplasmosis.

 ==HEMATINICS==

 (i)=IRON=

=Is used in iron deficiency anemia

=iron is absorped in the upper small intestine from food sources witth the help of HCL acid,is combined with transferrin and transported to the bone marrow for erythropoiesis.

=some are also transported to the liver for storage as ferritin.

=IRON PREPARATIONS.

=Iron is usually given orally to treat deficiency and should give a rise in blood Hb of atleast 0.7mg/dl per week.

=treatment should be continued for 4 months after the blood haemoglobin level has returned to normal to replace depleted iron stores.

=they are also given in pregnancy when the iron requirements increase.

1. Ferrous sulphate tablets

=are a satisfactory way of giving iron to most people

=ferrous salts are rapidly oxidized to ferric salts in the air and therefore are given as coated tablets.

=therapeutic dose is 200mgs tds

=Adverse effects includes;gastric discormfort,nausea or diarrhea or sometimes constipation.

=keep away from reach of children because of their sugar-coating which tempts children to overdose.

1. Ferrous gluconate

=it is less irritating to the stomach than most ferrous salts.

 =ferrous glycine sulphate is another preparation of ferrous sulphate and amino acid glycine. It is the least irritative to the stomach and has liquid preparations.

1. Iron sorbital

=is an iron preparation for IM injection.it is rapidly absorped from the injection site

=it contains 50mgs of iron per ml. solution

=side effects may include shock-like reactions and care should be taken when injecting not to stain the skin.

 (II)=COBALAMINS=(VIT B12)

=Works togather with folic acid to regulate formation of red blood cells and promote the utilization of iron

=its major sources are;milk, eggs, clams, liver and kidneys

=vit b12 is absorped in the intestine with the help of intrinsic factor produced in the stomach.lack of this factor will lead to vit B12 defficiency.

=vit B12 defficiency will result in pernicious or addison’s anaemia where there are large and irregular erythrocytes in shape and size.accompanied by glossitis and degenerative changes in the CNS.

=Treatment is to give cobalamin by injection.there are Two types of cobalamins;-cyanocobalamin

 -hydroxocobalamin

=hydroxocobalamin is now the drug of choice because of its long half life

=Therapeutic use

=For pernicious anaemia without neurological involvement;give 1mg IM.three times weekly for two weeks,followed by 1mg every 3 months.

=For pernicious anaemia and other macrocytic anaemias with neurological involvement;give 1mg on alternate days until there is no further improvement,followed by 1mg ever 2 months.

 (iii)=FOLIC ACID=

=Folic acid is obtained from animal and vegetable sources and is also synthesized by gut bacteria.it is necessary for maturation of red blood cells.

=deficiency will result in symptoms similar to pernicious anaemia.and neural tube defects.

=common causes of deficiency are malabsorptionsyndromes caused by diseases like coeliac disease and in pregnancy.

=Preparations

=includes folic acid tablets or a combination of ferrous fumarate+folic acid tablets

=Therapeutic use

=folic aci d can be given orally in doses of 15mg daily.

=combinations containing ferrous fumarate 100mgs+folic acid 350mcgs are currently in use mch.dose being 1 tab. Daily.

 (iv)=EPOETINS=

=Erythropoietin is a hormone produced in the kidney and is necessary for erythrocyte formation.in renal failure, their levels fall resulting in anaemia.

=Epoetin is an analogue of erythropoietin and is synthesized by recombinant DNA technology to produce two forms:alpha and beta available commercially

=In patients with renal failure and anaemia,epoietin is given 3 times weekly by SC or IV until satisfactory hb level is achieved.

=Treatment then continues with a maintenance dose

=Darbepoetin is a modified form of epoetin with a longer half life hence less frequency of administration.

=Adverse effects

=hypertension is fairly common and may be severe

=BP should be taken weekly in initial stages of treatment then at 6weekly intervals.

=Thrombosis and flu-like symptoms ocassionally occur.

**Circulatory system**-

1. **Coagulants**-promote blood clotting process by hepatic synthesis of clotting factors.

**Vitamin k. has 2** forms**-Vit K1-**phytonadione or phylloquinone or phytomenadione-plant sources

 **vit K2-**menaquinone-animal sources

 - intestinal bacteria(E.Coli) synthesise vit k2 .

MOA-promotes hepatic synthesis of clotting factors II,VII,IX&X used for synthesis of prothrombin-thrombin,fibrinogen-fibrin.

**INDs**-prophylaxis&Rx of hemorrhagic disease on Newborn (HDN) due to insufficient maternal stores&poor passage to newborn via placenta.

-Mx of overdose of anticoagulants-warfarin.

-pts with fat-mal absorption/fat soluble vitamin disorders.

-Rx&prophylaxis of various coagulation disorders due to impaired synthesis in the liver of factors;II,VII,IX&X.

-Impaired activity of Vit K (Hypoprothrombinemia) due to coumarin-warfarin.

**CIs-**allergy to vit K,Liver function impairment,kernicterus in children,hemolytic aneamia,premature infants –menadiol.

**S/Effects**-anaphylaxis,cyanosis,dizziness,profuse sweating,rapid weak pulse,hemolytic anemia&liver toxicity.

1. **Anticoagulants-**drugs that interfere or inhibit clotting factors**.**

coumarin oral –warfarin 5-15mg OD & Phenindione

**MOA**-interfere with synthesis of vit K depedent clotting factors VII,IX,X,XI.

 **IND**s-prophylaxis&Rx of venous thrombosis

 –Rx of atrial fibrillation with embolization in CHF.

-Prophylaxis&Rx of PE.

-Transcient ischaemic attacks.

**CIs**-Hypersensitivity,active PUD,severe liver disease&renal failure.

-1st trimester of pg due to teratogenic effect.

**S/effects**-hemorrhage,thrombocytopenia,skin rashes,fever,jaundice(phenindione)&fetal abnormalities.

**DIs-**increased by antibiotics,ASA,Alcohol,cimetidine,phenytoin.

 -reduced by barbiturates.

 **Antidote**-Vit K.

 **Parenteral**-**heparin** &Hirudin-bivalirudin&lepirudin (used in the UK)

**Heparin-**20-40mg sc or infusion in 1L of N/S or dextrose.

**MOA**-inhibits coagulation by binding to antithrombin III which regulates blood clotting factors XII,XI,IX rendering them inactive hence prolonging clotting time(time taken for blood or plasma to coagulate).

**INDs** –prevention &Rx of venous thrombosis.

 -PE (thromboembolism)-blood clot in lungs.

 -Prevention of venous thrombosis related to surgical complicationslike hip&knee replacement due to immobility.

 -Unstable angina.

**CIs**-hypersensitivity,hepatorenal failure,thrombocytopenia,severe hypertension,active PUD,active bleeding,hemophilia,purpura,intracranial hemorrhage,active TB&threatened abortion.

**S/Effects**-hemorrhage due to overdosage

 -hemorrhagic shock.

 -thrombocytopenia,alopecia,osteoporosis,skin necrosis,spontaneous #s,mineralocorticoid def due to prolonged used.

**Antidote**-protamine sulphate IV-causes hypotension.

**Nurses roles-**Admnister rt dose overdosage leads to hemorrhage

 **-**advise pt to avoid traumatic activities involving sharp objects,sports increases risk of bleeding.  **-**Avoid OTC drugs-ASA increases effect of heparin.

  **-**Report to hosp immediately in case of injury.

  **-**pt should carry name tag for easy notificationtion&assistance in case of an accident.

 -DON'T use razor blades for shaving esp in men

  **-**Regular monitoring of prothrombin time&INR (International Normalized Ratio)=pts prothrombin time/normal prothrombin time(2.0-3.5)>5 risks of bleeding.pt-time taken for clotting to occur in asample of blood+thromboplastin&ca added.

 **-**comply with MOPC for follow up.

**Antiretrovirals**

**Antiviral drugs-**Acyclovir,famciclovir,valacyclovir&amantadine.

**MOA-**Inhibits viral DNA replication to RNA Strand.

**IND-**ISS,prophylaxis in herpes simplex virus,prophylaxis herpes zoster HSV-1(Oral)&HSV-2(Genital)-800mgx5x7/7,herpes zoster (shingles) ophthalmic branch of trigeminal nerve affected&short course of varicella (chicken pox) especially in ISS patients.

 **CIs**-hypersensitivity,S/Effects-skin rashes,fatique,GI disturbances-D,N&V,headache,vitiligo

**HAART**-Highly active anti-retroviral therapy-d4t+3tc, AZT+3TC

 -Reduces resistance,cost,increases adherence&improves coping with compliance/s/effects.

**NRTIs-**didanosine,lamivudine,stavudine,zalcitabine,zidovudine.

**MOA-**Inhibits viral RNA/DNA synthesis &subsequent viral replication.

**INDs-**Mx of HIV in combination with other ARVs,Pmtct,PEP,HEI

**NNRTIs-**delavirdine,efavirenz,niverapine.

**MOA**-Binds to reverse transcriptase inhibiting viral DNA synthesis.

**INDs**- Mx of HIV in combination with other ARVs.

-prophylaxis in HEIs.(NVP),Pmtct

**Protease inhibitors-**Indinavir,nelfinavir,ritonavir,saquinavir,lopinavir.

**MOA-**Inhibits the action of HIV protease and prevents the cleavage of viral polyproteins.

**Fusion inhibitors-**enfuvirtide

**MOA-**binds to viral glycoprotein subunit &hence block viral fusion with CD4 receptors of host cells and thus viral entry to the cells.

**CIs-**hypersensitivity,hepatorenal failure,severe anemia.

**S/Effects**;headache,D,N&V,BM suppression,insomnia,

**Antitumour/anticancer drugs**

**Main classes**

 **i)**Cytotoxic drugs-kill dividing cells

 ii)Sex hormones&Hormone antagonists-diethylstilbestrol,tamoxine

 iii)Immunotherapy-steroids-prednisolone

 iv)other immunomodulating drugs

 I)CYTOTOXIC DRUGS.

 =Cytotoxic drugs-kill dividing cells,toxic to cancer cells&healthy dividing body cells. Consists of;

**1.Alkylating agents** chlormethine (mustine),ifosfamide,busulfan,melphalan,cyclophosphamide,chlorambucil, lomustine, carmustine, estramustine (chlormethine+ostrogen)

**MOA**-interfere with DNA replication&transcription of RNA,damage or kill the cell&healthy body cells.

**INDs** chlormethine(mastine)-hodgkins disease.rarely used due to toxicity

cyclophosphamide-malignant lymphomas, hodgkins disease,lymphatic lymphoma,burkitts lymphoma,multiple myeloma,leukemias,ovarian carcinoma,retinoblastoma.

Chlorambucil-chronic lymphatic leukemia,malignant lymphomas, hodgkins disease,walden strom’s macroglobulinemia

Busulfan-chronic myeloid leukamia

**CIs**-hypersensitivity,hepatorenal damage.

**S/Effects-**

**=**Bone Marrow depression,Diahrroeah,Nausea&Vomitting,Oral ulceration,tremors,muscular twitching,confusion,agitation,ataxia,hallucinations,Steven Jhonson syndrome,jaundice,peripheral neuropathy,lung fibrosis,infertility&gynaecomastia.

**2.Cytotoxic antibiotics**

 =These are derived from anthracycline glycosides a/b produced by the Streptomyces.these includes; Doxorubicin,epirubicin,daunorubicin,bleomycin,dactinomycin,mitomycin,idarubicin.

MOA

=Inhibits DNA dependent RNA synthesis involved in cell replication.They act either by acting directly on the DNA,or by blocking the enzymes in DNA replication eg topoisomerase II,or through both actions.

ADVERSE EFFECTS

=similar to those of alkylating agents.

**3.Antimetabolites**

=methotrexate,Fluorouracil,mercaptopurine,cladribine,fludarabine,cytarabine,tegafur,raltitrexed,capecitabine

MOA

=Inhibit production of cell nuclear material from folic acid.many resemble purines and pyrimidines which are the building blocks of DNA.They become incorporated in the growing strand and stop the process.

INDICATIONs

= Immunosuppresant in Rheumatoid Athritis&psoriasis, gestational choriocarcinoma,hydatidiform mole,acute lymphocytic leukamia,breast cancer,lung cancer,non-Hodgkin's lymphoma,hydroxyurea,sickle cell crisis and chronic myelonous leukemia.

CONTRA INDICATIONS

=1st trimester Pregnancy,hepatorenal failure,hypersensitivity

SIDE EFFECTS

=Bone marrow depression,anemia,Dhiareah,Nausea&Vomitting,dizziness,hematemesis,headache,blurred vision,pruritus,alopecia,ecchymosis,acne,GI ulceration.

**4.Vinca alkaloids**

=vinblastine,vincristine,vinorelbine,vindesine.

MOA

=Inhibits DNA dependent RNA replication.

INDICATIONS

=Hodkins disease,Leukemias,Malignant lymphomas,neuroblastoma,Whilms tumour,Aids related karposis Sarcoma,small cell lung cancer,advanced breast cancer.

CONTRA-INDICATIONS.

=Hypersensitivity,Ist trimester pg,severe hepatorenal failure.

SIDE EFFECTS.

=fatigue,back pain,arthralgia,dyspepsia,anorexia,bleeding,hepatotoxicity,peripheral oedema,anorexia,D,N&V,abd pain,constipation,dyspnea,abd pain.alopecia,polyuria,dysuria,Bone marrow depression,muscle wasting.

5.TAXANES.

=Paclitacel(taxol) and docetaxel

=they are derived from the plant yew

MOA

=They inhibit cell division

INDICATIONS

=Treatment of ovarian and breast cancer when the other regimens have failed

=patients are usually given a steroid and an anti-histamine before infusion because of its side effects.

SIDE EFFECTS

=Depressed blood count,flushing,rashes,dyspnea and collapse.

6.CAMPOTHECINS

=Irinotecan and topotescan

=they are chemicaly related to taxanes

MOA

=They inhibit cancer growth by inhibiting topoisomerase I,used in DNA replication.

INDICATIONS

=Advanced colorectal and metastatic ovarian cancer.

SIDE EFFECTS

=Gastrointestinal upsets and myelosupression.

II)SEX HORMONES AND HORMONE ANTAGONISTS

A)HORMONES

=Consists of both estrogens and androgens depending on the sex of the patient

=Estrogens-Diethylstilbestrol,Ethinylestradiol,Fosfestrol and progestogens

=Androdens-testosterone,testosterone enantate,testosterone propionate,testosterone undecanoate and mesterolone.

MOA

=Most reproductive system cancers are dependent on sex hormones for growth and are halted when opposite sex hormones are administered

INDICATIONS

=Prostate cancer,endometrial cancer,renal cell carcinoma,breast cancer,

IND-prostate cancer,Postmenopausal women with breast cancer.

S/E-Oedema,Nausea,gynaecomastia,impotence,Dvt,

Hormone antagonists-Tamoxifen,Toremifene

MOA-Estrogen receptor antagonists.

INDs-Advanced breast Ca, gynaecomastia,endometrial carcinoma

CIs-Hypersensitivity,Hepatorenal failure,pregnancy,lactation

S/E-Oedema,nausea,flushing,bone pain,hypercalcamia,

Immunosuppresants-immunotherapy-minimize inflammatory process.

prednisolone,prednisone,methyl prednisolone.

ASSIGNMENT

**Fibrinolytics**-reteplase,streptokinase

**Antiplateletes-**aspirin MOA-inhibits COX-1 hence inactivation of thromboxane (A2) plateletsaggregation.

**cholesterol lowering agents/antihypercholestrolaemia**.

**1.statins (HMG-COA)-Administered at night due to bile formation**

-atorvatatin/ezetimide,fluvastatins,simvastatin,pravastatin,rosavastatin,lovastatin.

MOA-block synthesis of cholesterol in the liver lowering blood levels.

**2. Bile acid binding resins-**cholestyramine XENATIDE, Colestipol.Suppress glucagon release&reduce appetite.

MOA-Combine with bile acids&cholesterol in the gut preventing absorption&increasing elimination hence lowering blood cholesterol levels.

3. Fibrates-Bezafibrate,Ciprofibrate,Clofibrate,Fenofibrate,Gemfibrozil

MOA-Alter metabolism of lipoproteins lowering blood cholesterol&triglycerides

**GIT System**

**-Antiulcers/PUD**- production of HCL&Pepsin is by stimulation of vagus nerve-release of ach which increases secretion of HCL. Distension of stomach by food causes production of gastrin-parietal cells to produce HCL.

Both mechanisms mediated by histamine from histaminocytes H2 receptors.it stimulates proton pump in parietal cells to produce hcl.

**Aims of Rx**

-Reduce acidity hence

relieving pain&help in healing process.

-Protect ulcer from further damage by acid-sucralfate,bismuth chelate(cytoprotective agents)

-Eradicate H.Pylori infection.(H. pylori kit)

-Discourage or avoid use of NSAIDS.

**Drug classification**

**1.Antacids-**mg trisillicate(actal),AL Hydroxide(alugel),mg hydroxide,na bicarbonate.

**2.Histamine H2 receptor blockers/antihistamines**- cimetidine(Tagamet),famotidine,nizatidine,ranitidine(Zantac)

**Ind** -GERD,Zollinger Ellison syndrome

 -Hypersecretion of HCL.

 -Adjunct in RX to eliminate H.Pylori.

 -PUD associated with NSAIDS.

**CIs**-hypersensitivity,hepatorenal failure.

**S/Effects**-D,N&V,Headache,rashes,alopecia,muscle weakness,gynaecomasticia,jaundice,galactorrhea,confusion,hallucinations-elderly

**3.Proton pumb inhibitors**-Lansoprazole,omeprazole,pantoprazole,esomeprazole,rabeprazole.

**MOA**-inhibition of stimulation of proton pump in parietal cells hence producing HCL is inhibited.

 **Ind**-conditions unresponsive to H2 blockers

 -GERD,Zollinger Ellison syndrome

 -Hypersecretion of HCL.

 -Adjunct in RX to eliminate H.Pylori.

 -PUD associated with NSAIDS.

**CIs**-hypersensitivity,hepatorenal failure,pregnancy

**4. Eradication of H.Pylori(H pylori kit)**-A normal flora bacteria of the stomach.that normally causes PUD.Involves use of various triple drug therapies.

-omeprezole+metronidazole+amoxyl(1 week)

-Omeprazole+clarithromycin+amoxicillin(1 week but more expensive)

-Omeprazole+clarithromycin+metronidazole(1 week)

-Ranitidine+amoxicillin+metronidazole(2 weeks.cheapest but takes longer)

**5. Prostaglandins inhibitors**-misoprostol-inhibits prostaglandins hence relieving pain.

Inhibits PgE1 synthesis which increases bicarbonate secretion&inhibits Hcl secretion.

**6.Adjuncts**-antispasmodics-camylofin,clinidium bromide(chlordiazepoxide)

**Nurses responsibility-**modify lifestyle

 -stop NSAIDS

 -H/educate on side effects

 -cimetidine-reduces fertility in men by lowering testosterone

 -avoid stimulants, avoid coated drugs, use of pillow.

**-Laxatives/purgatives/lubricants/anticonstipation/Aperients-**drugs that loosen bowel in case of constipation.

**Classification**

**1.Bulk forming**-Bran ,ispaghula husk(isogel),cellulose. \_increases fecal mass thus stimulating peristalsis

**2.stimulant laxatives**-glycerin, docusate Na, bisacodyl (Dulcolax).

Increase intestinal motility causing abd. cramps. Mainly used in Rx of constipation due to narcotic or opioid analgesics.

**3.stool or feacal softeners**-medicinal liquid paraffin-.Lubricates impacted feaces &promote bowel action.

**4. osmotic laxatives**-MgSo4,lactulose,glycerine suppositories-.They promote bowel output by osmotic effect.

**General uses-**short term RX of constipation, evacuation of the colon for bowel &rectal exam.

-fecal impaction.

-Prophylactically in pts who need not to strain while defecating

-hemorrhoids, bowel syndrome, spastic colon.

-pre-op for barium enema.

**CIs-**IO, Undiagnosed abd condition or acute abdomen. atony. Hypersensitivity.

**s/effects**-excessive bowel activity-diarrhoea ,abd pain/cramps, N&V, flatulence

**Adverse s/effects or of abuse**-diarrhoea, -lipoid pneumonia ie liquid paraffin,abd pain

**Nursing responsibilities=**

**-**Hx taking to R/O IO diarrhea.

-high fibre diet. increase fluid intake.

-avoid prolonged intake of purgatives due to dependence.

**Antidiarrhoeals.**

-several drugs may act to reduce peristaltic activity during diahrreal bouts.

A)ANTICHOLINERGIC DRUGS.

MOA- Decreases the gastrointestinal tone by blocking the action of the parasympathetic nervous system.they are particularly useful when spasms of the colon is involved.

-examples are atropine, hyoscine(scopolamine) and their derivatives eg oxybutynin,flavoxate,tolteridine etc.

B)OPIOIDS.

MOA- Opioids actually increases the GIT tone but reduces peristalsis thus controlling diahrroeah.they are therefore not recommended when there are GIT spasms.

C) CO-PHENOTROPE(LOMOTIL)

MOA- This is a combination of atropine and diphenoxylate hydrochloride and therefore incorporates their respective mechanisms of action.diphenoxylate is an opioid derivative.

-this drug is a widely used anti-diahreal for adults and older children,but caution should be taken to avoid overdose which will result in respiratory depression.

D)LOPERAMIDE

MOA- Loperamide decreases large intestine motility thus curtailing diahrrea.they have the highest therapeutic index and can be sold over the counter.

ANTIEMETICS

=These are drugs used to control vomiting. It is believed that; Ach,histamine(h1),dopamine and 5-HT(5-hydroxytryptamine)neurotransmitters acts on the CTZ and vomiting centre in the brain to induce vomiting. Antiemetics therefore targets to block their respective receptors.

i)MUSCARINIC ACH.RECEPTOR ANTAGONISTS.

MOA-Eg hyoscine-blocks the action of acetylcholine on the vomiting centre and is useful for the short-term control of motion sickness.

-can be administered orally or transdermally as a patch behind the ear before beginning of a journey.

SIDE EFFECTS-drowsiness,blurred vision,paralysis of ocular accommodation.

ii)ANTIHISTAMINES(H1 RECEPTOR BLOCKERS)

Examples-cyclizine,promethazine,cinnarizine.

MOA-They block the action of histamine on its receptors.most of the antihistamines also block Ach receptors making them very effective antiemetics.

-they are particularly useful in hyperemesis gravidarum,sea sickness other conditions like menieres disease.

-usually doesn’t cause significant sedation.

iii)DOPAMINE ANTAGONISTS.

Examples- prochlorperazine,chlorpromazine,haloperidol,levopromazine,domperidone and metoclopramide.

MOA- most are of the phenothiazine group.they are powerful antiemetics due to their ability to block the effects of dopamine on the chemoreceptor trigger zone(CTZ).But most are none specific and therefore have other psychoactive uses like sedation and antipsychotic effects.

=prochlorperazine; suppresses opioid-induced vomiting and can be given orally or IM,but not subcutaneous.if given IV it must be well diluted before use.

=chlorpromazine;is similar in action to prochloperazine

=haloperidol;is also similar but is longer acting and less sedating.

=levomepromazine; is used particularly in terminal care to reduce vomiting and reduce agitation

=domperidone;is less sedative than chlorpromazine and less likely to produce dystonic reactions than metoclopramide because its action in the CNS is only confined to the CTZ,it also enhances gastric emptying.howver,only oral formulations are available and yet its first pass metabolism is 85%;therefore only 15%reaches systemic circulation.It is therefore only used to suppress vomiting that accompanies long term treatment with opioids,levodopa and mildly emetic cytotoxic drugs.

=metoclopramide;increases gastric tone and dilates the duodenum.this causes the stomach to empty more quickly.it also has some CNS action on the vomiting centre.it can be administered orally or IM.

-it is used postoperatively,in opioid induced vomiting and in management of migraines.in very large doses it also blocks 5-HT receptors and is therefore used to prevent vomiting due to cytotoxic drugs.

-adverse reactions are rare with metoclopramide but may include,dystonia of the facial and neck muscles which can be controlled by us e of diazepam.prolonged use however can cause tardive dyskinesia.

iv) 5-HT ANTAGONISTS.

Examples: ondansetron and granisetron

MOA-They block the 5-HT receptors associated with the central connections of the vagus nerve in the brain stem near the CTZ.

=they are used to prevent vomiting in patients receiving highly emetic cytotoxic drugs like cisplatin which releases 5-HT.

V) CANNABINOIDS

Examples: nabilone

MOA- cannabinoids are derivatives of cannabis sativa and have been demonstrated to have antiemetic,sedative and sometimes causes mental confusion.

=they have been used in patients receiving cytotoxic drugs

=cannabis sativa itself is currently illegal in Kenya and cannot be used.

vi)OTHERS

Examples:

=Betahistine; its use is confined to menieres disease in which vertigo and vomiting is due to disturbances in the inner ear.MOA-it lowers pressure in the inner ear thus relieve symptoms.

=dexamethasone& benzodiazepines may be used as adjuncts to other antiemetics.

MAJOR ADVERSE EFFECTS OF DOPAMINE ANTAGONISTS

=Jaundice –this occurs with chlorpromazine due to blocking of bile canaliculi in the liver.recovery occurs when the drug is stopped

=parkinsonism;akathisia,dystonia or tardive dyskinesia in which case administer an anticholinergic

=low leucocyte count

=skin rashes

=low blood pressure

=dry mouth

=weight gain(gynaecomastia)

**Endocrine system**-steroids/corticosteroids (adrenal cortex) 1-mineralocorticoids-Aldosterone increases water&Na absorption=HTN

2.-glucocorticoids(corticosteroids)

**Natural -**cortisol,cortisone

**Synthetic-**betam

ethasone,prednisolone,prednisone,methyl prednisolone-deprofost(inj),hydroctisone 200mg,dexamethasone 10mg ,fludrocortisone-inhaler

3.adrenal sex hormones(androgens)-testosterone-virilism

**Physiological effects of steroids**

Raise blood sugar-anabolic effect-gluconeogenesis-production of glucose from non carbohydrate.

 -catabolic-lipolysis-breakdown of fat or muscle tissue to mobilize glucose

Promotes survival response to stress-(general adaptation syndrome-GAS).

COMPONENTS

i) alarm reaction by release of adrenaline&nor-adrenaline stimulate steroids release.

ii) Resistance to the stress leads to prolonged effects of cortisol in stimulating gluconeogenesis-liver&lipolysis-muscle tissue.

iii) Exhaustion-prolonged use of sterois or stress leads to muscle wasting, immune suppression&atrophy of tissues,hyperglycaemia,gastric ulceration,vascular damage&reduced sensitivity to insulin**.(pathological use of steroids)-refer page-205-207**

**clinical use/indications**

**-**anti-inflammatory-SLE,polyarthritis nodosa,R/A or OA-Prednisolone.

-Antiallergic action-asthma-hydrocortisone,beclometasone-inhaler,hay fever,eczema.

-suppression of immunity in organ transplant to prevent rejection

.-antitumour agents(immunotherapy) cancers-brain tumours-dexa,prednisolone.-iodiopathic thrombocytopenic purpura,acute hemolytic anemia-nephrotic syndrome, shock(cardiogenic/anaphylactic)

**CIs**-hypersensitivity,Obesity,DM,Osteoporosis,hepatorenal damage.

S/E-prolonged use;atrophy of adrenal cortex,hyperglycaemia,oedema,immunosuppression,gastric ulceration,suppresion of stress response,growth retardation in children,skin thinning,acne&striae,

Bone thinning&osteoporosis,muscle weakness&wasting,euphoria,mon face,hirsutism,high Bp.

**Antidiabetics-**

Glucagon,adrenaline,glucocorticoids-**hyperglycaemic** agents.

-insulin-only endocrine hormone ie-**hypoglycaemic** agent.protein hormone produced from pancreatic beta cells stimulated by glucose.sources-pancrease of cows bovine& pigs porcine.

**Actions/effects of insulin or MOA of insulin**

Binds to specific receptors on the cell membranes&trigger cell response.

-Stimulate uptake of glucose by the tissues (adipose).

-Convert glucose to glucagon for storage in the liver.

-Increase production of energy from fats(lipolysis)&proteins (gluconeogenesis) from the skeletal muscle.

**INDs**-IDDM,DKA

 **CIs-**Hypersensitivity, hypoglycaemia, pg

**S/effects-**hypoglycaemia-faintness,dizziness,tremors,restlessness,palpitations,sweating,abnormal behavior,convulsions,coma&death.

**Types of insulin**

**Short acting insulin-**rapid action after 30mins&continues for 8hrs.used in emergencies like DKA.

Soluble insulin-humulin&human actrapid.insulin aspart&glulisine.

**Intermmediate acting insulin**-rapid onset after 1-2hrs &lasts for 16-24hrs.OD or BD daily.InsulinZinc suspension,Biphasic isophane insulin-human mixtard.

**Long acting insulin**-action after 6hrs&lasts 24-30hrs.OD.Protamine Zinc insulin(bovine insulin),human ultratard,insulin detemir.

**Nurses role**

Regular glucose monitoring-FBs,RBs&HbA1C-glycosylated red blood cells(normal-<8.8%).

-modify lifestyle –h/educate pt on longterm medication - h/educate pt on side effects like hypoglycaemia. -h/educate pt on importance of MOPC follow up.-importance of avoiding injuries to lower limbs.-importance of eating first before injecting insulin.

**OHA-insulin secretagogues-**promote insulin release from beta cells of the pancrease.

Sulphonylureas

-**1st gen**-Acetohexamide,chlorpropamide(diabenese)250-750mg OD,BD,Tolbutamide,Tolazamide,glibenclamide-5-10mg OD

 **2nd gen**-Glipizide-2.5-5mg OD,Glyburide,gliclazide

 3rd generation-Glimiperide-4mg OD.

**MOA**-increase insulin synthesis or production by pancreatic beta cells lowering blood glucose levels.Increase sensitivity of tissues to insulin.

**INDs**-NIDDM or type 2 DM,Maturity onset type 2 DM,Uncomplicated or non-ketonic DM.CIs-DKA/juvenile DM-Young pts requiring insulin.Hypersensitivity,renal/hepatic failure,hypoglycaemia.

**S/effects**-GI upsets,blood dyscrasias,fluid retention-oedema,hypoglycaemia,headache,dizziness,hyponatremia,parasthesia,photosensitivity.

**Insulin sensitizers-Biguanides-metformin/glucomet/Glucophage**

**MOA-**Reduce glucose absorption from GIT.Stimulate uptake of glucose into muscle.Inhibit gluconeogenesis-biosynthesis of glucose from non carbohydrate source eg amino acids.

Reduce glucose release from liver.

**INDs**-combined with sulphonylureas in NIDDM.

**CIs-**hypersensitivity,DKA,hypoglycaemia.

**S/Effects**-hypoglycaemia,neuropathy due to interference with Vit B 12 absorption.

**Thiazolidinediones**-glitazones(pioplitazone,rosiglitazone)

MOA-increase insulin sensitivity to the tissues.effective after a meal.

**IDs-**NIDDM.

**CIs**-hypersensitivity,liver/renal failure,pg,B/F,pts on insulin.

**S/Effects**-hypoglycaemia,jaundice,GI disturbance.

**Prandial glucose**-Nateglinide,Repaglinide

**MOA**-Stimulate insulin release from pancrease.

**INDs**-NIDDM.

**CIs**-hypoglycaemia,hepatorenal damage.

**S/effects**-loss of appetite,nausea,drowsiness,vomiting&shock

**Alpha glucosidase inhibitor**-miglitol,Acarbose-Oligosaccharride obtained from fermentation process of micro organism actinoplanes utahensis.

**MOA**-Is enzyme inhibitor of intestinal&glucosidase which converts CHO to glucose.inhibits digestion of complex CHO eg sucrose &starches preventing absorption.

**INDs**-adjunct in Rx NIDDM.

**CIs-**Hypoglycaemia, Hypersensitivity.

**S/effects-**Hypoglycaemia,flatulence,diarrhea.

**Nurses roles-**Ensure regular glucose monitoring eg FBS.

 -Advise pts to take drugs after a meal.

 -Drug compliance due to long term intake of medication.

 -Advise on diet-high fibre/plenty of water/lo w salt.

**Antithyroid/antihyperthyroidism** drugs.

=Hyperthyroidism leads to increased metabolic rate and is manifested by;

-excess T3 and T4 in the bloodstream

-raised temperature and sweating

-excessive sensitivity to heat

-nervousness and tremors

-susceptibility to fatigue

-tachycardia

-weight loss with associated increase in appetite

-exopthalmosis.

TYPES OF GOITRE

1.Graves disease(diffuse toxic or exophthalmic goiter)-autoimmune disease (LATS)

2.Toxic nodular goiter-due to a tumour

3.Non-toxic nodular goiter-dietary insufficiency of iodine.

=Hyperthyroidism, also called thyrotoxicosis can lead to a thyroid crisis in an acute severe attack,and is a medical emergency.

TREATMENT OF THYROTOXICOSIS.

=Surgery (thyroidectomy) may be necessary but medications are usually started first.The following drugs are usually used:

a) aqueous iodine solution(lugols solution)

b) radioactive iodine

c) thiourylenes

1. AQUEOUS IODINE SOLUTION

=Also called lugols solution, is administered orally and is metabolized in the body to iodide ion which temporarily inhibits thyroid hormone release.

=The thyroid looses some of its vascularity,and is therefore good preoperatively.

=S/Es—allergic effects eg;

-thyroid d gland shrinks and looses its vascularity

-is usually used as a premed.before sugery

-doesn’t taste pleasant and should be taken with food

=ADVERSE EFFECTS-patients may develop allergic responses like skin rashes,sneezing,lacrimation,conjunctivitis and salivary gland pain.

1. RADIO-IODINE

=Radio-active iodine is a radioactive isotope of iodine.as it decays to a more stable form,it emits powerful rays that kills cells undergoing cell division. Its actions are mainly concentrated on the thyroid gland.

=administration-radioactive iodine is given orally and is rapidly absorbed from the stomach and intestines.

=mechanism of action- it is taken up by the thyroid and incorporated into the thyroglobulin where it stops production of the thyroid hormone. Its prolonged usage usually leads to hypothyroidism which can be treated with administration of thyroxine.

=precautions-radioactive iodine should not be used to treat thyrotoxicosis during pregnancy and breastfeeding.

-not recommended for use in children and young women.

-care when handling urine and excreta as they will be radio-active.

1. THE THIOUREYLENES

=These drugs comprises of;

 -carbimazole

 -thiamazole

 -propylthiouracil

=MOA- These drugs act by inhibiting thyroid hormone production, possibly by preventing the oxidation of iodide to iodine.

-in addition, propylthiouracil blocks the conversion of T4 to T3 in target tissues.

=Dosage= carbimazole-20 to 60mg bd, thiamazole and propylthiouracil-300-900mg od.

=Therapeutic uses

\_Thioureylenes are given orally.

\_ after administration, carbimazole is rapidly metabolized in the blood to thiamazole which has a half-life of 5-15 hrs. but its effects may not be felt upto 2 months due to pre-circulating T3 and T4 in blood.

\_ the drug is usually continued upto 18 months but at a reduced dose gradually then finally stopped.

\_ about 60% of the patients will remain well albeit with still enlarged thyroid while the rest may relapse and require further management.

=Adverse effects.

-These includes;joint pains, rashes, enlarged lymph nodes and fever

- transient leukopenia and mild agranulocytosis may occur

- carbimazole should be given with care to pregnant and lactating mothers because it can depress the fetal and infant thyroid leading to goiter and hypothyroidism.

**Nurses responsibility**-High iodine salt diet,

 -Comply medication,

 -Comply with follow up at SOPC

 -Advice on drug side effects.

**HYPOTHYROIDISM**

**=** Thyroid deficiency means a reduced availability to the body of thyroid hormone and can result from:

-impairment of the TRH-TSH system of the brain and pituitary

- insufficient iodine in the diet (simple/non-toxic goiter)

-hashimoto”s disease (an autoimmunological disorder where the body reacts against thyroglobulin or any other protein in the thyroid gland)

- overtreatment with radio-active iodine in managing thyroid tumours.

- hypothyiroidism leads to MYXOEDEMA

SYMPTOMS

=mental impairment

=slow or slurred speech and deep low voice

=bradycardia

=lethargy

=sensitivity to cold

Coarse,dry skin

CRETINISM

= If severe thyroid deficiency occurs in infants from birth and is left untreated for long, cretinism will result.

= This is characterized by; stunted growth, dwarfism, mental retardation and coarsened facial features and skin.

= It is also called congenital hypothyroidism.

TREATMENT OF HYPOTHYROIDISM

=Hypothyroidism is treated either by increasing iodine in diet and/or with T3 or T4 both of which are available as oral tablets.

= two drugs are currently available for management of hypothyroidism

 -levothyroxine

 -liothyronine

a)LEVOTHYROXINE

= This is a pure hormone synthetically prepared for long time treatment.it is an oral formulation whose effects are seen after about 10 days.

=if given to patients with cretinism or myxoedema, they return to normal metabolic function

=early initiation of treatment in newborn infants is recommended to avoid irreversible changes of cretinism

=in myxedema,it is very important to start with small doses to avoid overstimulation of the heart leading to arrhythmias and angina pain.

=Early in treatment,the patient should be kept warm,hypnotics should be avoided and constipation should be relieved.

b)LIOTHYRONINE

=This is the official name for triiodothyronine(T3).

=its actions are similar to those of thyroxine but has a more rapid onset of action at 3 days.

=liothyronine is not as effective as thyroxine in treating myxedema but is useful if rapid onset of action is required.

=in both myxedema and cretinism, life-long treatment is necessary.

 == ANAESTHESIA==

=there are two types of anaesthesia;

 -general

 -local

 = GENERAL ANAESTHETHICS.

 =Some of the earlier includes;

-ether

-nitrous oxide(laughing gas)

-chloroform

 ==PRE-OPERATIVE ASSESSMENT.

=Medical history should be properly taken

- -previous drug history

 -use of any drugs for a chronic disease

 -pre-existing medical condition

-=pre-operative Exam to include ;

 -take bp

 -locate pulse and position

 -monitor the lungs;-auscultate and do an x-ray as ordered

 -ECG

 -Examination for any carotid bruit

 -heart murmurs

 -rule out rheumatoid arthritis complications

 -do necessary blood tests.-LFTS,FHGM….\

 ==PREMEDICATION

 OBJECTIVES

-To relieve anxiety

-to reduce production of saliva

-Reduce gastric motility

-increase GIT ph.

PRE-MEDICATIONS.

=ANXIOLYTICS

-mainly given an hour to two before surgery.

-main purpose is to

a)relieve anxiety

b)reduce the production of saliva

c)maintain nitrogen balance in the GIT.

=DRUGS

-several drugs can be used to include; tamezapam,midazolam,diazepam and lorazepam.

-majorly benzodianzebines

-opioids can also be used for terminally ill patients.

=SALIVA REDUCTIION

 =Atropine is the drug of choice.

 -usually given IM but can be given oral to paeds

 -oral dose is about twice the parenteral route

 -it crosses the blood brain barrier but CNS effects are minimal.

 =Glycopyrronium may be given IV before induction of anaesthesia

 -cannot be given orally

 -is fast acting –given when ROA is needed.

 =Hyoscine-is effective in reducing secretions

 -no longer widely used because of its marked sedation effect

 -it also causes confusion and restlessness to the elderly.

=GIT CONTROL

 =There is need to reduce the volume and increase the PH of gastric contents pre-ops.

 -this reduces the risk of vomiting,and aspirationa.

 =metoclopramide hastens gastric emptying.

 -it is given in the morning of,or afew hours before surgery

 -can be oral or IV

 =sodium citrate raises the PH of gastric secretions by neutralizing acid in the stomach

 -it is given orally 30 mins before surgery

 =ranitidine also raises the gastric PH.

 -it is an h2 receptor blocker that reduces acid secretion

 -it is given on the night before or on the morning of the operation

 -can be given orally or IV

=INTRAVENOUS INDUCTION AGENTS.

 =THIOPENTAL.

-unconciousness occurs about 20secs after adminnstration and continues for 5-10mins.

-the drug is then redistributed from the brain into muscles and fat leading to loss of its effects.

-it has a long half-life and is therefore not recommended for long term usage as it would lead to prolonged sleepiness and unconsciousness when discontinued.

=SIDE EFFECTS.

-loss of muscle control leads to respiratory depression and apnoea

-it causes bradycardia due to reduction in peripheral resistance

-the bradycardia may be marked if the drug is given;too rapidly,too large dose,to an elderly patient or to a cardiac or hypovolaemic patient.

-accidental intra-arterial injection will lead to severe pain in the area distal to the site,arterial spasms,loss of peripheral pulse or permanent ischemic damage.

-injection extravascular can also cause tissue damage.

=ETOMIDATE

-it was first used in 1973

-it is more quickly metabolized

-it has minimal effect on BP and therefore recommended for use in cardiac patients

-it is however not commonly used.

=PROPOFOL

-generally used since 1986

-recovery from its effects is more complete and rapid than any other induction agent

-it is recommended for short and day surgeries

-it can be used for prolonged anaesthesia by low dose IV infusion

-it is painful on injection and is usually mixed with lidocaine.

=KETAMINE

=Ketamine is unique amongst all the induction agents in that;

-it can be given IV and IM

-it has a potent analgesic effect leading to dissociative analgesia

-muscle tone is maintained hence no respiratory depression and no need for intubation

-it causes a rise in blood pressure thus useful in children with cardiac diseases

-during recovery, emergence phenomena occurs (unpleasant nightmares and hallucinations).

 ==MAINTENANCE ANAESTHESIA

= INHALATIONAL ANAESTHETHICS

1. Nitrous Oxide

-also called the laughing gas

-it causes some patients to laugh hysterically if used on its own

-it is a weak anaesthetic and needs to be used with other inhalational or intravenous drugs

-it has a strong analgesic effects in sub-anesthetic doses

B)Etonox

-is a 50:50 mixture of nitrous oxide and oxygen

-it is used for pain relief in labour wards and ambulances

-it is also used in short but potentially painful procedures like very painful dressings.

1. Halothane,enflurane ,isoflurane and sevoflurane

-are potent halogenated hydrocarbons

-they are also called volatile anaesthetic agents since they are liquid at room temperature but their vapour is inhaled for anaesthesia

-they require a carrier gas,usually oxygen or etonox

-unlike NO ,they have no analgesic effect in sub-anesthetic concentrations

-halothane is the oldest but is seldom used because it causes cardiac arrhythmias/hepatitis

-isoflurane is the most commonly used,it is associated with rapid recovery from anesthesia with minimal cardiac effects

-sevoflurane is the most expensive and is most preffered for children.

-ether used to be popular but is no longer used clinically but in laboratories because of slow induction,delayed recovery and an unpleasant smell.it is also explosive.

=SHORT ACTING OPIOID ANALGESICS

 -Eg fentanyl, alfentanil and remifentanil. Antidote/reversal agent is naloxone

 ==MUSCLE RELAXANTS

=There are three main indications for administration of muscle relaxants in surgery

 i)to facilitate intubation of trachea at the beginning of surgery

 ii)to relax muscles sufficiently to facilitate surgical incisions

 iii)to permit artificial ventilation by relaxing respiratory muscles.

=There are two classes of muscle relaxants depending on their action at the neuromuscular junction

1. Non-depolarising/competitive
2. Depolarising/non-competitive
3. NON-DEPOLARISING/COMPETITIVE

=These acts by binding to acetylcholine receptor sites thus blocking the receptors from acetylcholine released during a nerve stimulation

=there are two groups of competitive muscle relaxants

1. Aminosteroid group eg pancuronium,rocuronium and vecuronium
2. Benzylisoquinolinium ie atracurium,cisatrcurium,gallamine and mivacurium

=atracurium and vecuronium are the most widely used in this class of muscle relaxants.they have a medium duration of 30-60 mins.

-however,they tend to trigger histamine release which leads to allergic reactions.the other variants were therefore developed

-rocuronium has the fastest onset of action and can be used as alternative to a competitive relaxant when rapid intubation is required

 b)DEPOLARISING/NON-COMPETITIVE MUSCLE RELAXANTS

 =SUXAMETHONIUM is the only drug of this group in current use.

-They bind to the acetylcholine receptor sites and initially stimulate the muscle to contract. However, it then causes a persistent state of depolarization of the sarcolemma during which no further stimulation of the muscle fibre is possible.

 =Characteristics of suxamethonium

-it has a quick onset of action of about 60 seconds

-it has a short duration of action of 5-10 mins

-some people with genetic predisposition may suffer from suxamethonium apnoea in which its effects may last upto 2-3hrs.

-a common side effect of the drug is muscle pain and tenderness in the chest and abdomen

-it may cause marked bradycardia,hyperkalemia or cardiac arrhythmias

-there is no known antidote

 ==REVERSAL OF MUSCLE RELAXANTS

=Their effects can be left to wear off spontaneously but cn be reversed faster by use of anticholinesterases like neostigmine and endrophonium.

=however anticholinesterases causes side effects like;

 -bradycardia

 -an increase in salivation and tracheobronchial secretions

 -an increase in peristaltic activity in the GIT

=Therefore, anticholinergic drugs are given to reverse the above side effects.there are two anticholinergic drugs in use –atropine and glycopyrronium.

 ==ANTI-CONVULSANTS==

=These are drugs used to manage seizures as in epilepsy

=certain drugs can also cause convulsions eg;

-anaesthetics like halothane,enflurane,ketamine

-antibiotics like;amphotericin B,cephalosporins,cycloserine,fluconazole,isoniazid,penicillins

-antidepressants and antipsychotic drugs like;baclofen,cocaine,lithium,tricyclics

-cardiovascular drugs like;intravenous lidocaine,procaine

-endocrine drugs eg;desmopressin,insulin,oxytocin,prednisolone-

-radiographic contrast media like;certain meglumine derrivatives,metrizamide

-stimulant drugs eg;aminophylline,caffeine,theophylline

=A nurse should therefore have anticonvulsant drugs handy when administering some of these drugs.

 =GENERAL MANAGEMENT APPROACHES

I)Enhancement of the activity of the inhibitory brain neurotransmitter gama- aminobutyric acid (GABA)

II) inhibition of the activity of the excitatory brain neurotransmitter glutamate

iii) Directly blocking sodium and/or calcium channels in the nerve cell membrane

 =PHENYTOIN=

=It is a member of hydantoin group of compounds similar to barbiturates.

=MOA= It appears to act by blocking sodium channels in nerve membranes. This reduces the excitability of nerve cells and prevents the abnormal discharge from spreading in the brain.

 =THERAPEUTIC USE=

=Phenytoin is well absorbed by mouth and does not cause drowsiness or sleep’

=however it can be difficult determining the correct dose for every patient because

 -patients vary considerably in the rate at which the break down phenytoin

 -the relationship between dose taken and plasma levels is not linear,a small dose increase plasma

 Levels disproportionately.

 -phenytoin is slowly metabolized and therefore takes about a week before plasma levels stabilizes.

 =ADVERSE EFFECTS=

=These are faily common with phenytoin and may include

-if dosage is too high, the patient is sedated,ataxic and may show nystagmus(rapid,involuntary eye movements)

-greasy skin and hirsutism

-macrocytic anaemia due to folic acid deficiency

-gum hypertrophy;dental care is important

-lymph node enlargement

-rashes.

 =DRUG INTERACTIONS=

=Phenytoin is largely bound to plasma proteins in blood and drugs like sodium valproate and aspirin can displace it leading to increased plasma concentrations.

=phenytoin also induces liver enzymes that metabolises drugs like hydrocortisone,oral contraceptives,theophylline,tricyclic anti-depressants and thyroxine.this will decrease the efficacy of these drugs.

=N/B

=Fosphenytoin is a parenteral pro-drug that is converted to phenytoin in the body after injection.

 ==CARBAMAZEPINE==

=Carbamazepine is a drug similar chemically to tricyclic antidepressants.

=MOA=It is believed to act by blocking sodium channels and keeping the conducting nerve in refractory phase.

 =THERAPEUTIC USE=

=Carbamazepine is widely used in the control of tonic-clonic and partial sizures

=mgx of pain of trigeminal neuralgia

=treatment of bi-polar depression.

=carbamazepine is given orally and is fairly slowly absorbed from the intestines

=it induces liver enzymes with prolonged use and therefore should start with a low dose that is increased over time

=children metabolises carbamazepine faster than adults and should therefore be given more frequently(3 to 4times)daily’

=there are slow release(retard) formulations and suppositories.

 =ADVERSE EFFECTS=

=The most common side effects includes

-rashes

-dizzines and drowsiness

-blurred vision

-depression of leukocytes

=occasionally it can cause;

-jaundice

-excessive salivation

=At higher doses it can;

-have antidiuretic effect

-cause dyskinesia

-cause photosensitivity

-arrythmias

=it should be used with caution in patients with renal or hepatic conditions.

 =DRUG INTERACTIONS=

=Occurs with warfarin and erythromycin.

 ==PHENOBARBITAL==

=It is the oldest drug in use and is a barbiturate

=MOA=It enhances the action of the inhibitory neurotransmitter GABA by binding to sites on GABA receptors.it also inhibits the action of excitatory neurotransmitter glutamate.

 =THERAPEUTIC USE=

=It is not the drug of choice in epilepsy because of its potential neurotoxicity

=it is only given when patients cannot tolerate other drugs and are preferred because they are cheap.

=majority of plasma phenobarbitone is metabolized in the body and the rest excreted unchanged in the kidneys.

 =ADVERSE EFFECTS=

=Includes ;drowsiness and ataxia

=rash resembling measles

=in adults it may cause sedation and depression

=in children it can cause hyperactivity,aggression and insomnia.

=phenobarbital can cause osteomalacia due to vit.d deficiency and megaloblastic anemia due to folic acid deficiency

=all barbiturates can cause physical dependence and sudden cessation can cause serious withdrawal symptoms.

 =DRUG INTERACTIONS=

=Smilar to phenytoin

 ==SODIUM VALPROATE &VALPROIC ACID==

=MOA=they have several CNS actions

-they maintain levels of GABA after the neurotransmitter has been released by inhibiting enzymes that breaks it down

-it also increases the breakdown of excitatory neurotransmitter glutamate

-it has a weak blocking action of sodium channels on nerve cell membrane.

 =THERAPEUTIC USE=

=sodium valproate is well absorbed after oral administration and has a half-life of about 15 hrs.

=it is effective against both petit and grand mal epilepsy

=it is particularly useful for treating children since it has relatively low toxicity and few sedative effects.

 =ADVERSE EFFECTS=

=The drug is known to cause teratogenic defects like spina bifida

=can cause depressed platelet count

=can cause liver damage

=drowsiness,thinning of hair and weight gain may occur.

 ==CLONAZEPAM AND DIAZEPAM==

=Both are benzodiazepines

=they exert their anticonvulsant activity by enhancing the inhibitory effects of GABA

=they are effective against all forms of epilepsy but causes sedation

=withdrawal symptoms will manifest when these drugs are stopped

=they are useful in treating status epilepticus

=other benzodiazepines used as anticonvulsants includes;clobazam and lorazepam

 =OTHER ANTICONVULSANTS=

=Includes gapapentin and pregabalin which acts on the voltage gated calcium channels in the CNS.

=oxcarbazepine which is a pro-drug converted to an active metabolite in the body.its moa is similar to carbamazepine.

=Tigabine,topiramate and vigabatrin all of whom inhibits breakdown of GABA in the CNS.

=Paraldehyde used to treat status epilepticus.

=primidone which should never be combined with phenobarbital.

 ==ANTIPSYCHOTICS ==

=There are three types of psychiatric disorders that requires management with antpsychotic medications i) psychosis-loss of contact with the environment.

 ii) anxiety-all-pervasive fear featured by a patient”s innapropiate emotional response to

 the environment.

 iii) depression-affective disorder with mood changes.

=These drugs targets to either agonise or antagonise the CNS”S main neurotransmitters namely; acetylcholine(Ach),adrenaline,noradrenaline,dopamine,5-hyroxytriptamine(5-HT,serotonin),GABA and neuropeptides.

 = ANTIPSYCHOTIC DRUGS(NEUROLEPTICS)=

= Are classified into two i) TYPICAL-benberidol,chlorpromazine,flupentixol,fluphenazine,haloperidol,

 Levomepromazine,perphenazine,trufluoperazine etc.

 ii)ATYPICAL-amisulpride,aripiprazole,clozapine,olanzapine ,zotepine etc.

=The typical neuroleptics are composed of the following group of drugs:

A)PHENOTHIAZINES

=These includes; chlorpromazine,levomepromazine,promazine,pipotiazine,fluphenazine,

Trifluorophenazine,perphenazine etc.

 >Therapeutic uses

=They have antipsychotic effects.restlessness,agitation and hallucinations are reduced.They produce some sedation and a feeling of detachment from external worries.many of them also have antiemetic action

=They are useful in managing schizophrenic patients

=They act by blocking dopamine action in the brain

 >Adverse effects

=varies from drug to drug but includes;

-jaundice

-parkinsonism,akathisia,dystonia,tardive dyskinesia, which can be controlled by use of benzodiazepines.

-depressed leukocyte count

-skin rashes

-hypotension and dizziness

-hypothermia in the elderly

-weight gain

-dry mouth

-Sedation particularly by chlorpromazine

-rarely can cause neuroleptic malignant syndrome

=most of the above adverse effects are due to their antimuscarinic and extrapyramidal effects.

 B)THE BUTYROPHENONES

=haloperidol and droperidol

=They are rather similar to phenothiazines but are less sedating but produces more extrapyramidal effects

=haloperidol is particularly useful in the management of manic or confused patients.droperidol is similar but acts more rapidly.

C)THE THIOXANTHENES

=Eg flupentixol

=Are also similar to phenothiazines, are less sedative but have high incidence of akathisia.

=They are used as antiemetic and antipsychotic and are used in the treatment of schizophrenia

=Are formulated as two weekly injectable or tablets for daily intake’

D)OTHER NEUROLEPTICS

=Eg sulpiride and and pimozide

=Are used as antipschotic drugs used in the treatment of schizophrenia and manic states

=they are longer acting and less sedative than chlorpromazine

=they can cause adverse effects like cardiac arrhythmias,movement disorders and hepatitis and an ECG must first be done particularly with pimozide and be repeated half-yearly.

2)ATYPICAL NEUROLEPTICS

=Eg;clozapine,risperidone,olanzapine,amisulpride and aripiprazole.

=Are an improvement from the typical neuroleptics

=They have less extrapyramidal effects,less prolactin secretion and hardly causes any postural and movement disorders.

=They act by selectively blocking D2 dopamine receptors in the mesolimbic system of the brain and also block serotonin and adrenoreceptors thus the fewer extrapyramidal effects.

=They are used as second line treatment but can be quite expensive

 >Adverse effects

=clozapine can cause severe neutropenia,seizures,hypotension,excessive salivation and sedation

=olanzapine can cause drowsiness and weight gain.

 =ANXIOLYTICS=

=Anxiolytic drugs comprises:benzodiazepines,buspirone,beta blockers and antidepressants.

1)BENZODIAZEPINES

=Includes;diazepam,alprazolam chlordiazepoxide,clorazepate,lorazepam and oxazepam.

 MOA

=They act on the reticular formation and the limbic system of the brain.They enhance the actions of the neurotransmitter GABA at their receptors leading to depression of the brain function.

 THERAPEUTIC USES

=They are used as both anxiolytics and hypnotics

=They should be used as anxiolytics only in extreme cases of agitation,panic attacks and severe anxiety but using the lowest therapeutic dose and for no more than two weeks.

=They become less effective with prolonged use with withdrawal symptoms accompanying like sleeplessness and anxiety.

=slow weaning off is advised if patient has been on benzodiazepines for more than two weeks.

=They can also be used for other therapeutic purposes like Rx of status epilepticus,in combination with analgesics to manage lumbago related disorders.

 ADVERSE EFFECTS

=Prolonged use can cause;seizures,psychotic symptoms,muscle pain and twitching.

=overdose can cause;marked sedation,poor coordination,memory difficulties and sometimes respiratory depression.

N/B

=Flumazenil is a benzodiazepine antagonist.and is given IV to reverse benzodiazepine sedation either due to overdose or after surgery.

2)BUSPIRONE

=Was formulated to produce an anxiolytic effect without unwanted adverse effects.

=It reacts with a group of 5-HT(serotonin) receptors and has no sedative effect nor risk of addiction.

=it has minimal side effects like nausea and headache

=Its only downturn is the delayed onset of action of about two weeks.

3)BETA BLOCKERS

=Like propranolol suppresses the physical concomitant of anxiety eg tremors and palpitations

 ==ANTIDEPRESSANTS==

=Note that antidepressants can be used as part of anxiety management but is also used in the management of depression per se.

=depression is associated with a reduction in the levels of neurotransmitters serotonin and noradrenalin and many antidepressants acts to increase their levels.

=There are various groups of antidepressants namely;

-tricyclic antidepressants

-tricyclic anxiolytics

-selective serotoninin receptor inhibitors.

-monoamine oxidase inhibitors(MAOIs)

-lithium

-other antidepressants

1)TRICYCLIC ANTIDEPRESSANTS

=These includes ;amitriptyline,clomipramine,desipramine,imipramine,lofepramine,notriptyline and protriptyline.

=They exert their action by preventing the reuptake of amines(serotonin,noradrenalin) at the nerve endings in the brain thus increasing their concentrations for interaction with the receptors.

=imipramine is a pro-drug that is metabolized in the liver to its active form-desipramine.

 TERAPEUTIC USE

=They relieve sleeplessness associated with depression fairly quickly but depression itself may take longer to be relieved.

=Imipramine is the drug of choice to relieve bedwetting in children

 ADVERSE EFFECTS

=Anticholinergic effects(dry mouth,difficulty in urinating,constipation,visual disturbances)

=postural hypotension

=increased appetite and weight gain

=tendency to induce seizures in epileptics-increase dose of antiepieptics

=depresses cardiac conduction-avoid in cardiac patients

=overdosing causes CVS disturbances,seizures and coma

=withdrawal symptoms develops if drug is stopped suddenly

2)TRICYCLIC ANXIOLYTICS

=Doxepin and dosulepin

=Are similar to tricyclic antidepressants but have weaker antideoressant effects.

=They are more rapidly acting than standard tricyclics and are therefore useful when anxiety complicates mild depression.

=Adverse effects are similar to those of the tricyclics but less marked.

3)SELECTIVE SEROTONIN REUPTAKE INHIBITORS-SSRIs

=Eg citalopram,fluoxetine,fluvoxamine,paroxetine,escitalopram,sertraline.

=5-hydroxytryptamineis concerned with mood and deficiency of serotonin in the brain causes depression.

=These drug were developed to specifically inhibit 5-HT reuptake at nerve junctions

=they are preferred over tricyclics in that

-they are not cardiotoxic

-they generally donnot cause hypotension

-they have no anticholinergic effects

-donot cause weight gain.

**Respiratory system**;

**Histamines**-Mediators of allergies produced by basophils&mast cells in response to immune reactions.increase permeability of capillaries to WBCs&some proteins allowing them to engage pathogens in infected tissues.

**effects-Histamine H1 receptor stimulate-**allergy,inflammation&vasodialation.

 **-**Histamine H2 receptors stimulate parietal cells to secrete Hcl.

**Bronchodilators -**Salbutamol,aminophylline,theophylline(franol)

**Histamine (H1) inhibitors** (antihistamines)

**Expectorants/cough suppressors/antitussives**-loosen secretions for easy expectorations eg mucosulvan,ascoril,trichohist,flemnil,ambrodil,sputex,coscof etc.

1. **Bronchodilators-**bronchial spasms relaxants

 1.**Oral beta agonists-salbutamol (ventolin) 4mg tids 5/7 ,syrup, inhaler &injection**

**MOA**-Stimulates beta-2 agonist in the lungs to relax bronchial smooth muscle relieving bronchospasms.

Increase production of cAMP&ensuring reduction in intracellular CA2+ ions conc in smooth muscles,bronchial&uterine.

**INDs-**bronchospasms in asthma.-bronchitis,chronic bronchitis.-emphysema,bronchiectasis&premature labour in threatened abortion(tocolytic)

**CIs-**Hypersensitivity,palpitations,HTN/beta blockers,pg.

 **S/effects**-palpitations,headache,tachycardia,sweating&increased BP, GI disturbance, acidosis,hypokalemia,resistance after prolonged use.

 **2. Phosphodiesterase inhibitors (Methylxanthines)**

 Aminophylline-250-500mg IV, Theophylline (franol)10-30 Mg bd/tds, oxtriphylline.

**MOA-**inhibit enzyme phosphodiesterase in bronchial muscle concentrations of cyclic adenosine monophosphate(cAMP)causing relaxation hence relieving bronchospasm,CNS stimulation,pos inotropic&chronotropic effects,diuresis,gastric acid secretion.

 I**NDs**-Rx&prophylaxis of bronchospasm in COPD ass.with asthma,chronic bronchitis,emphysema.

**CIs**-hypersensitivity,peptic ulcers, epilepsy

**S/effects**-tarchycardia,palpitations,angina,headache,sweating,hypokalemia,anxiety,cardiac arrhythmias,convulsions,seizures,N&V,anorexia,cramps

 **3. Adrenergic drugs or agonists-**epinephrine/adrenaline,Noradrenaline/norepinephrine.

**MOA**-inhibit alpha&beta adrenergic receptors hence relaxation&subsequent relieve of bronchial smooth muscle.

 **INDs**-severe hypersensitivity-anaphylactic shock,bronchospasms,severe hypotension,cardiogenic shock, nasal decongestant, ophythalnic vasoconstriction&mydriatic,chronic open angle glaucoma,to prolong the duration of LA, Epistaxis.

**CIs-**HTN, hypersensitivity, MI, CHF.

**S/effects**-Anxiety ,headache, precipitate angina, MI, Arrhythmias, hypotension,hypertension.

1. **Antihistamines (antiallergy drugs)-Histamine H1 inhibitors**

**Alkylamines-**Chlorpheniramine (piriton) 4mg TDS

**Phenothiazines-**promethazine-25MG OD

**Piperidines-**fexofenadine-non sedating, loratadine (desloratadine)

**Ethanolamines-**ebastine,

 **piperazines**-citrizine/levocitrizine-10mg od,meclizine.

**MOA-**Compete with histamine (H1) receptor sites on effector cells.

**IND-** Symptomatic relief of allergic reactions-rhinitis/rhinorrhea, conjunctivitis &chronic urticarial rash.

  **-** Emergency Rx of anaphylactic shock-insect/animal bites, drugs, food.

 **-**Vomiting associated with food poisoning (promethazine).

 **-**Adjunct in rx of asthma.

**CIs-**premature infants,epilepsy,renal/hepatic failure,hypersensitivity.

**S/effects**-drowsiness,headache,hypersensitivity rxns,dry mouth,N&V,dizziness,blurred vision,constipation/diarrhea,tremors,anxiety &euphoria.

**C) Mast cell stabilizers/leukotriene /Modifiers**-Montelukarst,Zafirlukast,Na cromoglycate-nebulizer

Montel (Montelukarst 5mg+ levocitrizine) ,.

 ==ANTICOAGULANTS==

=These are drugs that interfere with blood clotting and are used to prevent and treat venous thrombosis.

=They include;-heparin and heparin-like compounds

 -hirudin

 -the coumarins(warfarin and phenindione)

 =HEPARIN AND HEPARIIN-LIKE SUBSTANCES

=Heparin is a complex mixture of acidic substances that occurs naturally and is stored in mast cells and basophils.

=it is a very potent anticoagulant.

 MOA

=It inhibits coagulation by binding to antithrombin III and other clotting factors.this enhances antithrombin activity with the clotting factors thus prolonging clotting time.

PREPARATIONS OF HEPARIN

=There are two major preparations

a)unfractionated heparin

b)low molecular weight heparins

=heparin is a large molecule that can be fragmented into several components some of which donot have anticoagulant properties.

=those components that have anticoagulant properties are called low molecular weight heparins.

=unfractionated heparin may therefor vary considerably in potency depending on the batches and sources of supply.

=preparations of low molecular heparins includes;dalteparin’enoxaparin and tinzaparin.

=Advantages of low molecular weight heparins’

-they are better than unfractionated heparin in preventing post operative venous thrombosis.

-given subcutaneously they are effective in treating and preventing venous thrombosis and pulmonary embolism

-they are used in unstable angina

-they donot cross the placental barrier and can safely be used in pregnancy

-they donot require as much monitoring as unfractionated heparin

-they have more prolonged duration of activity in the body

-lower doses can be used.

=heparin is not absorbed by mouth .it is only given IV or subcutaneously.

=kaolin cephalin time or activated partial thromboplastin time are then monitored to avoid overdose.

 ADVERSE EFFECTS

=A common adverse effect is bleeding due to overdose which is usually manifested in hematuria

=prolonged use may lead to osteoporosis

=very rarely may result in severe thrombocytopenia.a platelet count should be done if patient is on heparin more than 5 days.

=osteoporosis and thrombocytopenia are less common if low molecular weight heparin is used.

 ANTIDOTE

=Protamine sulphate is the antidote for heparin.it is a basic protein’

=its chief adverse effect is it may cause hypotension.

 =HEPARINOIDS=

=danaparoid sodium

=These are substances similar to heparin in structure and action.

=it contains as active ingredients;low molecular weight heparin,dermatan and chondroitin.

=it accts like heparin by inhibiting coagulation factor Xa..

=it is used to prevent deep venous thrombosis before surgery and in patient who have suffered heparin induced thrombocytopenia.

 =FONDAPARINUX=

=Is a synthetic pentasaccharide which is identical to the binding site for antithrombin III and acts by selectively inhibiting activated factor X.

=it has a significantly lower risk of thrombocytopenia than heparin

=it is contraindicated in patients with impaired renal function since it is excreted via kidneys

 =HIRUDIN=

=bivalirudin and lepirudin

=Hirudin was originally obtained from leeches and has been used as anticoagulant for many years

=it is nowadays made synthetically by means of recombinant technology.

=it difers from heparin in its MOA in that it directly inhibits thrombin

=it is as effective as low molecular weight heparins

=its major side effect is bleeding.

 =THE COUMARINS-ORAL ANTICOAGULANTS=

=Warfarin and phenindione

=were discovered from spoiled spoiled sweet clover silage

=they are called oral anticoagulants since they are active thru’ this route

MOA

=Warfarin and phenindione exert their effect by interfering with synthesis of vitamin K-dependent clotting factors like factors VII,IX,X and XI.

ADMINSTRATION

=Warfarin and phenindione are administered orally which is very convenient for outpatient treatment

=their onset of action is delayed for many hours since they will only be active once the body stores of vit.k-dependent factors have been depleted.

=for this reason,anticoagulant therapy is usually started with heparin which acts immediately then followed by oral anticoagulants’.

=phenindione is shorter acting than warfarin and is nowadays rarely used.

MONOTORING ANTICOAGULANT THERAPY

=The initial stages of anticoagulation therapy is traditionally carried out in hospitals then thereafter controlled at outpatient and community level.

=patients on anticoagulation therapy need to be carefully and regularly monitored for the level of anticoagulant activity since excess can cause bleeding and insufficient leads to clotting.

=the prothrombin time should be measured before starting treatment then daily and the dose adjusted until the INR is stabilized.

=INR(international normalized ratio) is obtained by dividing the patient’s prothrombin time by the normal prothrombin time and it should range between 2 and 3.5.

=this range gives effective anticoagulation with minimal risk of bleeding.

C/Is

=includes active peptic ulcer,severe liver disease and renal failure

ADVERSE EFFECTS

=haemorrhage

=skin rashes,fever and jaundice(phenindione)

=teratogenic effects

=warfarin crosses the placenta and may cause fetal abnormalities in the first trimester.heparin may therefore be used upto 16 weeks before switching to warfarin.

DRUG INTERACTIONS

=Warfarin activity is increased by;

-antibiotics,aspirin,alcohol,cimetidine,phenytoin

=Activity is decreased by;

-barbiturates’

ANTIDOTE

=Vitamin k.

FIBRINOLYTIC AGENTS

=Streptokinase,plasminogen activators,urokinase,acylated plasminogen-streptokinase activator complex(APSAC)

=are used in managing an already formed blood clot as in DVT &CVA

=All fibrinolytic agents acts directly or indirectly as plasminogen activators.

NURSES ROLES.

=administer right dose.overdose can lead to bleeding.

=advise patient to avoid traumatic activities involving sharp objects and sports.they increase risk of bleeding.

=avoid OTC drugs and alcohol,they increase effects of heparin

=report to hosp.immediately incase of an accident

=patient should carry a name tag for easy notification and assistance incase of an accident

=don’t use razor blades for shaving esp.for men

=regular monitoring for INR.

=liase with MOPC for follow-up.

 ==COAGULANTS==

=These are substances that enhances homeostasis thru’ various means.they generally encourage coagulation of blood.

=drugs used for homeostatic therapy are classified as:

i)agents acting locally

ii)transfusional agents

iii)non-transfusional agents

 i)Agents acting locally

=these agents control oozing of blood from minute vessels but are not effective in controlling bleeding from large vessels.

=they are applied topically to injured site either as powder form or impregnated in a gauze.

=they are effective when manual pressure is addittionaly applied

=they include;thrombin,thromboblastin,fibrin,gel foam,oxidized cellulose and microfibrillar collagen.

=they are simply exogenously sourced clotting factors applied locally.

 ii)Transfusional agents

=These are administered systemically and includes;

a)human fibrinogen

=are fractions obtained from human plasma used to restore normal fibrinogen levels in hemorrhagic complications caused by afibrinogenemia

=fibrinogen and thrombin may be used togather for local homeostasis.

b)antihaemophilic globulin(AHG)

=used to treat haemophilia A

=it is a concentrate of clotting factor VIII.

=It can be prepared from pooled normal plasma or by recombinant DNA technique.

=in patients with hemophilia B(Christmas disease) plasma infusion is indicated to replenish factor IX.

c)Plasma or blood

=Fresh frozen plasma or blood is suitable for the treatment of most coagulation disorders,since it provides all the clotting factors.

=whole blood transfusion however carry the additional risk of transfusion reactions.

 iii)Non-transfusional agents

=Includes the following;vitamin K,epsilonaminocproic acid(EACA),tranexamic acid,desmopressin&conjugated estrogens.vit c and some snake poisons.

a)vitamin k.

=vitamin k consists of three distinct fatt soluble compounds which participates in biosynthesis of several clotting factors.

1)vitamin k1(phytonadione) obtained from plants

2)vitamin k2-produced by bacteria(E coli) in the GIT.

3)vitamin k3(menadione) synthetically produced.is water soluble

 =Therapeutic uses

=Adult vit k deficiency due to:malabsorption syndrome,long term IV feeding,prolonged periods of malnutrition-menadione may be used

=vit k deficiency in infants during acute diahrrea.use menadone

=neonatal vit k deficiency

=bleeding state during coumarin anticoagulant therapy.

 Adverse reactions

=rarely anaphylactoid reactions

=hemolytic anemia

=hyperbilirubinaemia and kernicterus in new born

=jaundice

 b)Epsilon aminocaproic acid(EACA)

=This is a water soluble analogue of the amino acid lysine

MOA

=they reversibly occupy the lysine binding sites on plasminogen.this results in inhibition of fibrin binding to plasminogen.plasminogen cannot be converted to plasmin and fibrinolysis is impaired and the blood clot is stabilized

 Therapeutic use

=primary menorrhagia

=during prostatic surgery

=major trauma with risk of bleeding

=upper GI bleeding

=bleeding after tooth extraction in pts.with bleeding disorders

=thrombocytopenic bleeding

=post-partum hemorrhage.

 Adverse reactions

=nasal stuffiness

=abd. Discomfort

=dyspepsia

=hypotension

=conjuctival erythema

=D,N&V

=skin rash-all of which are mild

=rarely fatal disseminated intravascular thrombosis

 c)Tranexamic acid

=is also a derivative of lysine but is about 10 times more potent than EACA.

=indications and side effects are also similar.

=it togather with EACA are contraindicated in patients with subarachnoid hemorrhage as they may induce vasospasm and ischemic stroke.

**MOA**-Antagonizes the effects of leukotrines from mast cell&eosinophils which mediate the following;airway oedema,smooth muscle constriction&altered cellular activity resulting in decreased inflammatory process.

**Inds-**Prophylaxis&chronic treatment of asthma.

 **-**Symptomatic relief of seasonal allergic rhinitis.

**CIs**-Hypersensitivity, lactation &1st trimester pregnancy.

**S/Effects**-fatique,headache,drowsiness,irritability,restlessness,insomnia,dyspepsia,vertigo,dry mouth, weakness,nasal congestion,otitis in children,sinusitis,cough,abd pain,diarrhea,dyspnea,nausea,elevated liver enzymes,rash&esinophilic conditions,fever.

**Drugs Acting in the CNS**

**Analgesics/antipyretics**-**NSAIDS/Non-opiod**-PCM,ibuprofen,diclofenac,Asa,indocid,mefanamic acid,piroxicam,meloxicam ,ketoprofen,acetaminophen

**MOA**-Inhibits COX-2 mediates production of Prostagladins hence reduces inflammation relieves pain&fever. COX-1(Protective effect on the gastric lining by secreting mucous.&prevents platelet agression to the walls of blood vessels by blocking synthesis of thrombaxane A2.

**Aspirin(acetyl salicylic acid-ASA)** 600MG TDS 3/7

.INDs-relieving pain antinflammatory action,fever by inhibiting prostaglandins synthesis in hypothalamus,RA,Acute rheumatic fever,Toothache,sore throat,headaches

,prophylaxis in CHF/MI prevent(thromboxane) platelet aggregation

.CIs-PUD,Hemophilia,liver disaeases,pt on anticoagulants,Reyes syndrome in children,Asthma,Gout

S/e-D,N&V,hypersensitivity rxns,blurred vision,thirst,fever,increased bleeding time&bronchospasms.

**Adverse effects-**causes bronchospasm asthma like attack,gastric irritation/alceration-hematemesis due to reduced production of prostaglandins,salicylism-dizziness,tinnitus,deafness&vomiting,mental confusion,aspirin poisoning-hyperventilation due to stimulation of respiratorycentre,acidosis manifested by fever.Remedy-gastric lavage.

**Diclofenac-**50-100mg **MOA**-inhibit prostaglandin synthesis.

**IND-**gout,R/A,Fever,mild-moderate pain,OA,spondylitis arthritis.

**Indomethacin (Indocid)**-Ind-Ankylosing spondylitis,RA,Pericarditis/pleurisy,Acute gouty attacks.

**Ibuprofen(brufen)/ketoprofen, naprofen, aceclofenac.**

 **INDs-**RA,OA,STI,Pain-headache,dysmenorrhea,fever,mennorhagia/metrorhagia due to hormonal imbalance.

**CIs**-PUD,liver damage,renal damage,hypersensitivity.

**Mefanamic acid** **ind-**pain,heavy menses.

Nurses responsibility

Screen for CIs-pud/asthma/bleeding disorders.-Take drugs after meals –modify lifestyle.advice on side effects.Avoid OTC drugs.

Disease modifying antirheumatic drugs-DMARDs-reduce pain&joint damage-6months effect-methotrexate,sulfasalazine,penicillamine,chloroquine.(assignment)

 **Opiod/Narcotics-GA**- **1.** **Agonists**; morphine,pethidine/meperidine,diamorphine(heroine), codeine &dextropropoxyphene.

**MOA**-inhibits synthesis of prostaglandins hence relieving pain/fever by stimulation of receptors in the neurons.

**IND**-pre-op medication prior to theatre,allay anxiety in anticipation&fear of pain,mild hypnotic-sleep/dizziness,cough,pain control in cancer,diarrhea-intractable profuse diarrhoes,pain relieve during laour-pethidine/morphine

**Adverse effects-**unconsciousness/drowsiness in overdose, allergy/hypersensitivity, bradycardia, confusion,constipation,dependence,dry mouth,hallucinations&night mares,nausea,sedation,urinary retention,pregnancy-cross placenta.

 **2. Partial agonists**-tramadol,nalbuphine,meptazinol,buprenorphine

 **MOA**-stimulation&partial blockage of pain at receptors.

 **3.** **Antagonists/antidote**-naloxone Hcl,naltrexone

 **MOA** –Block or reverse effects of agonists.

**Ind**; overdosage/poisoning,addiction-during withdrawal symptoms,reverse resp centre in newborns.

**Local anaesthesia**-lidocaine,Lignocaine

 **MOA-**stabilizes membranes of the nerve cells by decreasing there permeability to Na+ions.

 **NB/**Adrenaline is added to prolong its effect during operation.

**General anaesthesia**-

Stage A.**Premedication**-A.**opiods**-pethidine/morphine,

 B.**Anticholinergic-**Atropine,

 C.**Anxiolytics**-valium,lorazepam

 D.**Antihistamines**-ranitidine,cimetidine.

stage B.**Initiation**-ketamine,Profol,thiopental.

**Stage C.Maintenance**-**inhalational-**nitrious oxide (laughing gas) ,halothane&fentanyl.

 -**Skeletal muscle relaxation** (neuromuscular blockers)

 1.**competitive non-deplorising**-vecuronium,rocuronium,tracurium,atracuronium

 2.**depolarizing**-suxamethonium(scolin)

 Stage D.Reversal of muscle relaxants-chlorxazone,baclofen.

ge

**anticonvulsants or minor trinquillizers**

1. **anxiolytics**-benzodiazepines-diazepam/valium,clonazepam,lorazepam,chlordiazapoxide.

**MOA**-inhibit neurotransmitter GABA which causes excitation of muscles.

**IND**-convulsions eg status epilepticus,myoclonic seizures,hysteria,anxiety/neurosis,withdrawal symptoms of alcohol,pre-op medication&stimulation of appetite.

 **CIs-**hypersensitivity,respiratory distress.

**S/Effects**-drowsiness,lethargy,ataxia,hypotension

1. **barbiturates**-phenobarbitone,primidone,mephobarbitone,methabarbitone

**MOA-**inhibits activity of neurotransmitter glutamate blocking its effects In the brain.

1. **succinimides-**ethosuximide
2. **valproic acid**-Sodium valproate

 **5. Iminostilbines-**carbamazepine 200mg nocte-trigeminal neuralgia-HSV,Post herpetic pain

 -phenytoin- trigeminal neuralgia.cardiac arrhythmias.

 **MOA**-directly block Na/Ca channels in the nerve cell membrane.

 **Ind-**epilepsy,febrile convulsions

 **CIs-**hypersensitivity,respiratory distress.

 **Hypnotics, Sedatives**, **Antipsychotics (major trianquilizers)**

**MOA-**Block dopamine receptors in the brain hence inhibiting its effects.

**1**.**phenothiazines**-cpz(largactil),promethazine,fluphenazine,prochlorperazine,thioridazine,trifluoperazine.

**INDs**-Acute&chronic psychoses with increased psychomotor activity,n&v,intractable hiccups,pre-operative sedation&Rx of acute intermittent porphyria.

**2.Butyrophenone-Haloperidol**

 **MOA**-it has anticholinergic&alpha-adrenergic blocking activity.

**INDs-**acute&chronic psychoses,Tourettes syndrome,severe behavioural problems in children.

**CIs-**hypersensitivity,narrow angle glaucoma,BM depression,CNS depression,severe liver or cardiovascular disease.

**S/Effects**-seizures,extrapyramidal reactions,confusion,drowsiness,restlessness,tardive dyskinesia,blurred vision,dry eyes,resp depression,hypotension,tachycardia,constipation,dry mouth,anorexia,drug induced hepatitis,ileus,urinary retention,diaphoresis,photosensitivity,rashes,galactorrhea,hyperpyrexia.

**3.Miscellaneous-**clozapine,olanzapine,quetiapine,risperidone**.**

**INDs-**treatment of schizophrenic patients who are unresponsive to or intolerant of standard therapy with other antipsychotics.

**CIs**-Hypersensitivity,BM depression,lactation&severe CNS depression/coma.

**S/effects**-dizziness,sedation,visual disturbances,hypotension,tachycardia,hypertension,constipation,abdominal discomfort,dry mouth,increased salivation,N&V,rash,sweating,agranulocytosis,leukopeni,extrapyramidal reactions,fever&wt gain.

**Rigidity and tremor controllers**

**Antiparkinsonism( Antimuscarinic) drugs –**Benzhexol (Artane)-5mg OD,Benzotropine.

**Dopaminergic inhibitors-**Levodopa, Bromocriptine

**MOA-**Partially block central cholinergic receptors hence balancing cholinergic &dopaminergic activity in the basal ganglia. (Decreases salivation and relaxation of smooth muscles).

**Inds-** Parkinsonism, Drug induced extrapyramidal symptoms.

CIs-Tardive dyskinesia, Cardiac arrhythmias,Myasthenia gravis,Urinary retention,hypersensitivity.

**S/Effects**-dry mouth, blurred vision,urinary retention,GI disturbances,nervouseness,allergic reactions,drowsiness, increased IOP(glaucoma)

**Antidepressants**

**1.Tricyclic**-Imipramine (bedwetting-nocturnal enuresis),Amitriptyline,Clomipramine,Nortriptyline

**MOA**-Increases the synaptic concentration of norepinephrine and serotonin in the CNS.

**INDs-**depression, depression ass with anxiety &disturbances, chronic neurogenic pain, bulimia nervosa, temporary Rx of nocturnal enuresis.

**CIs-**hepatorenal failure,acute MI,hypersensitivity,BPH.

**Side effects**-anticholinergic-dry mouth,retained urine(male),constipation,postural hypotension-faintness,dizziness,increased appetite&wt gain.epilepsy-seizures,palpitations,constipation,blurred vision,sweating,arrhythmias,convulsion

**2.Tricyclic anxiolytics (TCA)**-doxepin,dosulepin

**3.Selective serotonin** (5-HT) **Reuptake inhibitors** (SSRIs)- citalopram, fluvoxamine, fluoxetine, Paroxetine, Sertraline.

**MOA**-Selectively inhibiting the re-uptake of serotonin.

**Ind**; depression, obsessive-compulsive disorders, bulimia nervosa

**CIs-**hepatorenal failure,acute MI,hypersensitivity,BPH.

**Side effects**-anticholinergic-dry mouth,retained urine(male),constipation,postural hypotension-faintness,dizziness,increased appetite&wt gain.epilepsy-seizures,palpitations,constipation,blurred vision,sweating,arrhythmias,convulsion,headache.

**4.Monoamine oxidase inhibitors (MAOIs)-**phenelzine, isorcarboxazid,Tranylcypromine

**MOA**-inhibits the enzyme MOA resulting in an accumulation of various neurotransmitters in the body (dopamine,epinephrine,norepinephrine&serotonin).

**Mood stabilizers**-Lithium

**MOA**-modify neurotransmission in the brain.

**Ind**- Prophylaxis in mania-unipolar&bipolar depression.( MDP)

**CIs**-1st trimester of pg,Hepatorenal failure,Lactation,Leukamia.

**S/Effects**-GI disturbance,hand tremor,thirst,fatique,muscle weakness,polydipsia,wt gain&leukocytosis.

**6. Other antidepressants**-Nefazodone,Venlafaxine,Trazodone,Mirtazapine,bupropion.

 **Anticholinergics-** Atropine 10mg oral/sc/iv/im,gylcopymonium(glycopymolate).Ipratropium bromide,(antidote for organophosphate poisoning)

MOA-block effects of ach at postganglionic parasympathetic nerve ending

 **Inds**-releive of involuntary muscle spasms eg intestinal ,biliary,renal colic pain.

-premedication pre-op to dry up salivary,intestinal&bronchial secretions&protect the heart from undue vagal depression.

-Relieve bronchial spasms by inhalation especially bronchoasthma.

-OPP to dilate pupils to prevent blindness &also facilitate eye exam (mydriasis-fundoscopy).

-Rx of parkinsonism

-Prevention of bradycardia.

-Atropine derivative(Ipratopium) inhaler to relieve bronchospasms in asthma.

**CIs-**hypersensitivity,constipation,Glaucoma,elderly with BPH&Pyloric stenosis.

S/E-Anaphylaxis,rashes,hypotension,renal injury,ocular toxicity,Bm depression &growth retardation.

Photophobia,dry mouth,mydriasis,urinary hesitancy&retention,tachycardia,loss of taste sensation,headache,nervouseness,D,V&N,drowsiness,dizziness

**Muscle relaxants-**centrally acting-Neuromuscular blockers

 Competitive(non-depolarizing) blocking atracurium,pancuranium,vecuronium,tubocurarine.

MOA-Compete with neurotransmitter ach for cholinergic receptor sites on the motor end plate antagonizing the actions of Ach.

IND-Adjunct to Gen.anaesthesia in facilitating endotracheal intubation and induce skeletal muscle relaxation in surgical pts.

Depolarizing blocking agents-Suxamethonium(Scoline),Decamethonium

MOA-Inhibits cholinergic receptors blocking neurotransmitter Ach at motor end plate to produce depolarization.

Ind-Adjunct to gen.anaesthesia

CIs-Hx malignant hyperthermia,hypersensitivity,hyperkalemia

S/E-Hypertension,hypotension,bradycardia,tachycardia,hyperkalemia,resp depression,excessive salivation.

 Direct acting(skeletal)banclofen,chlorzoxazone.

MOA-Inhibits transmission at spinal level as well as depressing CNS.

INDs-Chronic severe spasticity of voluntary muscles.

CIs- hypersensitivity,pUD,

S/E-Headache,dizziness,drowsiness,ulceration,dry mouth,nausea,tremor,GI disturbance

**Anticholinesterases**-neostigmine,Donepezil,pyridostigmine

Local anaesthesia-Lidocaine(Lignocaine),Adrenalined lidocaine(prolongs effect)

MOA-Stabilizing the membranes of the nerve cells by decreasing their permeability to Na ions.

Ind-local anaesthesia in minor surgical ops

CIs-Hypersensitivity,Hypotension,Heart failure

S/E-Drowsiness,confusion,lightheadedness,tinnitus,numbsee,hypotension,D,N&V,parasthesia,dyspnea&slured speach

**Antispasmodics-**buscopan(Hyoscine Butyl-N-bromide) 10-30mg bd or tds.MOA-anticholinergic

IND-billiary colic,colicky pain in renal conditions,dysmenorrhea,PUD,Rx of frequency of micturition.Labour-ripen cervix...

CIs-prostate enlargement,paralytic ileus,pyloric stenosis,high ambient temps.

**S/Effects**-skin rashes,dry mouth/skin,flushings,visual disturbances,drowsiness.

**Anti gout**-alluprinol.proben colchine(assignment)

Uricosuric agents-Probenecid,Sulfinpyrazone

MOA-Increases uric acid excretion in the urine from kidneys.

Decrease Uric acid production-Allopurinol

MOA-Slow uric acid production by inhibiting an enzyme(Xanthine Oxidase).

Others-Colchicine,Indomethacin

MOA-Inhibits inflammatory cells in gouty tissue. Hence pain relieve.

INDs-Gout,Hyperuricaemia with ass conditions.

CI-Hypersensitivity,Pg,Lactation&Children,Hepatorenal failure

S/E-Skin rashes,D,N&V,blood dyscrasias,Wt loss,headache,sore gums,flushing,anemia,dizziness,renal colic,uric acid stones with or without haematuria,nephrotic syndrome

Disease-Modifying Antirheumatic Drugs(DMARDs)

Methotrexate,Sulfasalazine,penicillamine,cyclophosphamide.

MOA-Inhibit effects of immune system on the rheumatic process.

INDs-RA,cancers

CIs-Hypersensitivity,hepatorenal failure,1st trimester pg,lactation.

S/E- rashes,D,N&V,anemia,stomatitis,renal damage

Reproductive system

Msoprostol (cytotec)

MOA-PgE1 sythesis,ripens cx&increasing uterine tone and contractility.

PGE2

Oxytocin

Syntocinon

ergomrtrine

Viagra

 **Antidotes**

**Benxodiazepines-flumenzanil**

**beta blockers-Ca gluconate or glucagon**

**CCBs-Ca gluconate**

**Digoxin-Digoxin specific antibodies**

**Isoniazid-Pyridoxine**

**mg-Ca gluconate**

**Methanol-Ethanol and folinic acid**

**Opiods-Naloxone Hcl**

**organophosphates-Atropine**

**paracetamol-N-aceylcysteine**

**Coumarins-Vit K**

**Heparin-Protamine sulphate.**

**Disinfectants-used on environment-hard surfaces**

 **jik(Na Hypochlorite)**

**Glutaraldehyde-Cidex-sterilize plastic equipments-endoscopes,MVA kit**

**Antiseptics-disinfectants used on the skin&mm.**

**Iodine-destroys spores as well as vegetative bacteria.**

**Povidone-iodine( Bethadine)10% alcoholic soln**

**Povidone-iodine 10% acqueous soln**

**chlorhexidine-Savlon-effective against gram+ive bact( staph&strep)-pre-op scrub**

**Cream&soln for umbilical cord**

**Isopropyl Alcohol-cleansing skn prior to injection.**

**H202-irrigating infected wounds.**

**Hand disinfectant.....**