PHARMACOLOGY

SECOND STAGE

Introduction to Pharmacology

Pharmacology / is the science that deals with study of the drugs and it's interaction with living systems.

Drugs / are chemicals that act on living systems at the chemical (molecular) level.

Medical pharmacology / is the study of drugs used for the diagnosis, prevention, and treatment of disease.

Toxicology / is the study of the untoward effects of chemical agents on living systems. It is usually considered an area of pharmacology.

Pharmacodynamics / describe the action of the drug on the body. Including:

receptor interactions , dose-response phenomena , and mechanisms of therapeutic and toxic action.

Pharmacokinetic /describe the action of the body on the drug.

including

absorption , distribution , metabolism , and excretion (Elimination).

*Not: Elimination of a drug may be achieved by metabolism or by excretion.

Concept of the Pharmacodynamics

Concentration-Response : Relationship exists between the concentration of a drug at its site of action and its beneficial or toxic action.

Properties of Drug Receptors: Most receptors are proteins .

Types of Drug-Receptor Interactions : When a drug activates a receptor that it binds to, the drug is an **agonist**.

Concept of the Pharmacokinetics:

Absorption of Drugs:

Drugs usually enter the body at sites remote from the target tissue and are carried by the circulation to the intended site of action. Before a drug can enter the bloodstream, it must be absorbed from its site of administration. The rate and efficiency of absorption differs depending on the route of administration.

Distribution of Drugs:

The distribution of drugs from the site of absorption, through the bloodstream and to the target tissue depends upon:

1-The blood flow: The tissues that receive a high degree of blood flow (e.g., brain, kidney) have a fast rate of uptake whereas tissues with a low degree of blood flow (e.g., adipose tissue) accumulate drug more slowly.

2-Solubility of the drug in the tissue Some tissues, e.g., **brain**, have high lipid content and dissolve a higher concentration of lipophilic agents.

3-Binding of the drug to macromolecules in the blood or tissue limits their distribution.

4-The ability to cross special barriers : Many drugs are poorly distributed to the brain and the testis because these tissues contain specialized capillaries (the smallest type of blood vessel).

Metabolism of Drugs:

The action of many drugs, especially lipophilic compounds, is terminated by enzymatic conversion, or metabolism, to biologically inactive derivatives. In most cases, the enzymatic conversion forms a more hydrophilic compound that can be more readily excreted in the urine. **Most of the enzymes that catalyze drug-metabolizing reactions are located in the** : gastrointestinal tract and the liver. Some drugs inhibit

drug-metabolizing enzymes and thus cause drug-drug interactions when co-administered with drugs that depend upon metabolism for elimination.

Elimination of Drugs (Excretion**):**

The most common route for drug excretion is through the:

kidney and out of the body in the urine to be excreted by the kidney ,a few drugs enter the bile duct and are excreted in the feces.

*** NOT** : Patients with impaired kidney function usually have a reduced ability to eliminate hydrophilic drugs. To avoid excessively high drug concentrations in these patients, you will need to reduce their dosages or give dosages less frequently.

Home work:

Q1/what the different between pharmacology and medical pharmacology?

Q2/what the different between Pharmacokinetic and Pharmacodynamics?

The dose

Effective dose /Amount of drug given to patient to exert therapeutic effect

Minimal dose /Smallest amount of drug given to patient to exert therapeutic effect

Maximal dose /Largest amount of drug given to patient to exert therapeutic effect

Toxic dose /Amount of drug more than maximal dose, exert toxic effect

Fatal dose /Amount of drug more than toxic dose cause death of patient (kill the patient)

Important factors that affecting the dose of drug :

- ✓ Type of the drug
- ✓ Route of administration of the drug
- ✓ Time of drug taken
- ✓ Age
- ✓ Sex
- ✓ General health of the patient(as fever)
- ✓ Habitual use(common use of the drug)

Estimation of the dose, According to

Age of the patient

Young's role $\text{Child dose} = \frac{\text{Child age}}{\text{Child age} + 12} \times \text{Adult dose}$

Dilling’s role

$$\text{Child dose} = \frac{\text{Child age}}{20} \times \text{Adult dose}$$

Weight of the patient

$$\text{Child dose} = \frac{\text{Wt. Of child (pound)}}{150} \times \text{Adult dose}$$

Lecture 3 **pharmacology**

The route of drug administration

Dosage form / Is the physical form of a dose of medication , such as capsule, injection , the route of administration is depend on the dosage form of a given drug various dosage forms may exist for the same compound e.g. metoclopramide? can be exist in solution for injection, tablet, syrup….etc.

1-Inhaled dosage forms

- ✓ Gas
- ✓ Inhaler
- ✓ Solution for nebulizer

2-Ophthalmic dosage forms

- ✓ Eye drop (solution or suspension)
- ✓ Ophthalmic gel
- ✓ Ophthalmic ointment

3-Oral dosage form

- ✓ Capsule
- ✓ Buccal or sublingual tablet
- ✓ Thin film

4-Parenteral dosage form

- ✓ Solution or suspension for injection
- ✓ Rectal dosage forms
- ✓ Enema

5-Topical dosage form

- ✓ Cream: emulsion of oil and water in equal proportions

- ✓ Ointment: combines oil 80% and water 20%
- ✓ Liniment
- ✓ Transdermal patches

Autonomic nerves system

Cholinergic drugs

Acetyl-choline / An acetic acid ester of choline, normally present in the body. It is a neurotransmitter at the neuromuscular junction, in sympathetic and parasympathetic ganglia, and at parasympathetic nerve endings.

Autonomic nervous system / portion of the nervous system that controls the involuntary visceral functions of the body.

***Not: Cholinergic** :stimulated, activated, or transmitted by acetylcholine or a similar substance

Neurotransmitter / chemical substance secreted by the neuron at the synapse that acts on receptor proteins in the membrane of the adjacent neuron or muscle to stimulate, inhibit, or modify its activity .

Parasympathetic nervous system / cholinergic division of autonomic nervous system.

Para sympathomimetic / agent that produces effects similar to those from stimulation of the parasympathetic nerves; also called cholinergic or muscarinic.

*Not : Disordered release of acetylcholine from these nerves or impaired binding with skeletal muscle leads to profound muscle weakness (myasthenia gravis).

Drug mimics Ach.

- ✓ Edrophonium

- ✓ Neostigmine
- ✓ Physostigmine
- ✓ Ambenonium
- ✓ Bethanechol

Major uses

- ✓ Ambenonium, neostigmine, physostigmine, and pyridostigmine are used to treat symptoms of myasthenia gravis.
- ✓ Edrophonium and neostigmine aid differential diagnosis of myasthenia gravis.
- ✓ Neostigmine is used to prevent and treat postoperative urine retention.
- ✓ Neostigmine and pyridostigmine reverse the effect of neuromuscular blocking agents used in surgery.
- ✓ Physostigmine is antidote in anticholinergic poisoning , such as poisoning caused by caused by tricyclic antidepressants(TCAS).
- ✓ Bethanechol is used to prevent and treat postoperative urine retention, postoperative gastric a tony and retention, abdominal distension and megacolon

Mechanism of action

- ✓ Ambenonium, edrophonium, neostigmine physostigmine and pyridostigmine inhibit the destruction of Ach released from the parasympathetic nerves. Ach accumulates increased the stimulation of the receptor.
- ✓ Bethanechol directly, binds to muscarinic receptors, mimicking the action of Ach.

Adverse reaction

Increase level of Ach directly or indirectly but symptoms of increase cause adverse reaction which is:

- ✓ Sweating
- ✓ GI disturbances (nausea, diarrhea, abdominal cramping).
- ✓ Cardiac problems
- ✓ Bradycardia, hypotension and arrhythmias.
- ✓ Respiratory difficulties due to increase airway secretions.
- ✓ CNS reactions
- ✓ Headache, confusion, nervousness in high dosage seizures
- ✓ Visual reactions (effect on eyes)
- ✓ Problem of accommodation, miosis, excessive lacrimation and diplopia.

Autonomic nerves system

Adrenergic drugs

Sympathomimetic produce their effect either by mimicking the actions of dopamine, epinephrine, or norepinephrine at receptor sites in the sympathetic N.S. or by displacing natural norepinephrine from neural storage sites.

*Not:These drugs do not stimulate all types of adrenergic receptors equally, their effects and indications for use differ .their action is not organ- or site- specific and may occur at other than the desired sites.

Three major types of receptors within sympathetic N.S

Alpha, beta, and dopaminergic

The sympathetic nerves system innervates numerous organs (e.g. heart, blood vessels, respiratory tract, liver, urinary bladder, and intestines, regulate of many body functions. When stimulated, sympathetic nerves release norepinephrine except for sympathetic nerves that innervate sweat glands, which release Ach. Norepinephrine combines with receptor sites on the innervated organ to elicit a response. Stimulation of alpha receptors causes vasoconstriction and uterine and sphincter contraction.

Beta divided into $B_1$and B_2

- ✓ $Beta_1$ receptors are largely in the heart; when stimulated, they increase the rate and force of contraction and the rate of AV node conduction.

- ✓ $Beta_2$ receptors are primarily in bronchi, blood vessels, and uterus; stimulation produce bronchodilation, vasodilatation and uterine relaxation.
- ✓ Dopaminergic receptors in splanchnic blood vessels; stimulation dilates these vessels.

*Not: The adrenal medulla is a major part of sympathetic nervous system. During times of danger or acute stress, the sympathetic N.S. can activate the adrenal medulla to release epinephrine into the systemic circulation.

Epinephrine activates alpha and beta receptor, producing physiologic and metabolic effects that prepare the person to cope with the stress(as in the fight- or-flight response).

Drug used as adrenergic stimulant

- ✓ Albuterol (Salbutamol)
- ✓ Adrenaline and noradrenaline
- ✓ Ephedrine
- ✓ Phenylephrine
- ✓ Pseudoephedrine

Uses of adrenergic drug :

- ✓ Raise blood pressure and cardiac output.
- ✓ Relieve bronchoconstriction.
- ✓ Treat heart block and certain arrhythmias and to restore cardiac rhythm in cardiac arrest.
- ✓ Epinephrine and phenylephrine are used to treat anaphylaxis and other allergic reactions.

- ✓ Pseudoephedrine is nasal decongestants.
- ✓ Phenylpropanolamine is used in weight- control aid by increase the release of glucose from the liver, increase the heart rate and ventricular contractility.

Drugs Acting the Digestive system

Antacids

Action: Antacids act by neutralizing or reducing gastric acidity, thus increasing the pH of the stomach and relieving hyperacidity.

- ✓ Antacids containing magnesium have a laxative effect.
- ✓ Antacids containing aluminum or calcium have a constipating effect.

Uses:

- ✓ 1-Treatment of hyperacidity. (Heart- burns).
- ✓ 2-Peptic ulcer & duodenal ulcer (adjunct treatment)
- ✓ 3-Gastro-esophageal reflux.

Contraindications of Antacids:

- ✓ Sodium containing products are contraindicated in C.H.F., hypertension
- ✓ Pregnancy
- ✓ Children less than 6 years of age.

*Not: chronic use of aluminum containing antacids may contribute to development of Alzheimer's disease.

Drugs in this group:

- ✓ Aluminum carbonate
- ✓ Aluminum hydroxide
- ✓ Calcium carbonate
- ✓ Magnesium trisilicate

Antiulcer Drugs

1. Cimetidine:

Trade name : Tagamet

Class: Histamine H2-receptor blocking agent.

Action: decreases the acidity of the stomach by blocking the action of histamine which involved in triggering gastric acid secretion.

Uses:

- ✓ 1-Short-term (up to 8 wks.) & maintenance treatment of duodenal ulcer & treatment of benign gastric ulcer.
- ✓ 2-Management of hyper secretion of gastric acid.
- ✓ 3-Reflux esophagitis.

Contraindications:

- ✓ Children under 16 years.
- ✓ Lactation
- ✓ Impaired renal & hepatic function.

Side effects: Diarrhea, hepatic fibrosis, Hepatitis, Pancreatitis, Hallucinations, Dizziness, Headache, confusion, Hypotension, Arrhythmias following I.V. administration.

Dose: 300 mg, 4 times daily with meals & at bedtime.

2. Ranitidine Hcl:

Trade name : Zantac

Class: H2-receptor antagonists.

Action: It competitively inhibits gastric acid secretion by blocking the effect of histamine on histamine H2-receptors.

Uses: see cimetidine (The same).

Contraindications: Liver cirrhosis, renal failure & hepatic failure.

Side effects: Constipation, nausea, vomiting, diarrhea, malaise, vertigo, bradycardia or tachycardia.

Dose: 150 mg 2 times daily, Maintenance 150 mg at bed-time.

3. Omeprazole

Trade name: Losec, Pepticum, Mepral

Uses:

- ✓ 1-Gastro esophageal reflux disease
- ✓ 2-Esophagitis
- ✓ 3-Duodenal ulcer (short-term treatment), to eradicate H. pylori, Short-term treatment of active benign gastric ulcer

Action: Inhibits activity of proton pump to block formation of gastric acid.

Dose: 20-40 mg daily for 4-8 weeks

Side effects:

- ✓ 1-CNS: headache, dizziness.
- ✓ 2-GI: diarrhea, abdominal pain, nausea, vomiting, constipation, flatulence.
- ✓ 3-Musculoskeletal: back pain.
- ✓ 4-Respiratory: Cough upper respiratory tract infection.
- ✓ 5-Skin: rash.

Contraindications: Contraindicated in patients hypersensitive to drug or its components.

Laxatives

1. Saline laxatives:

Action: It increases the bulk of the stools by attracting & holding large amounts of fluid. The increased bulk results in the mechanical stimulation of peristalsis.

***Not**: The saline cathartics should be administered with sufficient fluid so as not to cause dehydration.

Onset: 0.5 – 3 hrs.

Uses:

- ✓ To empty the bowel prior to diagnostic or surgical procedures.
- ✓ To eliminate parasites following anti-helminthic therapy.
- ✓ To remove toxic substances following poisoning.

2. Mineral oil:

Class.: Emollient laxative.

Action:

- ✓ lubricates the intestines
- ✓ It also decreases absorption of fecal water from the colon.

Onset: P.O. Q 6-8 hrs. Enema 2-15 minutes.

Uses:

- ✓ Constipation
- ✓ To soften feces during fecal impaction.

Contraindications: nausea, vomiting, abdominal. Pain, intestinal obstruction.

Side effects:

- ✓ Pruritus.
- ✓ In pregnancy, it decreases vitamin k absorption leading to hypo-prothrombinemia in the newborn.

3. Glycerin Suppositories:

Class: miscellaneous laxative.

Action: promote defecation by irritating the rectal mucosa as well as by hyperosmotic action, It also softens & lubricates fecal material.

Onset: 15-60 minutes.

Uses:

- ✓ To evacuate the colon prior to rectal & bowel examination or surgery.
- ✓ To establish normal bowel function in patients dependent on laxatives.

Contraindications: Anal fissure, fistula, ulcerative hemorrhoids.

Other laxatives including

- ✓ Castor oil
- ✓ Bisacodyl tablets
- ✓ Docusate tablets
- ✓ Apple, Honey & Apricot.

Digestants

Digestant / promote digestion in the gastrointestinal tract, used in patient lacking such digestive substances as bile salts, gastric acid, and pancreatic enzymes most widely used digestant are:

- ✓ Bile salts and hydrochloric acid: stimulate bile flow from the liver, promote digestion and absorption of fats, fat- soluble vitamins, and cholesterol.
- ✓ Pancreatin
- ✓ Pancrelipase
- ✓ Glutamic acid Hcl replaces gastric acid, inhibit growth of putrefactive microorganisms in ingested food.

Anti-diarrheas

reduce the fluidity of the stool and frequency of defecation. Diarrhea may be caused by foods or drugs, laxative abuse, allergies, endocrine dysfunction, malabsorption, neurological or inflammatory diseases, mechanical obstruction parasitic infection, gastric resection, or radiation poisoning

Drugs used as anti-diarrhea

- ✓ Bismuth subgallate
- ✓ Diphenoxylate Hcl
- ✓ Kaolin & pectin
- ✓ Loperamide Hcl

*Bismuth salts have a mild water- binding capacity; may absorb toxins and provide protective coating for intestinal mucosa

*Diphenoxylate and loperamide: increase smooth muscle tone in GI tract, inhibit motility and propulsion, and diminish digestive secretions

*Kaolin and pectin: decrease the stool's fluid content by adsorption of bacteria and toxins that may cause diarrhea.

Emetics & Anti-emetics

Used in cases of acute poisoning to induce vomiting when it is desirable to empty the stomach promptly & completely after ingestion of toxic materials.

Vomiting can be elicited in two methods :

- ✓ direct action on the Chemoreceptor trigger zone(CTZ) in the medulla.

- ✓ indirect stimulation of the GIT.

1. Apomorphine Hcl:

Class: Emetic.

Action: is a synthetic derivative of morphine which produces vomiting by stimulating the CTZ.

Uses: In drug overdose. - Poisoning.

Contraindications:

- ✓ Shock
- ✓ Drug induced CNS depression.

Side effects: Depression, tremors, tachypnea , overdose may lead to excessive emesis, cardiac depression and finally death.

Dose: 5-6 mg as a single dose.

2. Ipecac syrup

Class. : Emetic

Action: Acts locally on the gastric mucosa & centrally on the CTZ.

Uses: Drug overdose, poisoning to empty stomach.

Contraindications:

- ✓ With corrosives - Unconscious patients.
- ✓ Shock. - Children under 6 months.

Dose: 5-10 ml preceded or followed by 240 ml of water.

Anti-emetics

Nausea & vomiting can be caused by a variety of conditions such as infections, drugs, motion, organic disease or psychological factors.

The selection of antiemetic depends on the cause of the symptom as well as on the manner in which the vomiting is triggered.

Metoclopramide Hcl

Trade name: Plasil

Class: Antiemetic

Action: It is dopamine receptor antagonist, increases the peristalsis of the duodenum resulting in accelerated gastric emptying & intestinal transit.

Indications:

- ✓ Digestive disorders.
- ✓ Nausea & vomiting as in chemotherapy.
- ✓ Facilitate diagnostic procedure e.g. barium meal.

Side effects: GI disturbances, supraventricular tachycardia, dizziness & convulsion.

Contraindications: Seizure (epilepsy), intestinal obstruction.

Other anti-emetics: Diphenidol Hcl "ventrol" & Vitamin B6.

Anti-cholinergic Drugs

1-Atropine sulphate

2-Scopolamine

Cholinergic blockers (also called parasympatholytics) / inhibit the action of acetylcholine released by parasympathetic and some sympathetic nerves. The effects of parasympatholytics are typically opposite those of parasympathetic stimulation.

Major uses of Atropine and Scopolamine:

- ✓ Atropine may be used for treatment of poisoning by organic phosphate insecticides and certain mushrooms.
- ✓ As preanaesthetic medications, atropine and scopolamine are used
- ✓ To reduce salivary and respiratory secretions.
- ✓ Scopolamine may be used to prevent motion sickness.

Mechanism of action of cholinergic blockers in general:

Cholinergic blockers inhibit the effect of acetylcholine (as the neurotransmitter for impulses in parasympathetic nervous system) at the junction between postganglionic parasympathetic nerve endings and effectors organs. These receptor sites are also called muscarinic sites.

Adverse reactions:

- ✓ GI reactions :Dry mouth, thirst, constipation, nausea, and vomiting
- ✓ Urinary symptoms: Hesitancy and retention
- ✓ Cardiovascular reactions: Tachycardia, palpitations, and activation of angina

- ✓ Dermatologic reaction: Hot ,flushed skin
- ✓ Visual changes: Mydriasis , blurred vision and photophobia.
- ✓ CNS reactions: Headache, restlessness, ataxia, disorientation, hallucination, delirium, agitation, mental confusion, insomnia and coma with excessive dosage.

Drug uses for respiratory system

Two types of cough:

- ✓ *Productive:* leads to removal of sputum from the lungs
- ✓ *Dry cough*: no removal of sputum

Drug which acted and used in respiratory system include

- ✓ Expectorant.
- ✓ Antitussive.
- ✓ Bronchodilators.
- ✓ Mucolytic

*Not : Normally respiratory tract secret about 100ml of fluid, in some cases it produce more quantity and patient can't clearing his chest.

1- Expectorants:

Act by reflex from stomach stimulate cough and causes increase bronchial secretion. These agents should be used only in conjunction with a total care plan that includes adequate fluid intake and a cool mist or steam vaporizer, example for these:

- Guaifenesin
- Iodinated glycerol

Facilitate expectoration in pneumonia, bronchitis, T.B., cystic fibrosis and bronchial asthma

2- Anti-tussives: or called cough suppressants, reduce the frequency of cough, when it is dry and nonproductive, desirable when chronic cough produces extreme fatigue(as in lung cancer) like:

- Benzonatate
- Codeine phosphate

3-Bronchodilators:Are used for patients with respiratory diseases, include asthma, bronchitis, and emphysema.

Classified into:

- ✓ Adrenergics
- ✓ Anticholinergics
- ✓ Methylxanthines

Adrenergic

1. Ephedrine
2. Epinephrine Hcl

Cause bronchodilation by acting on smooth muscle of bronchial tree also act on $Beta_2$ adrenergic receptors facilitating relaxation of bronchial smooth muscle

Anti-cholinergic :Atropine sulphate /Block muscarinic receptors, bronchodilating agents are administered by inhalation, minimizing absorption into the systemic circulation, thereby decreasing systemic effects.

Methylxanthines

1-Aminophylline

2-Dyphylline

Acting on smooth muscle of the bronchial tree, stimulate the respiratory center in the brain, increasing rate and depth of respiration.

4-Mucolytic

Acetylcystein / is used to decrease the viscosity of respiratory tract secretion in chronic pulmonary diseases such as bronchitis, cystic fibrosis, and emphysema.

Cardio tonics: Digitalis

Cardiac glycosides / are the most effective drugs for treatment of congestive heart failure (C.H.F).

- ✓ **Digitoxin:** crystodigin Class: Cardiac glycoside
- ✓ **Digoxin:** Lanoxin Class: cardiac glycoside.

Actions:

- ✓ They increase the force of myocardial contractions (positive inotropic).
- ✓ They increase the contractility of the heart
- ✓ It decreases the heart rate due to increase in parasympathetic nervous system and decrease in the sympathetic tone.

Excretion:

They are primarily excreted through the kidneys.

Indications (uses of digitalis):

Congestive heart failure (C.H.F).

Side & toxic effects of digitalis:

- ✓ They are extremely toxic and may cause death.
- ✓ Bradycardia (below than 60 beat/ minute)
- ✓ Nausea, vomiting, and diarrhea.
- ✓ Headache, malaise and muscle weakness.
- ✓ blurring of vision

Anti-arrhythmic drugs

Anti-arrhythmic / are medications that prevent and treat a heart rhythm that's too fast or irregular.

1. Amiodarone hydrochloride

Trade name:- (Procor)

Classification:- Anti-arrhythmic

Action:- Increases the duration of the myocardial cell action potential as well as alpha & beta anti-adrenergic effect.

Indications: Should be reserved for life threatening ventricular arrhythmias which don't respond to other therapy.

Contraindications:

- ✓ Sensitivity.
- ✓ Sinus bradycardia
- ✓ AV block
- ✓ Thyroid dysfunction

Side effects:

- ✓ Bradycardia
- ✓ CHF
- ✓ Tremors.
- ✓ Visual disturbances
- ✓ Hepatotoxicity.

Dose: Tabs 200 mg.

2. Procainamide

3. Propranolol

4. Verapamil

Anti-anginal drugs (Vasodilatations)

Angina pectoris / is a clinical syndrome characterized by paroxysm of pain in the anterior chest caused by:

- ✓ insufficient coronary blood flow
- ✓ inadequate oxygen supply to the myocardial muscle.
- ✓ Atherosclerosis.
- ✓ Vaso-compression.

There are three groups of drugs used for treatment of angina:

1. Nitrates/nitrites.
2. Beta-adrenergic blocking agents.
3. Calcium channel blocking agents.

1-Nitrates/nitrites: Action: Direct relaxation of blood vessels and coronary arteries and smooth muscles vasodilatation for O2 requirements.

Drugs:

- ✓ **Nitroglycerin (Angised)**
- ✓ **Isosorbide Dinitrate**

Isosorbide dinitrate / Present in the forms of capsules chewable, sublingual, tablets.

Trade names: Isordil, Cordil

Class: coronary vasodilator.

Dosage forms: caps 20-40 mg, tabs 20-40 mg.

Uses:

- ✓ Tabs for only prophylaxis of anginal pain.
- ✓ Chewable, sublingual to terminate acute attack and relieve acute pain.
- ✓ Esophageal spasm.

Side effects: Headache, hypotension.

Calcium channel blocking agents

Action: for contraction of cardiac and smooth muscle to occur, extracellular calcium must move into the cell through openings called calcium channels. These agents inhibit the influx of calcium through the cell membrane.

Nifedipine:

Crude name: Adalat

Class: Calcium channel blocking agent (anti-angina, antihypertensive).

Uses: Vasospastic angina, essential hypertension.

Contraindications: hypersensitivity, lactation.

Side effects: pulmonary and peripheral edema, MI, hypotension, palpitation, headache.

Dosage: 10- 30 mg.

Heparin

Action: Inhibits reactions that lead to clotting of blood and formation of fibrin clots.

Absorption: Heparin is not absorbed from GI, must be given IV or subcutaneously.

Elimination: Excreted in the urine, primarily as metabolites.

Indications and Usage

- ✓ Prophylaxis and treatment of venous thrombosis
- ✓ Pulmonary embolism (PE)
- ✓ Peripheral arterial embolism
- ✓ Atrial fibrillation with embolization
- ✓ Prevention of C (DVT) and PE.
- ✓ Anticoagulant in blood transfusions, extracorporeal circulation, dialysis, and laboratory samples.

Contraindications

- ✓ Severe thrombocytopenia
- ✓ Uncontrolled bleeding
- ✓ Hypersensitivity to heparin or any other product ingredients

Side effects:

1. Hemorrhage

2. Hypersensitivity

3. Miscellaneous: Osteoporosis following long-term administration of high doses of heparin , Coetaneous necrosis after systemic administration, suppression of aldosterone synthesis

Drug used for cholesterol

Classification of statins:

Lipophilic	Hydrophilic	Partial
1-Simvastatin 2-Fluvastatin [Weak] 3-Atorvastatin [Strong] 4-Lovastatin	1-Pravastatin	1-Rosuvastatin *Not: It's the best statin reduces (Cholesterol) Partial

HMG CoA Reductase Inhibitors (Statins)

- ✓ Lovastatin
- ✓ Atorvastatin

Adverse effects:

- ✓ Hepatotoxicity
- ✓ Myopathy
- ✓ Renal obstruction

Contraindications:

- ✓ Hepatic disease, jaundice and cholestasis
- ✓ Renal insufficiency
- ✓ Children and teenage

Indications:

- ✓ Hyperlipidemias & atherosclerosis
- ✓ Primary prevention of IHD
- ✓ Stroke prevention

Antihypertensive drugs

Hypertension: is a condition in which the mean arterial blood Pressure is elevated.

- ✓ **Essential hypertension:** could be mild, moderate, or sever and may lead to dangerous changes in kidneys, eyes and blood vessels
- ✓ **Secondary hypertension:** a certain disease or condition leads to elevation of blood pressure such as toxemia or pregnancy, acute kidney failure, etc.

Antihypertensive agents: are initiated when diastolic blood pressure is higher that 90mm/Hg.

Treatment of hypertension includes:

- ✓ Weight reduction.
- ✓ Sodium restriction.
- ✓ Alcohol restriction.
- ✓ Stop smoking.
- ✓ Exercise.
- ✓ Behavior modification.

Single drug should be considered from the following classes:

- ✓ Diuretics.
- ✓ Beta-blocking agents.
- ✓ Calcium channel blocking agents.
- ✓ Angiotesin converting enzyme inhibitors.

*Not: Initial therapy is continued for one month. If there is no response, combination therapy is needed.

Angiotensin-converting enzyme inhibitors (ACE-Inhibitor):

Captopril:

Trade name: Capotin, inhabace.

Class: antihypertensive, inhibitor of angiotensin synthesis**.**

Action: Effect on the enzyme is responsible for the conversion of angiotensin I to angiotensin II which decrease BP, Decrease aldosterone secretion which works to increase level of serum potassium.

Indications:

- ✓ Hypertension.
- ✓ CHF.

Contraindication: Hypersensitivity and pregnancy.

Side effects:

- ✓ Skin rash
- ✓ Hypotension, proteinuria
- ✓ Renal failure
- ✓ Hyperkalemia.

Other drugs: **Enalapril maleate**

Beta-adrenergic blocking agents:

Action: β-adrenergic receptors have been classified as beta 1 (in the cardiac muscle) and beta 2 (in the bronchi and blood vessels).

Used drugs

- ✓ Atenolol (Tenormin)
- ✓ Propranolol (Indral)

1-Atenolol:

Trade name: (Tenormin).

Class: Beta-adrenergic blocking agent

Uses: Hypertension angina pectoris.

Dosage: Tablets 50 mg or 100 mg daily.

2-Propranolol hydrochloride

Trade name: Inderal

Class: beta-adrenergic blacking agent, antiarryhthmic.

Action: manifests both beta1 and beta 2 adrenergic blocking activity.

Indication:

- ✓ Angina pectoris.
- ✓ Hypertension.
- ✓ Cardiac arrhytmias.
- ✓ Prophylaxis of migraine.
- ✓ Prophylaxis of MI.

Side effects: Bradycardia, C.H.F., hypotension, dyspnea, hepatomegaly and bronchospasm.

Other Drugs: Methyldopa (Aldomin)

Diuretics

The kidney is a complex organ with 3 main functions:

- ✓ Maintain the acid-base balance.
- ✓ Elimination of waste materials & return of useful metabolites to the blood.
- ✓ Maintenance of an adequate electrolyte balance which in turn governs the amount of fluid retained in the body.

Action of diuretics:

It increase the urinary output of water and sodium prevention or correction of edema through one of the following mechanisms:

- ✓ Increasing the glomerular filtration rate.

- ✓ Increasing tubular reabsorption
- ✓ Promoting the excretion of sodium

Uses: Congestive heart failure, hypertension, edema.

Type of Diuretics:

- ✓ Carbonic Anhydrase Inhibitor Diuretics Acetazolamide (Diamox)
- ✓ Furosemide (Fused , Lasix) Class: Loop diuretic.'
- ✓ Mannitol (Osmitrol) Class : Osmotic diuretic.
- ✓ Potassium – Sparing Diuretics: Spironolactone (Aldactone) Class: Diuretic – potassium sparing.
- ✓ Thiazides & related diuretics

Drugs used for Urinary system

Drugs acting on the Kidney

Diuretics: The drugs which cause loss of sodium and water from the body by an action of kidney. The primary effect is decrease the reabsorption of sodium and chloride from the filtrate, increase the excretion of salt and water.

This can be achieved in to two ways :

1. A direct action on the cells of the nephron
2. Indirectly modifying the content of the filtrate

Drugs Which Alter the pH of the Urine:

Agent which increase the urinary pH

Sodium and Potassium citrate are metabolized and the cations are excreted with bicarbonate to give an alkaline urine

Why we need to alter the pH of urine?

- ✓ Increase the action of some antibacterial drug (sulphonamide, streptomycin)
- ✓ It self-have some antibacterial effects
- ✓ Increase excretion of drug (aspirin, barbiturates) by alkalinizing the urine

Agent which decrease urinary pH

Ammonium chloride the chloride displaces bicarbonate with hyperchloraemic acidosis results. The chloride, with accompanying sodium, appears in the glomerular filtrate and passes out in the urine with an osmotic equivalent of water, causing a mild diuresis.

Anti-spasmodic drugs :Cholinergic blocking drugs

Drugs:

- ✓ **Bucopan**
- ✓ **Scapolamine**
- ✓ **Hyoscin butyl bromide**

Actions: Inhibits bladder contractions.

Uses : Urinary colic **,** Dysuria **,**Urinary urgency **,**Urge urinary incontinence

Adverse Reactions

Dry mouth, drowsiness, constipation or diarrhea, GI disturbances, Nausea and vomiting, nervousness, vertigo, headache, rash and mental confusion

Antibiotics for U.T.I (Urinary tract infection)

Drugs

- ✓ **Nalidixic acid**
- ✓ **Metheprem (Sulfamethoxazole + Methoprome)**
- ✓ **Nitrofurantoin**

Actions: High concentration in urine; Acts by interfering with bacterial multiplication in urine.

Uses: Used for urinary tract infections (UTIs) caused by susceptible bacterial microorganisms.

Adverse reactions:

- ✓ Anorexia , Nausea & Vomiting
- ✓ Diarrhea , Abdominal pain
- ✓ Drowsiness , Headache

Antihistaminic drugs

Histamine: is an organic nitrogenous compound involved in local immune responses **,** histamine is stored in almost every type of tissue in the body

Appropriate stimuli including:

tissue injury, antigen- antibody (allergic) reactions, and extreme cold trigger the release of histamine from its storage sites into the vascular system.

Histamine receptors / are a class of G protein–coupled receptors which bind histamine as their primary endogenous ligand.

There are four known histamine receptors:

- ✓ H_1 receptor
- ✓ H_2 receptor
- ✓ H_3 receptor
- ✓ H_4 receptor

Anti-histaminic drugs

Action: The effect of histamines may be reversed either by drugs that block histamine receptors (antihistamine) or by drugs that have effects opposite to those of histamine e.g. epinephrine.

Antihistamines used for the treatment of allergic conditions , used for treatment of GI disorders as peptic ulcer.

Antihistamines don't prevent the release of histamine they prevent or reduce increased permeability edema & itching & bronchospasm.

Uses:

- ✓ Treatment of seasonal allergic rhinitis, allergic conjunctivitis.
- ✓ Treatment of urticarial transfusion reactions.
- ✓ Treatment of topic dermatitis.
- ✓ Treatment of insect bites.
- ✓ Sneezing & rhinorrhea due to common cold.
- ✓ Prophylaxis & treatment of motion sickness "nausea & vomiting".
- ✓ Night – time sleep aid.

Contraindications:

- ✓ Hypersensitivity.
- ✓ Pregnancy.
- ✓ Glaucoma
- ✓ Prostatic hypertrophy
- ✓ CNS depression (phenothiazine type).
- ✓ Bone marrow depression
- ✓ Comatose patients.

Side effects: Sedation - deep sleep - Dizziness - Headache - muscle weakness - disturbed coordination - epigastric distress - dry mouth - nausea - vomiting - urinary frequency, anemia (pancytopnea) . Paradoxical excitation (especially in children & elderly) Restlessness, irritability, insomnia, hysteria, tremors euphoria, nervousness, hallucinations, disorientation & convulsion. Usually caused by overdose (acute toxicity).

1. Anti-histamine1 (H1)

Chlorpheniramine maleate trade name: Allermin (Anaphyl)

Class: Antihistamine

Action: sedation is less pronounced.

Dose: syrup each 5ml contains 5mg

Brompheniramine Maleate / Trade name: Ahiston.

Class. : Antihistamine.

Action: It has little sedative effect.

Dose: each tablet contains 2 mg

Antibiotics

Antibiotics / are substances produced by various species of microorganisms (bacteria ,fungi, actinomycetes) that suppress the growth of other microorganisms.

We have two types of Antibiotics according to their action

- ✓ Bacteriostatic antibiotics
- ✓ Bactericidal antibiotics

Classification of antibiotics according the mechanism of action:

- ✓ Cell wall synthesis inhibitors
  -Beta-lactams (penicillins, cephalosporins, aztreonam, imipenem)
  -Poly-peptides (bacitracin, vancomycin)
- ✓ Protein synthesis inhibitors
  -Tetracycline
  -Chloramphenicol
  -Clindamycin
- ✓ Folate antagonists
  -Sulfonamides
  -Trimethoprim
- ✓ Nucleic acid inhibitors :
  -DNA inhibitor (Mitomycin) .
  -RNA inhibitor (Rifampicin).
- ✓ Cell membrane inhibitors:
  - polymyxin

Principle of Antibiotics: Inhibit growth of bacteria without harming the host.

Resistance: loss of efficacy of a given antibiotics against a particular strain.

Penicillin Antibiotics

- ✓ Phenoxymethyl penicillin (penicillin V)

  Naturally occurring

  Poor oral availability (sensitive to stomach acid)

  Its half-life = 30 minutes

  Uses for Rx of acute tonsillitis, endocarditis

  given by injection (IM), in the form o vial.

  Active against gram-positive bacteria

- ✓ Benzyl penicillin (penicillin G)

  it has properties same as of that penicillinV, except it has longer time for action, which continue for many days, given parentally (IM inj.) in the dose of 400.000 iu, 600.000 iu or 800.000 iu.

- ✓ **Ampicillin (** Broad spectrum antibiotic**)**

  Good oral availability

  Active against gram-positive especially staphylococcus and gram negative bacteria like Neisseria.

  Active against enterobacteria

  Given orally or parentally (capsules 250 mg or 500 mg) or vails 500 mg.

  Indications include: bronchitis, otitis media, tonsillitis, laryngitis

- ✓ **Amoxicillin (** Broad spectrum antibiotic**)**

  Excellent oral availability

  Given orally or parentally (capsules 250 mg or 500 mg) or vails 500 mg or 1000 mg.

Indications include: respiratory indections (bronchitis and pneumonia), ear infections (otitis media), urinary infections (cystitis), gynecological infections, intra-abdominal infections, skin and soft tissue infections, typhoid and paratyphoid, joint infections and prevention of septicemia.

Cephalosporin Antibiotics

Cephalosporin can be classified into four generations depending mainly on the spectrum of antimicrobial activity. First-generation compounds have better activity against gram-positive organisms and the later compounds exhibit improved activity against gram-negative aerobic organisms.

- ✓ **First generation cephalosporins**

Are moderate spectrum agents. They are effective alternatives for treating staphylococcal and streptococcal infections and therefore are alternatives for skin and soft-tissue infections, as well as for streptococcal pharyngitis.

The first generation cephalosporins are:

1. Cephalexin
2. Cephalothin
3. Cefazolin

- ✓ **Second generation cephalosporin**

They are more resistant to beta-lactamase. They are useful agents for treating upper and lower respiratory tract infections, sinusitis and otitis media. These agents are also active against E. coli, Klebsiella and Proteus, which makes them potential alternatives for treating urinary tract

infections caused by these organisms. The second generation cephalosporins are:

1. Cefoxitin
2. Cefuroxime

✓ **Third generation**

It including the vast majority of microorganisms with intermediate and high level resistance to penicillin. These agents also have activity against N. gonorrhea .The third generation cephalosporins are:

1. Ceftriaxon
2. Cefotaxime
3. Cefixime

✓ **Fourth generation**

They have a greater resistance to beta-lactamases than the third generation cephalosporins. Many can cross blood brain barrier and are effective in meningitis.

Cefepime has broad gram-negative coverage with somewhat enhanced activity against pseudomonas but slightly lesser activity against pneumococci.

Cefepime is highly active against nosocomial pathogens such as Enterobacter and Acinetobacter and their use should therefore be restricted to the setting of nosocomial sepsis.

Drugs used for Diabetes

Diabetes mellitus

Diabetes is a heterogeneous group of syndromes characterized by the elevation of glucose levels due to a relative or absolute deficiency of insulin; frequently inadequate insulin release is complicated by excess glucagon release.

Type I (Insulin dependent diabetes).	Type II (Noninsulin dependent diabetes).
✓ Childhood" diabetes ✓ Loss of pancreatic β cells ✓ Decreased insulin ✓ Develops suddenly, usually before age 15. ✓ Caused by inadequate production of insulin because T cell-mediated autoimmune response destroys beta cells. ✓ Controlled by insulin injections	✓ Adult" diabetes ✓ Defective signal reception in insulin pathway ✓ Decreased insulin ✓ Usually occurs after age 40 and in obese individuals, genetics, aging, and peripheral insulin resistance also. ✓ Insulin levels are normal or elevated but there is either a decrease in number of insulin receptors or the cells cannot take it up. ✓ Controlled by dietary changes and regular exercise

*Not: Both cause hyperglycemia, glycosuria, lipid breakdown because tissues are deficient in glucose, ketone bodies

Insulin and Oral Hypoglycemic drugs

The peptide hormones directly involved in responding to and controlling blood glucose levels are located in the islets of Langerhans in the pancreas insulin is secreted by β-cells and glucagon by α2 cells.

Insulin

- ✓ Human insulin is chemically identical to endogenous insulin but it is not derived from the human pancreas
- ✓ Cannot be given orally
- ✓ Insulins differ in onset and duration of action.

Types of Insulin

1-Rapid acting insulin

- ✓ Insulin lispro (Humalog) or insulin aspart (Novolog) are very shorting acting insulins
- ✓ More effective in decreasing post-prandial hyperglycemia
- ✓ Less likely to cause hypoglycemia before the next meal
- ✓ Onset is 15', peaks in 1-3 hours, duration is 3-5 hours

2-Short acting Insulins

- ✓ Humulin R, Novolin R
- ✓ May be given sub Q or IV
- ✓ May be given as a continuous IV drip
- ✓ The only insulin that may be given IV

- ✓ Onset is ½-1 hour, peak is 2-3 hours and duration is 5-7 hours

3-Intermediate-acting Insulins

- ✓ Isophane insulin suspension (NPH, Humulin N, Novolin N)
- ✓ Onset is 1-1.5 hours, peaks in 8-12 hours and duration is 18-24

4-Long-acting Insulin

- ✓ Extended insulin zinc suspension
- ✓ Onset is 4-8 hours, peaks in 10-30 hours and duration is 36+ hours

5-Insulin Mixtures

- ✓ NPH 70/30 (Humulin or Novolin 70/30)
- ✓ Durations of actions same as individual components

Oral Hypoglycemic Drugs

Several oral Antidiabetic agents are available for patients with noninsulin dependent diabetes.

Classification:

First generation:

- ✓ Chlorpromide (Diabenase)
- ✓ Glibenclamide (daonil)

Second generation:

- ✓ Glyburide (Micronase)

Action of oral Anti-diabetic agents:

- ✓ Increases the sensitivity of pancreatic islet cells.
- ✓ Increases insulin secretion by beta cells.
- ✓ Increase in the number of insulin receptors
- ✓ Increase the insulin ability to combine with receptors.

Uses (Indication): Non Insuline Dependent Diabetes Mellitus (type II).

***Note:**Patients should be subjected to a 7 day therapeutic trial **,** Decrease in blood sugar, decrease in glucosuria & disappearance of polyuria, & polyphagia indicate that patient can be managed on oral Antidiabetic agents.

***Note:** Diabetes complicated by recurrent episodes of ketoacidosis.

Side effects of oral hypoglycemic agents:

- ✓ Hypoglycemia (most common).
- ✓ Nausea, heartburn, diarrhea
- ✓ Headache, dizziness, general weakness.
- ✓ Chronic use increases risk of cardiovascular mortality.
- ✓ Renal & liver disease.

Drugs acting on central nervous system

Anti-inflammatory: these drugs are used to treat inflammatory diseases and injuries.

Antipyretic: reduce fever; lower elevated body temperature by their action on the hypothalamus; normal body temperature is not reduced

Antiplatelet: inhibit platelet aggregation, prolong bleeding time; have anticoagulant effects

Analgesic: Any drug that relieves pain selectively without blocking the conduction of nerve impulses, markedly altering sensory perception, or affecting consciousness. This selectivity is an important distinction between an analgesic and an anesthetic.

Anti-inflammatory analgesics / Most anti-inflammatory analgesics are derived from two compounds salicylic acid and acetophenetidin.

Drugs:

Acetylsalicylic acid or aspirin / which is derived from salicylic acid is the most widely used mild analgesic.

Mechanism of work:

inhibition of the synthesis of prostaglandins (natural products of inflamed white blood cells) that induce the responses in local tissue that include pain and inflammation.

Opioid analgesics

Opioid substances encompass all the natural and synthetic chemical compounds closely related to morphine.

- ✓ hydrocodone (Vicodin)
- ✓ oxycodone (OxyContin)
- ✓ oxymorphone
- ✓ morphine
- ✓ codeine.

Sedative-Hypnotic Drugs

Insomnia: trouble in falling asleep or too easily to be waken up; can be primary or secondary; harmful to daily life: excessive daytime sleepiness and a lack of energy, feel anxious, depressed, or irritable.

Anxiety: is characterized by excessive, exaggerated anxiety and worry about everyday life events with no obvious reasons for worry; can be extremely debilitating, having a serious impact on daily life.

Sedative/hypnotic drugs

Tranquilizers may be a more familiar term used to describe sedative-hypnotic agents these drugs used for:

- ✓ Drugs that take the edge off.
- ✓ Calming mood when a person feeling anxious.
- ✓ Induce sleep.

Drugs used as sedative/hypnotic / Benzodiazepines is a class of drugs that have an effect on the brain that, in turn, induces sleep and causes feelings of relief, relaxation and a state of euphoria.

Prescription Benzodiazepines

- ✓ Chlordiazepoxide (Librium)
- ✓ Diazepam (Valium)
- ✓ Temazepam (Restoril)
- ✓ Triazolam (Halcion)
- ✓ Clonazepam (Klonopin)
- ✓ Lorazepam (Ativan)
- ✓ Alprazolam (Xanax)

Indications (uses):

- ✓ Reduce anxiety levels
- ✓ Helps people to cope with stress
- ✓ Trouble sleeping
- ✓ In combination with amphetamine-like drugs
- ✓ Many people use sedatives to calm themselves back down from the rush associated with amphetamine use

Short-Term Effects

- ✓ Paranoia
- ✓ Aggression
- ✓ Easily agitated
- ✓ Difficulty remembering

Anti-epileptic drugs (AEDs): (Anti-seizure drugs)

- ✓ Carboxamides.
- ✓ Phenytoin.
- ✓ Barbiturates (Phenobarbital).
- ✓ Sodium valproate (Depakin).
- ✓ Benzodiazepines(Clonazepam, Clorazepate, Diazepam).
- ✓ Gabapentin.

Antidepressant drugs: Drugs

Imipramine and Amitriptyline.

- ✓ Prototypical TCAs.
- ✓ Desipramine (Norpramin) .
- ✓ Nortriptyline (Pamelor) .

Serotonin - Specific Reuptake Inhibitors (SSRI's)

- ✓ Fluoxetine (Prozac)
- ✓ Sertraline (Zoloft)
- ✓ Paroxetine (Paxil)

Non-steroidal anti-inflammatory drugs (NSAIDs)

Some common examples of NSAIDs are: aspirin, ibuprofen, and naproxen. The newer specific COX-inhibitors are not classified together with the traditional NSAIDs even though they presumably share the same mode of action , on the other hand, there are analgesics that are commonly associated with anti-inflammatory drugs but that have no anti-inflammatory effects. An example is paracetamol, called acetaminophen.

Side-effects:

Long-term use of NSAIDs can cause gastric erosions , which can become stomach ulcers

Extreme cases can cause severe hemorrhage, resulting in death.

1. Diclofenac (Voltaren)

Diclofenac is a nonsteroidal anti-inflammatory drug (NSAID). This medicine works by reducing substances in the body that cause pain and inflammation.

Indications: Voltaren (diclofenac sodium) is indicated:

- ✓ For relief of the signs and symptoms of osteoarthritis
- ✓ For relief of the signs and symptoms of rheumatoid arthritis
- ✓ For acute or long-term use in the relief of signs and symptoms of ankylosing spondylitis

Common diclofenac side effects may include:

- ✓ heartburn, indigestion, gas, stomach pain, nausea, vomiting;

- ✓ diarrhea, constipation;
- ✓ headache, dizziness, drowsiness;
- ✓ itching, increased sweating;
- ✓ increased blood pressure; or
- ✓ swelling, pain in your arms or legs.

2. Mefenamic acid (Ponstan)

Mefenamic acid is a non-steroidal anti-inflammatory drug used to treat pain, including menstrual pain. It is typically prescribed for oral administration.

Indications:

Decreases inflammation (swelling) and uterine contractions by a still-unknown mechanism.

Side effects

Mild side effects of mefenamic acid include:

headaches, nervousness and vomiting.

Serious side effects may include:

diarrhea, hematemesis (vomiting blood), hematuria (blood in urine), blurred vision, skin rash, itching and swelling, sore throat and fever.

*Not: It is advised to consult a doctor immediately if these symptoms appear while taking this medication.

*Not: Mefenamic acid is recommended to be taken with food.

3. Drugs used for Uric acid.

Uric acid / is a heterocyclic compound of carbon, nitrogen, oxygen, and hydrogen with the formula $C_5H_4N_4O_3$. Uric acid is a product of the metabolic breakdown of purine nucleotides.

High blood concentrations of uric acid can lead to gout.

Drugs that used for treatment of uric acid called **xanthine oxidase inhibitors** including:

- ✓ Allopurinol (Aloprim, Lopurin, Zyloprim)
- ✓ Febuxostat (Uloric).

Pharmacology of Hormones in general

Hormone: A chemical substance produced in the body that controls and regulates the activity of certain cells or organs. Many **hormones** are secreted by special glands, such as thyroid **hormone** produced by the thyroid gland.

Hormones of the Pituitary

- ✓ Growth hormone
- ✓ ACTH
- ✓ Gonadotropins
- ✓ Prolactin
- ✓ Melanocyte stimulating hormone

Hormones of the Posterior Pituitary

- ✓ Antidiuretic hormone
- ✓ Oxytocin

The Thyroid Gland

- ✓ Thyroxine (T4)
- ✓ Triiodothyronine (T3)

The Parathyroid Gland

- ✓ Parathyroid hormone

The pancreas produces insulin and glucagon

- ✓ The primary blood glucose regulatory hormones
- ✓ Insulin produced in the beta cells of the islets of Langerhans
- ✓ Glucagon produced in the alpha cells

The Testes and the Ovaries

- ✓ The testes produce testosterone

- ✓ The ovaries produce estrogen and progesterone.

Female Sex Hormones

- ✓ Estrogens.
- ✓ Progestogens.
- ✓ LH .
- ✓ FSH secreted from the anterior pituitary gland.

Anti-thyroid Drugs:

- ✓ Carbimazole .
- ✓ Methimazole .
- ✓ Propylthiouracil.
- ✓ A less common anti-thyroid agent is potassium perchlorate**.**

Effects of Hyperthyroidism: May be caused by tumors on the thyroid gland (thyrotoxic crisis), pituitary, or hypothalamus or Autoimmune disease (Grave's Disease) .

Clinical Indication

Replacement or supplement in hypothyroidism of any cause

- ✓ cretinism- mental & physical retardation in
- ✓ children with chronic untreated hypothyroidism
- ✓ nontoxic goiter in adults
- ✓ myxedema in adults

Cautions and Contraindications:

Thyroid hormone therapy

- ✓ is contraindicated in patients with myocardial infarction
- ✓ is not recommended for weight reduction in the management of obesity
- ✓ should be used with caution in patients:

  -With cardiovascular disease, diabetes, adrenal insufficiency

-Who are elderly

Female hormones:

Clinical Indication

- ✓ Replacement therapy in hypogonadism and menopause, or fertility enhancement.
- ✓ Adjunctive therapy for cancer.
- ✓ Prevent ovulation or implantation in the uterus
- ✓ Alleviate menstrual disorders in non-menopausal women

Pharmacological Actions

Contraception

Estrogen and progesterone combinations mimic the natural secretory cycle so that :

- ✓ FSH and LH secretions are suppressed
- ✓ ovulation is blocked
- ✓ cervical mucus is thickened decreasing the possibility of implantation

Adverse Effects of Estrogen and Progesterone

- ✓ Nausea & Vomiting
- ✓ Headache & Dizziness
- ✓ Depression
- ✓ Fluid retention
- ✓ Breast tenderness
- ✓ Weight gain
- ✓ Thrombophlebitis (pain in legs)
- ✓ Double-vision

Androgens Pharmacologic Action

- ✓ Anabolic action - Stimulate protein synthesis
- ✓ Clinical benefit- Increase body weight and appetite
- ✓ Nontherapeutic use- Increase muscle mass and enhance athletic performance
- ✓ Erythropoiesis-Stimulate production of RBCs
- ✓ Inhibit tumor growth.

Adverse Effects

Result from chronic high dose use

Men may develop	Women may develop	Men and women
Addiction syndrome	Hirsutism	Jaundice
	Menstrual irregularities	Nausea
Sustained erection	Acne	Vomiting
Tumors	Deepening voice	Diarrhea
Increased breast tissue	Hirsutism	Retention of Na and H2O
Decreased sperm count	Menstrual irregularities	Jaundice

Vitamins

Vitamins / are organic compounds that regulate metabolism and make possible more efficient use of carbohydrates, proteins, and fat within the body.

Types and classification of vitamins :

Vitamins are usually classified on the basis of their solubility as either:

- ✓ **Fat-soluble vitamins** are absorbed along with ingested dietary fats by the small intestines. The fat-soluble vitamins are A, D, E, and K.
- ✓ **Water-soluble vitamins** by contrast, are absorbed along with water in the gastrointestinal tract and dissolve in the body fluids. The water-soluble vitamins are vitamin C (ascorbic acid) and the family of B vitamins.

***Note:** Water-soluble vitamins cannot be stored in the body, so you need to get them from food every day. They can be destroyed by overcooking.

Fat-Soluble Vitamins

✓ **Vitamin A** (retinol & carotene)

Functions

- Necessary for the vision cycle process - adaption to light and dark
- Tissue growth, especially skin and mucous membranes; toxic in large amounts.

Results of Deficiency:

- Night blindness
- Exophthalmia

✓ **Vitamin D** (calciferol)

Functions:

- Absorption of calcium and phosphorus
- Calcification of bones; toxic in large amounts

Results of Deficiency:

- Rickets
- Faulty bone growth
- Poor tooth development

✓ **Vitamin E** (Tocopheral)

Functions:

- Anti-oxidant
- Normal growth
- Reproduction

Results of Deficiency:

- breakdown of red blood cells, anemia, sterility

✓ **Vitamin K** (Menadione)

Functions:

- Normal blood clotting; toxic in large amounts

Results of Deficiency:

1. Bleeding tendencies
2. Hemorrhagic disease

Water-Soluble Vitamins

✓ **Vitamin C** (ascorbic acid)

Functions:

- Intercellular cement substance
- Firm capillary walls and collagen formation
- Helps prepare iron for absorption and release to tissues for red blood cell formation

Results of Deficiency:

- Scurvy
- Sore gums
- Fevers and infections
- Poor wound healing and tissue formation
- Anemia

Complex vitamins

✓ Vitamin B1 (Thiamin)

Functions:

- Normal growth
- Coenzyme in carbohydrate metabolism
- Normal function of heart, nerves, and muscles

Results of Deficiency:

Beriberi; GI: Loss of appetite, gastric distress, indigestion, deficient hydrochloric acid; CNS: Fatigue, neuritis, paralysis; CV: Heart failure.

✓ Vitamin B2 (Riboflavin)

Functions:

- Normal growth; coenzyme in protein and energy metabolism.

Results of Deficiency:

- wound aggravation, cracks at corners of mouth, glossitis , Eye irritation and sensitivity to light, skin eruptions.

✓ Niacin (Nicotinic acid)

Functions:

- Coenzyme in energy production; normal growth, health of skin, normal activity of stomach, intestines, and nervous system.

Results of Deficiency:

- Pellagra; weakness, lack of energy, and loss of appetite; skin: scaly dermatitis; CNS: Neuritis, confusion

✓ Vitamin B6 (Pyridoxine)

Functions:

- Coenzyme in amino acid metabolism; protein synthesis, heme formation, brain activity.

Results of Deficiency:

- Anemia; CNS: Hyperirritablity, convulsions, neuritis.

✓ Pantothinic acid

Functions:

- Coenzyme in formation of fat, cholesterol, and heme formation, and amino acid activation

Results of Deficiency:

- Unlikely because of widespread occurrence and intestinal baceria synthesis.

✓ Folic acid

Functions:

- Growth and development of red blood cells.

Results of Deficiency:

- Certain types of anemia; megoblastic (large, immature red blood cells)

✓ Vitamin B12 (Cobalamin)

Functions:

- Normal red blood cell formation, nerve function, and growth.

Results of Deficiency:

Pernicious anemia

Treatment of Anemia, Iron- Drugs

Anemia / low hemoglobin, low RBC count and low RBC mass , usually presents with pallor, fatigability, weakness and pale conjunctivae

Therapeutic uses of Iron

- ✓ Iron Deficient Anemia
- ✓ Pregnancy
- ✓ Premature Babies
- ✓ Blood loss
- ✓ Hookworn infestation
- ✓ Malabsorption Syndrome
- ✓ GI Bleeding due to:
  - Ulcers
  - Aspirin
  - Excess consumption of coffee

Iron drugs:

- ✓ Ferrous Sulfate (Feosol)(Oral Iron)

Side Effects / are extremely mild like Nausea, upper abdominal pain, constipation or diarrhea. Cheapest form of Iron and one of the most widely used.

✓ Iron Dextran (Imferon)(**Parenteral**) IM or IV

Indicated for patients who cannot tolerate or absorb oral iron or where oral iron is insufficient to treat the condition i.e. Malabsorption syndrome, prolonged salicylate therapy, dialysis patients.

Toxicity

Toxicity: The degree to which a substance (a toxin or poison) can harm humans or animals.

- ✓ Acute toxicity involves harmful effects in an organism through a single or short-term exposure.
- ✓ Sub chronic toxicity is the ability of a toxic substance to cause effects for more than one year but less than the lifetime of the exposed organism.
- ✓ Chronic toxicity is the ability of a substance or mixture of substances to cause harmful effects over an extended period, usually upon repeated or continuous exposure, sometimes lasting for the entire life of the exposed organism.

Toxicity with some metals

Lead (Pb)

Absorption

- ✓ Skin
- ✓ Inhalation: up to 90% depending upon particle size
- ✓ GI: adults 5 to 10%, children 40%

Distribution

Initially carried in red cells and distributed to soft tissues (kidney and liver); redistributed to bone, teeth and hair mostly as a phosphate salt. Rates of absorption and distribution are greatly influenced by dietary intake and body stores of phosphate, calcium and iron relative to lead

Sources of exposure

paint, pottery, Inhalation - metal fumes , tetraethyl lead in gasoline

Mechanisms of toxicity: Inhibition of heme biosynthesis.

Treatment

- ✓ Remove from exposure
- ✓ CaNa2EDTA
- ✓ D-penicillamine

Mercury (Hg)

Distribution: depends upon sources of exposure

- ✓ Elemental Hg (vapor) crosses membranes well and rapidly moves from the lung to the CNS.
- ✓ Organic salts (lipid soluble) are evenly distributed, intestinal (intracellular)-fecal elimination.
- ✓ Inorganic salts concentrate in blood, plasma and kidney (renal elimination).

Sources of exposure

- ✓ Environmental from electronics and plastic industry
- ✓ Seed fungicide treatment, dentistry

Treatment

- ✓ Remove from exposure
- ✓ 2,3-dimercaptopropanol (BAL)

Toxicity with some commonly used drugs like Paracetamol, Diclofenac, Mefenamic acid & Diazepam.

Paracetamol toxicity:

- ✓ Widely available
- ✓ Potential toxicity underestimated
- ✓ Virtually all patients who ingest doses in excess of 350 mg/kg develop severe liver toxicity unless appropriately treated

Diclofenac toxicity:

Diclofenac is a commonly used nonsteroidal antiinflammatory drug (NSAID) used for the therapy of chronic forms of arthritis and mild-to-moderate acute pain. Therapy with diclofenac in full doses is frequently associated with mild serum aminotransferase elevations and, in rare instances, can lead to serious clinically apparent, acute or chronic liver disease.

Mefenamic acid toxicity:

PONSTAN has demonstrated analgesic, anti-inflammatory and antipyretic properties in human clinical studies. It inhibits the enzymes of prostaglandin synthesize.

Diazepam toxicity:

Diazepam is a prescription medication used to treat anxiety disorders. Diazepam overdose occurs when someone accidentally or intentionally takes more than the normal or recommended amount of this medication.

Treatment of Drugs Toxicity including :

- ✓ Activated charcoal
- ✓ Breathing support
- ✓ Fluids through a vein (by IV)
- ✓ Laxative
- ✓ Medicine (antidote) to reverse the effect of the overdose
- ✓ Tube through the mouth into the stomach to empty the stomach (gastric lavage)

Lecture 31 pharmacology

Emergency drugs

are those drugs which may be required to meet the immediate therapeutic needs of patients and which are not available from any other authorized source in sufficient time to prevent risk or harm to patients.

Some drugs that used in ICU:

- ✓ 1-Voltaren(diclofenac) / important to treat all kind of pain don't used in case of asthma and replace it with paracetamol.
- ✓ 2-Atropine / used for bradycardia
- ✓ 3-Dobutamine / increased the efficiency of heart.
- ✓ 4-Hyoscine(buscopan) / used to relieves stomach and period pains by helping your digestive system and bladder relax.
- ✓ 5-Dopamine / it works by improving the pumping strength of the heart and improve flow to the kidney.
- ✓ 6-Adrenalin / used to treat cardiac arrest , hypotension associated with septic shock.
- ✓ 7-Lasix (furosemide) / used to reduce extra fluid in the body (edema) caused by condition such as heart failure.
- ✓ 8-Nitroglycerin / it is vasodilator used to treat or prevent angina , heart failure and hypotension.
- ✓ 9-steptokinase / used to dissolve clots that have formed in the blood vessel .
- ✓ 10- Morphine / used to treat both acute and a chronic sever pain.
- ✓ 11-Tramal / used to relieve sever pain it is opioid analgesics .
- ✓ 12-Metoclopramide (pramin) / anti sickness (anti emetic) used to treat nausea and vomiting after radiotherapy or chemotherapy or when you may get with a migraine.

THANK YOU