محاضرة رقم -8-

Bronchodilators and Antiasthma Drugs

Asthma is a reversible obstructive disease of the lower airway , with asthma there is increasing airway obstruction caused by bronchospasm and bronchoconstriction, inflammation and edema of the lining of the bronchioles, and the production of thick mucus that can plug the airway . There are three types of asthma:

1. Extrinsic (also referred to as allergic asthma and caused in response to an allergen such as pollen, dust, and animal dander)
2. Intrinsic asthma (also called nonallergic asthma and caused by chronic or recurrent respiratory infections, emotional upset, and exercise)
3. Mixed asthma (caused by both intrinsic and extrinsic factors)

A-BRONCHODILATORS

A drug used to relieve bronchospasm associated with respiratory disorders, such as bronchial asthma, chronic bronchitis, and emphysema. These conditions are progressive disorders characterized by a decrease in the inspiratory and expiratory capacity of the lung..

1- Sympathomimetic

Examples of sympathomimetic bronchodilators include albuterol (Ventolin), epinephrine (Adrenalin), salmeterol (Serevent), and terbutaline (Brethine). Many of the sympathomimetics used as bronchodilators have the subclassification of beta-2 (B_2) receptor agonists

ACTIONS

When bronchospasm occurs, there is a decrease in the lumen (or inside diameter) of the bronchi, which decreases the amount of air taken into the lungs with each breath. Use of a bronchodilating drug opens the bronchi and allows more air to enter the lungs, which in turn, completely or partially relieves respiratory distress.

USES

Sympathomimetics are used primarily to treat reversible airway obstruction caused by bronchospasm associated with acute and chronic bronchial asthma, exercise-induced bronchospasm, bronchitis, emphysema.

ADVERSE REACTIONS

Administration of a sympathomimetic bronchodilator may result in restlessness, anxiety, increase in blood pressure, palpitations, cardiac arrhythmias, and insomnia.

CONTRAINDICATIONS, PRECAUTIONS,AND INTERACTIONS

The sympathomimetic bronchodilators are contraindicated in patients with known hypersensitivity to the drug, cardiac arrhythmias

The sympathomimetics are used cautiously in patients with hypertension, cardiac dysfunction, The sympathomimetic drugs are used cautiously during pregnancy, and lactation. When the sympathomimetics are used concurrently with other sympathomimetic drugs, additive adrenergic effects can occur.

2- Xanthine Derivatives

Examples of the **xanthine derivatives** (drugs that stimulate the central nervous system [CNS] resulting in bronchodilation, also called methylxanthines) are theophylline and aminophylline.

ACTIONS

The xanthine derivatives, although a different class of drugs, also have bronchodilating activity by means of their direct relaxation of the smooth muscles of the bronchi.

USES

The xanthine derivatives are used for symptomatic relief or prevention of bronchial asthma and reversible bronchospasm associated with chronic bronchitis and emphysema.

ADVERSE REACTIONS

Adverse reactions associated with administration of the xanthine derivatives include nausea, vomiting, restlessness, nervousness, tachycardia, tremors, headache, palpitations, increased respirations, fever,

CONTRAINDICATIONS, PRECAUTIONS, AND INTERACTIONS

The xanthine derivatives are contraindicated in those with known qhypersensitivity, peptic ulcers, seizure disorders, serious uncontrolled arrhythmias, and hyperthyroidism.

The xanthine derivatives are used cautiously in patients older than 60 years, those with cardiac disease, hypoxemia, hypertension, congestive heart failure, or liver disease. Aminophylline, used cautiously during pregnancy and lactation.

When xanthine bronchodilators are administered with sympathomimetic drugs , additive CNS and cardiovascular effects may occur. Certain foods contain xanthine (eg, coffee, colas, or chocolate) and may increase the risk of cardiac and CNS adverse reactions. Cigarettes.

B-ANTIASTHMA DRUGS

With asthma the airways become narrow, the muscles around the airway tighten, the inner lining of the bronchi swell, and extra mucus clogs the smaller airways. Along with the bronchodilators, several types of drugs are effective in the treatment of asthma. These include corticosteroids, leukotriene formation inhibitors, leukotriene receptor agonists, and mast cell stabilizers. A multidrug regimen allows smaller dosages of each drug, decreasing the number and severity of adverse reactions.

A- Corticosteroids

ACTIONS

Corticosteroids, such as beclomethasone (Beclovent), flunisolide (AeroBid), and triamcinolone (Azmacort), are given by inhalation and act to decrease the inflammatory process in the airways of the patient with asthma. In addition, the corticosteroids increase the sensitivity of the B_2- receptors. With increased sensitivity of the B_2-receptors, the B_2-receptor agonist drugs are more effective.

USES

The corticosteroids are used in the management and prophylactic treatment of the inflammation associated with chronic asthma or allergic rhinitis.

ADVERSE REACTIONS

When used to manage chronic asthma, the corticosteroids are most often given by inhalation. Adverse reactions to the corticosteroids are less likely to occur when the drugs are given by inhalation rather than taken orally.

Occasionally, patients may experience throat irritation causing hoarseness, cough, or fungal infection of the mouth and throat. Vertigo or headache also may occur.

CONTRAINDICATIONS, PRECAUTIONS, AND INTERACTIONS

The corticosteroids are contraindicated in patients with hypersensitivity to the corticosteroids, acute bronchospasm, status asthmaticus, or other acute episodes of asthma. The corticosteroids are used cautiously in patients with compromised immune systems, glaucoma, kidney or liver disease, convulsive disorders, or

diabetes, those taking systemic corticosteroids, and during pregnancy and lactation. Ketoconazole may increase plasma levels of budesonide and fluticasone.

B- Leukotriene Receptor Antagonists and Leukotriene Formation Inhibitors

Leukotriene receptor antagonists include montelukast sodium (Singulair) and zafirlukast (Accolate). Zileuton (Zyflo) is classified as a leukotriene formation inhibitor.

ACTIONS

Leukotrienes are bronchoconstrictive substances released by the body during the inflammatory process. When leukotriene production is inhibited, bronchodilation is facilitated. Zileuton acts by decreasing the formation of leukotrienes.

USES

Zafirlukast and zileuton are used in the prophylaxis and treatment of chronic asthma in adults and children older than 12 years. Montelukast is used in the prophylaxis and treatment of chronic asthma in adults and in children older than 2 years.

ADVERSE REACTIONS

Adverse reactions include headache, dizziness, myalgia, pain, nausea, diarrhea, abdominal pain, vomiting, and fever.

CONTRAINDICATIONS, PRECAUTIONS, AND INTERACTIONS

These drugs are contraindicated in patients with a known hypersensitivity to the drugs Administration of zafirlukast and aspirin increases plasma levels of zafirlukast, When zafirlukast is administered with warfarin, there is an increased effect of the anticoagulant. Administration of zafirlukast and theophylline or erythromycin may result in a decreased level of zafirlukast. Administration of montelukast with other drugs has not revealed any adverse responses.

Administration of montelukast with aspirin and NSAIDs is avoided in patients with known aspirin sensitivity. Administration of zileuton with propranolol increases the activity or the propranolol; with theophylline increases serum theophylline levels; and with warfarin may increase prothrombin time (PT). A prothrombin blood test should be done regularly in the event dosages of warfarin need to be decreased.

C- Mast Cell Stabilizers

Mast cell stabilizers include cromolyn sodium (Intal) and nedocromil sodium (Tilade).

ACTIONS

These drugs inhibit the release of substances that cause bronchoconstriction and inflammation from the mast cells in the respiratory tract.

USES

The mast cell stabilizers are used in combination with other drugs in the treatment of asthma and other allergic disorders, including allergic rhinitis (nasal solution), and in the prevention of exercise-induced bronchospasm. When the mast cell stabilizers are used in conjunction with other antiasthma drugs, a reduction in dosage of the drugs may be possible after using the mast cell stabilizer for 3 or 4 weeks. These drugs may be given by nebulization, aerosol spray, or as an oral concentrate.

ADVERSE REACTIONS

The more common adverse reactions associated with the mast cell stabilizers include headache, dizziness, nausea, fatigue, hypotension, or unpleasant taste in the mouth. These drugs may cause nasal or throat irritation when given intranasally or by inhalation.

CONTRAINDICATIONS, PRECAUTIONS, AND INTERACTIONS

The mast cell stabilizers are contraindicated in patients with known hypersensitivity to the drugs. The mast cell stabilizers are contraindicated in patients during attacks of acute asthma because they may worsen bronchospasm during the acute asthma attack.

It is important to use the mast cell stabilizers cautiously in patients with impaired renal or hepatic function and during pregnancy

محاضرة رقم -7-

Cardiotonic drugs

The cardiotonics are drugs used to increase the efficiency and improve the contraction of the heart muscle, which leads to improved blood flow to all tissues of the body. The drugs have long been used to treat congestive heart failure (CHF), a condition in which the heart cannot pump enough blood to meet the tissue needs of the body.

HF is a complex clinical syndrome that can result from any number of cardiac or metabolic disorders .Any condition that impairs the ability of the ventricle to pump blood can lead to HF.

The most common symptoms associated with HF include:

Left Ventricular Dysfunction

- Shortness of breath with exercise or difficulty breathing when lying flat
- Dry, hacking cough or wheezing
- Orthopnea (difficulty breathing while lying flat)
- Restlessness and anxiety

Right Ventricular Dysfunction

- Swollen ankles, legs, or abdomen, leading to pitting edema
- Anorexia
- Nausea
- Nocturia (the need to urinate frequently at night)
- Weakness
- Weight gain as the result of fluid retention

Other symptoms include:

- Palpitations, fatigue, or pain when performing normal activities
- Tachycardia or irregular heart rate
- Dizziness or confusion

Cardiotonics

Digoxin (Lanoxin) is the most commonly used cardiotonic drug. Other terms used to identify the cardiotonics are **cardiac glycosides** or **digitalis glycosides**.

The digitalis or cardiac glycosides are obtained from the leaves of the purple foxglove plant or the *Digitalis purpurea* and the *Digitalis lanata*. Miscellaneous drugs with positive inotropic action such as inamrinone and milrinone (Primacor) are nonglycosides used in the short-term management of HF.

ACTIONS

Digitalis acts in two ways:

1. Increases cardiac output through positive inotropic activity
2. Decreases the conduction velocity through the atrioventricular (AV) and sinoatrial (SA) nodes in the heart

CONTRAINDICATIONS

The cardiotonics are contraindicated in patients with known hypersensitivity, ventricular failure,

PRECAUTIONS

The cardiotonics are given cautiously in patients with electrolyte imbalance (especially hypokalemia, hypocalcemia, and hypomagnesemia), severe pulmonary disease, acute and impaired renal or hepatic function.

محاضرة رقم -3-

Diuretics

A **diuretic** is a drug that increases the secretion of urine (ie, water, electrolytes, and waste products) by the kidneys. Many conditions or diseases, such as heart failure, endocrine disturbances, and kidney and liver diseases can cause retention of excess fluid (**edema**). When the patient shows signs of excess fluid retention, the primary health care provider may order a diuretic There are various types of diuretic drugs such as :-

- Carbonic anhydrase inhibitors
- Loop diuretics
- Osmotic diuretics
- Potassium-sparing diuretics
- Thiazides and related diuretics

Diuretics are used in a variety of medical disorders. In some instances, hypertension may be treated with the administration of an antihypertensive drug and a diuretic. The diuretics used for this combination therapy include the loop diuretics and the thiazides and related diuretics.

ACTION

Carbonic Anhydrase Inhibitors

Carbonic anhydrase is an enzyme that produces free hydrogen ions, which are then exchanged for sodium ions in the kidney tubules. Carbonic anhydrase inhibitors inhibit the action of the enzyme carbonic anhydrase. This effect results in the excretion of sodium, potassium, bicarbonate, and water. Carbonic anhydrase inhibitors also decrease the production of aqueous humor in the eye, which in turn decreases intraocular pressure (IOP) (ie, the pressure within the eye).

Loop Diuretics

The loop diuretics, furosemide (Lasix) and ethacrynic acid (Edecrin), increase the excretion of sodium and chloride by inhibiting reabsorption of these ions in the distal and proximal tubules and in the loop of Henle.

This mechanism of action at these three sites appears to increase their effectiveness as diuretics.. Bumetanide (Bumex) primarily increases the excretion of chloride but also has some sodium-excreting ability.

Osmotic Diuretics

Osmotic diuretics increase the density of the filtrate in the glomerulus. This prevents selective reabsorption of water, which allows the water to be excreted. Sodium and chloride excretion is also increased.

Potassium-Sparing Diuretics

Potassium-sparing diuretics work in either of two ways : -

1-Triamterene (Dyrenium) and amiloride (Midamor) depress the reabsorption of sodium in the kidney tubules, therefore increasing sodium and water excretion. Both drugs additionally depress the excretion of potassium and therefore are called potassium-sparing (or potassiumsaving) diuretics.

2-Spironolactone (Aldactone), also a potassium-sparing diuretic, antagonizes the action of aldosterone. Aldosterone, a hormone produced by the adrenal cortex, enhances the reabsorption of sodium in the distal convoluted tubules of the kidney. When this activity of aldosterone is blocked, sodium (but not potassium) and water are excreted.

Thiazides and Related Diuretics

Thiazides and related diuretics inhibit the reabsorption of sodium and chloride ions in the ascending portion of the loop of Henle and the early distal tubule of the nephron. This action results in the excretion of sodium, chloride, and water.

USES

Carbonic Anhydrase Inhibitors

Glaucoma is an increase in the IOP that, if left untreated, can result in blindness . Acetazolamide (Diamox) is used in the treatment of simple glaucoma,. These drugs are also used in the treatment of edema caused by congestive heart failure (CHF), drug-induced edema, and control of epilepsy .

Loop Diuretics

Loop diuretics are used in the treatment of edema associated with CHF, cirrhosis of the liver, and renal disease, including the nephrotic syndrome. Furosemide is the

drug of choice when a rapid diuresis is needed or if the patient has renal insufficiency, Furosemide is used to treat hypertension.

Osmotic Diuretics

Mannitol (Osmitrol) is used for the promotion of dieresis in the prevention and treatment of the oliguric phase of acute renal failure, as well as for the reduction of IOP and the treatment of cerebral edema.

Potassium-Sparing Diuretics

Amiloride (Midamor) is used in the treatment of CHF and hypertension and is often used with a thiazide diuretic. Spironolactone and triamterene are also used in the treatment of hypertension and edema caused by CHF, cirrhosis, and the nephrotic syndrome. Amiloride, spironolactone, and triamterene are also available with hydrochlorothiazide, a thiazide diuretic that enhances the antihypertensive and diuretic effects of the drug combination while still conserving potassium.

Thiazides and Related Diuretics

Thiazides and related diuretics are used in the treatment of hypertension, edema caused by CHF, hepatic cirrhosis, corticosteroid and estrogen therapy, and renal dysfunction.

ADVERSE REACTIONS

Carbonic Anhydrase Inhibitors

Adverse reactions associated with short-term therapy with carbonic anhydrase inhibitors are rare. Long-term use of these drugs may result in fever, rash, numbness, photosensitivity reactions,

Loop Diuretics

Adverse reactions seen with the loop diuretics may include anorexia, nausea, vomiting, dizziness, rash, **postural hypotension** (dizziness and light- headedness , when rising suddenly from a sitting or lying position), **orthostatic hypotension** (hypotension after standing in one place for a long time).

Osmotic Diuretics

The osmotic diuretics urea and mannitol are administered intravenously (IV), whereas glycerin and isosorbide are administered orally. Administration by the IV route may result in a rapid fluid and electrolyte

imbalance, especially when these drugs are administered before surgery with the patient in a fasting state.

Potassium-Sparing Diuretics

Hyperkalemia (increase in potassium in the blood), a serious event, may be seen with the administration of potassium-sparing diuretics

Thiazides and Related Diuretics

Administration of thiazides and related diuretics may be associated with numerous adverse reactions. However, many patients take these drugs without experiencing adverse reactions other than excessive fluid and electrolyte loss, which often can be corrected with an adequate fluid intake, a balanced diet, supplemental oral electrolytes, or the eating of foods or fluids high in the electrolytes that are being lost.

CONTRAINDICATIONS, PRECAUTIONS, AND INTERACTIONS

Carbonic Anhydrase Inhibitors

The carbonic anhydrase inhibitors are contraindicated in patients with known hypersensitivity to the drugs, electrolyte imbalances, severe kidney or liver dysfunction, Diuretics are used cautiously in patients with renal dysfunction.

Loop diuretics

Loop diuretics are contraindicated in patients with known hypersensitivity to the loop diuretics or to the sulfonamides, severe electrolyte imbalances, hepatic coma, Loop diuretics are used cautiously in patients with renal dysfunction.. Furosemide is used in children but should be used cautiously. The loop diuretics are used cautiously in patients with liver disease.

Osmotic Diuretics

The osmotic diuretics are contraindicated in patients with known hypersensitivity to the drugs, electrolyte imbalances, severe dehydration, and those who experience progressive renal damage after instituting therapy (mannitol).

Potassium-Sparing Diuretics

The potassium-sparing diuretics are contraindicated in patients with known hypersensitivity to the drugs, serious electrolyte imbalances, significant renal impairment, and those receiving another potassium-sparing diuretic.

Thiazides and Related Diuretics

The thiazide diuretics are contraindicated in patients with known hypersensitivity to the thiazides or related diuretics, electrolyte imbalances, renal decompensation, hepatic coma . A cross-sensitivity reaction may occur with the thiazides and sulfonamides.

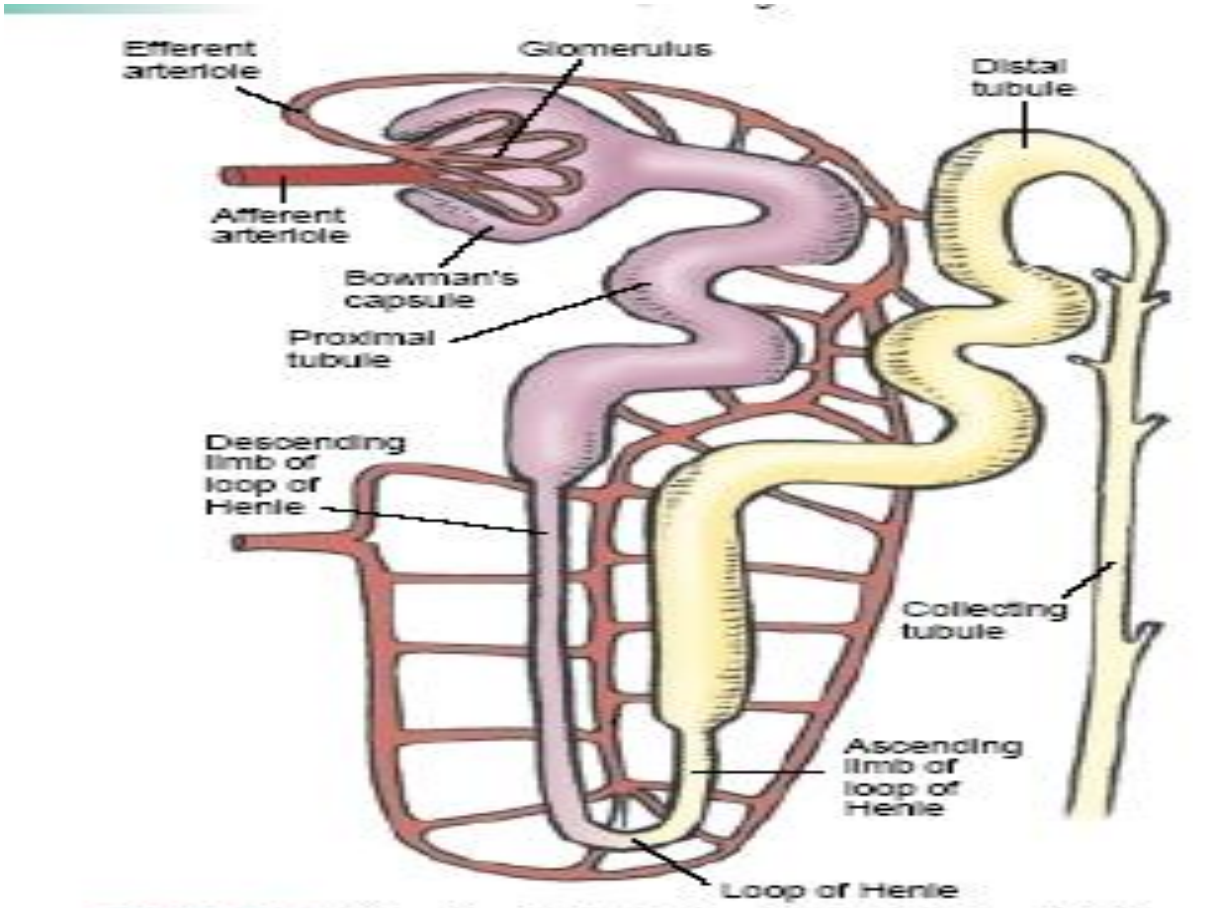

FIGURE 46-1. The nephron is the functional unit of the kidney. Note the various tubules, the site of most diuretic activity. The loop of Henle is the site of action for the loop diuretics. Thiazide diuretics act at the ascending portion of the loop of Henle and the distal tube of the nephron.

محاضرة رقم -2-

Antidiarrheals and Laxatives

I- Antidiarrheals

ACTIONS

Antidiarrheals decrease intestinal peristalsis, which is usually increased when the patient has diarrhea. Examples of these drugs include difenoxin with atropine (Motofen), diphenoxylate with atropine (Lomotil), and loperamide (Imodium).

USES

Antidiarrheals are used in the treatment of diarrhea.

ADVERSE REACTIONS

Diphenoxylate use may result in anorexia, nausea, vomiting, constipation, rash, dizziness, drowsiness, sedation, euphoria, and headache. This drug is a narcotic-related drug that has no analgesic activity but has sedative and euphoric effects and drug dependence potential. To discourage abuse, it is combined with atropine (an anticholinergic or cholinergic blocking drug), which causes dry mouth and other mild adverse effects. Loperamide is not a narcotic-related drug, and minimal adverse reactions are associated with its use.

Occasionally, abdominal discomfort, pain, and distention have been seen, but these symptoms also occur with severe diarrhea and are difficult to distinguish from an adverse drug reaction.

CONTRAINDICATIONS, PRECAUTIONS, AND INTERACTIONS

These drugs are contraindicated in patients whose diarrhea is associated with organisms that can harm the intestinal mucosa (*Escherichia coli, Salmonella, Shigella*) and in patients with pseudomembranous colitis, abdominal
pain of unknown origin, and obstructive jaundice. The antidiarrheal drugs are contraindicated in children younger than 2 years.

The antidiarrheal drugs are used cautiously in patients with severe hepatic impairment or inflammatory bowel disease. Antidiarrheals are classified as Pregnancy Category B drugs and should be used cautiously during pregnancy and lactation.

The antidiarrheal drugs cause an additive CNS depression when administered with alcohol, antihistamines, narcotics, and sedatives or hypnotics. There are additive

cholinergic effects when administered with other drugs having anticholinergic activity, such as antidepressants or antihistamines. Concurrent use of the antidiarrheals with a monoamine oxidase inhibitor increases the risk of a hypertensive crisis.

2-Laxatives

ACTIONS

There are various types of laxatives (see the Summary Drug Table: Drugs Used in the Management of Gastrointestinal Disorders). The action of each laxative is somewhat different, yet they produce the same result—the relief of constipation .

USES

A laxative is most often prescribed for the short-term relief or prevention of constipation. Certain stimulant, emollient, and saline laxatives are used to evacuate the colon for rectal and bowel examinations. Fecal softeners or mineral oil are used prophylactically in patients who should not strain during defecation, such as after anorectal surgery or a myocardial infarction. Psyllium may be used in patients with irritable bowel syndrome and diverticular disease. Polycarbophil may be prescribed for constipation or diarrhea associated with irritable bowel syndrome and diverticulosis. Mineral oil is useful for the relief of fecal impaction. Docusate is used to prevent dry, hard stools. Constipation may occur as an adverse drug reaction. When the patient has constipation as an adverse reaction to another drug, the primary care provider may prescribe a stool softener or another laxative to prevent constipation during the drug therapy.

ADVERSE REACTIONS

Laxative use, especially high doses or use over a long time, can cause diarrhea and a loss of water and electrolytes. For some patients, this may be a serious adverse effect. Laxatives may also cause abdominal pain or discomfort, nausea, vomiting, perianal irritation, fainting, bloating, flatulence, cramps, and weakness. Prolonged use of a laxative can result in serious electrolyte imbalances, as well as the "laxative habit," that is, a dependency on a laxative to have a bowel movement. Some of these products contain tartrazine, which may cause allergic-type reactions (including bronchial asthma) in susceptible individuals.

Obstruction of the esophagus, stomach, small intestine, and colon has occurred when bulk-forming laxatives are administered without adequate fluid intake or in patients with intestinal stenosis.

CONTRAINDICATIONS, PRECAUTIONS, AND INTERACTIONS

Laxatives are contraindicated in patients with known hypersensitivity and those with persistent abdominal pain, nausea, or vomiting of unknown cause or signs of acute appendicitis, fecal impaction, intestinal obstruction, or acute hepatitis. These drugs are used only as directed because excessive or prolonged use may cause dependence. Magnesium hydroxide is used cautiously in patients with any degree of renal impairment.

Laxatives are used cautiously in patients with rectal bleeding, in pregnant women, and during lactation. The following laxatives are Pregnancy Category C drugs: cascara, sagrada, docusate, glycerin, phenolphthalein, magnesium hydroxide, and senna. These drugs are used during pregnancy only when the benefits clearly outweigh the risks to the fetus.

Mineral oil may impair the GI absorption of fat-soluble vitamins (A, D, E, and K). Laxatives may reduce absorption of other drugs present in the GI tract, by combining with them chemically or hastening their passage through the intestinal tract. When surfactants are administered with mineral oil, surfactants may increase mineral oil absorption. Milk, antacids, H2 antagonists, and proton pump inhibitors should not be administered 1 to 2 hours before bisacodyl tablets because the enteric coating may dissolve early (before reaching the intestinal tract), resulting in gastric lining irritation or dyspepsia and decreasing the laxative effect of the drug.

المحاضرة رقم –6–
التطبيقات العلاجية – د . شهباء الخزرجي

Anti-arrhythmic drugs

The antiarrhythmic drugs are primarily used to treat cardiac arrhythmias. A cardiac **arrhythmia** is a disturbance or irregularity in the heart rate, rhythm, or both, which requires administration of one of the antiarrhythmic drugs. An arrhythmia may occur as a result of heart disease or from a disorder that affects cardiovascular function. Conditions such as emotional stress, hypoxia, and electrolyte imbalance also may trigger an arrhythmia. An electrocardiogram (ECG) provides a record of the electrical activity of the heart. Careful interpretation of the ECG along with a thorough physical assessment is necessary to determine the cause and type of arrhythmia. The goal of anti arrhythmic drug therapy is to restore normal cardiac function and to prevent life-threatening arrhythmias.

ACTIONS

The cardiac muscle (myocardium) has attributes of both nerve and muscle and therefore has the properties of both. Some cardiac arrhythmias are caused by the generation of an abnormal number of electrical impulses (stimuli). These abnormal impulses may come from the sinoatrial node or may be generated in other areas of the myocardium.

Class I Antiarrhythmic Drugs

Class I anti arrhythmic drugs, such as moricizine, have a membrane-stabilizing or anesthetic effect on the cells of the myocardium, making them valuable in treating cardiac arrhythmias. they are subdivided into classes I-A, I-B, and I-C.

Class I-A

The drugs disopyramide, procainamide, and quinidine are examples of class I-A drugs.

Class I-B Drugs

Lidocaine (Xylocaine), the representative class I-B drug,

Class I-C Drugs

Flecainide (Tambocor) and propafenone (Rythmol) are examples of class I-C drugs.

Class II Antiarrhythmic Drugs

Class II antiarrhythmic drugs include beta (B_)-adrenergic blocking drugs, such as acebutolol (Sectral), esmolol (Brevibloc), and propranolol (Inderal).

These drugs also decrease myocardial response to epinephrine and norepinephrine (adrenergic neurohormones) because of their ability to block stimulation of β receptors of the heart .

Class III Antiarrhythmic Drugs

Bretylium (Bretylol) , Amiodarone (Cordarone)

Class IV Antiarrhythmic Drugs

Class IV antiarrhythmic drugs include verapamil (Calan) and the other calcium channel blockers. Calcium channel blockers produce their antiarrhythmic action by inhibiting the movement of calcium through channels across the myocardial cell membranes and vascular smooth muscle.

CONTRAINDICATIONS

The antiarrhythmic drugs are reserved for emergency situations and are contraindicated in patients with known hypersensitivity to the antiarrhythmic drugs and during pregnancy and lactation.

PRECAUTIONS

All antiarrhythmic drugs are used cautiously in patients with renal or hepatic disease. When renal or hepatic dysfunction is present, a dosage reduction may be necessary.

محاضرة رقم -9-

Sulphonamides

The sulfonamides (sulfa) drugs were the first antibiotic drugs developed that effectively treated infections. Although the use of sulfonamides began to decline after the introduction of more effective anti-infectives, such as the penicillins and other antibiotics, these drugs still remain important for the treatment of certain types of infections.
Sulfonamides are antibacterial agents, meaning they are active against bacteria. Sulfadiazine, sulfisoxazole, and sulfamethizole are examples of sulfonamide preparations.

ACTIONS

The sulfonamides are primarily bacteriostatic, which means they slow or retard the multiplication of bacteria. This bacteriostatic activity is due to sulfonamide antagonism to para-aminobenzoic acid (PABA), a substance that some, but not all, bacteria need to multiply. Once the rate of bacterial multiplication is slowed, the body's own defense mechanisms (white blood cells) are able to rid the body of the invading microorganisms and therefore control the infection.

USES

The sulfonamides are often used to control urinary tract infections caused by certain bacteria such as *Escherichia coli*, *Staphylococcus aureus*, and *Klebsiella-Enterobacter*. Mafenide (Sulfamylon) and silver sulfadiazine (Silvadene) are topical sulfonamides used in the treatment of second- and third-degree burns. Additional uses of the sulfonamides are given in the Summary Drug Table: The Sulfonamides.

ADVERSE REACTIONS

The sulfonamides are capable of causing a variety of adverse reactions. Some of these are serious or potentially serious; others are mild. The following hematologic changes may occur during sulfonamide therapy:

- Agranulocytosis—decrease in or lack of granulocytes, a type of white blood cell
- Thrombocytopenia—decrease in the number of platelets
- Aplastic anemia—anemia due to deficient red blood cell production in the bone marrow
- Leukopenia—decrease in the number of white blood cells

.

CONTRAINDICATIONS

The sulfonamides are contraindicated in patients with hypersensitivity to the sulfonamides, during lactation, and in children less than 2 years old.

PRECAUTIONS

The sulfonamides are used with caution in patients with renal or hepatic impairment and bronchial asthma. These drugs are given with caution to patients with allergies.

INTERACTIONS

When a sulfonamide is administered with an oral anticoagulant, the action of the anticoagulant may be enhanced. Sulfonamides may inhibit the (hepatic) metabolism of the oral hypoglycemic drugs tolbutamide (Orinase) and chlorpropamide (Diabinese). This would increase the possibility of a hypoglycemic reaction.

محاضرة رقم -10-

Penicillins

The The antibacterial properties of natural penicillins were discovered in 1928 by Sir Arthur Fleming while he was performing research on influenza. There are four groups of penicillins: natural penicillins, penicillinase-resistant penicillins, aminopenicillins, and the extended-spectrum penicillins.

DRUG RESISTANCE

Because the natural penicillins have been used for many years, drug-resistant strains of microorganisms have developed, making the natural penicillins less effective than some of the newer antibiotics. Bacterial resistance has occurred within the penicillins. **Bacterial resistance** is the ability of bacteria to produce substances that inactivate or destroy the penicillin. One example of bacterial resistance is the ability of certain bacteria to produce **penicillinase,** an enzyme that inactivates penicillin.

ACTIONS

Penicillins prevent bacteria from using a substance that is necessary for maintenance of the bacteria's outer cell wall. Unable to use this substance for cell wall maintenance, the bacteria swell, rupture, assume unusual shapes, and finally die . The penicillins may be **bactericidal** (destroy bacteria) or **bacteriostatic** (slow or retard the multiplication of bacteria). They are bactericidal against sensitive microorganisms (ie, those microorganisms that will be affected by penicillin) provided there is an adequate concentration of penicillin in the body. An adequate concentration of any drug in the body is referred to as the blood level. An inadequate concentration or inadequate blood level) of penicillin may produce bacteriostatic activity, which may or may not control the infection.

USES

Infectious Disease

Penicillins may be used to treat infections such as urinary tract infections, septicemia, meningitis, intra-abdominal infection, gonorrhea, syphilis, pneumonia, and other respiratory infections.

Prophylaxis

Penicillin is of no value in the treatment of viral or fungal infections. However, the primary health care provider occasionally will prescribe penicillin as **prophylaxis**

(prevention) against a potential secondary bacterial infection that can occur in a patient with a viral infection. In these situations the viral infection has weakened the body's defenses and the person is susceptible to other infections, particularly a bacterial infection.

ADVERSE REACTIONS

Common adverse reactions include mild nausea, vomiting, diarrhea, sore tongue or mouth, fever, and pain at injection site. Penicillin can stimulate a **hypersensitivity** (allergic) reaction within the body. Another adverse reaction that may be seen with penicillin, as well as with almost all antibiotics, is a **superinfection** (a secondary infection that occurs during antibiotic treatment).

Superinfections

Antibiotics can disrupt the **normal flora** (nonpathogenic microorganisms within the body) causing a superinfection. The destruction of large numbers of **nonpathogenic** bacteria (normal flora) by the antibiotic alters the chemical environment. This allows uncontrolled growth of bacteria or fungal microorganisms, which are not affected by the antibiotic being administered.

Other Adverse Reactions

Other adverse reactions associated with penicillin are hematopoietic changes such as anemia, **thrombocytopenia** (low platelet count), **leukopenia** (low white blood cell count), and bone marrow depression..

CONTRAINDICATIONS

Penicillins are contraindicated in patients with a history of hypersensitivity to penicillin or the cephalosporins.

PRECAUTIONS

Penicillins should be used cautiously in patients with renal disease, pregnancy , lactation (may cause diarrhea or candidiasis in the infant), and in those with a history of allergies.

INTERACTIONS

Some penicillins (ampicillin, bacampicillin, penicillin V) may interfere with the effectiveness of birth control pills that contain estrogen. There is a decreased effectiveness of the penicillin when it is administered with the tetracyclines.

Cephalosporins

The cephalosporins are a valuable group of drugs that are effective in the treatment of almost all of the strains of bacteria affected by the penicillins, as well as some strains of bacteria that have become resistant to penicillin. The cephalosporins are structurally and chemically related to penicillin. The cephalosporins are divided into first-, second-, and third-generation drugs. Particular cephalosporins also may be differentiated within each group according to the microorganisms that are sensitive to them. Generally, progression from the first-generation to the second-generation and then to the third-generation drugs shows an increase in the sensitivity of gram-negative microorganisms and a decrease in the sensitivity of gram-positive microorganisms. For example, a first-generation cephalosporin would have more use against gram-positive microorganisms than would a third-generation cephalosporin.

ACTIONS

Cephalosporins affect the bacterial cell wall, making it defective and unstable. This action is similar to the action of penicillin. The cephalosporins are usually bactericidal (capable of destroying bacteria).

USES

The cephalosporins are used in the treatment of infections caused by susceptible microorganisms. Examples of microorganisms that may be susceptible to the cephalosporins include streptococci, staphylococci, citrobacters, gonococci, shigella, and clostridia. Pharyngitis, tonsillitis, otitis media, lower respiratory infections, urinary tract infections, septicemia, and gonorrhea are examples of the types of infections that may be treated with the cephalosporins. The cephalosporins also may be used perioperatively, that is, during the preoperative, intraoperative, and postoperative periods, to prevent infection in patients having surgery on a contaminated or potentially contaminated area, such as the gastrointestinal tract or vagina. In some instances, a specific drug may be recommended for postoperative prophylactic use only.

ADVERSE REACTIONS

The most common adverse reactions seen with administration of the cephalosporins are gastrointestinal disturbances, such as nausea, vomiting, and diarrhea. Hypersensitivity (allergic) reactions may occur with administration of the cephalosporins and range from mild to life threatening. **aplastic anemia** (anemia due to deficient red blood cell production). Because of the close relation of the cephalosporins to penicillin, a patient allergic to penicillin also may be allergic to the cephalosporins.

Other adverse reactions that may be seen with administration of the cephalosporins are headache, dizziness, **nephrotoxicity** (damage to the kidneys by a toxic substance).

CONTRAINDICATIONS

The nurse should not administer cephalosporins if the patient has a history of allergies to cephalosporins or penicillins.

PRECAUTIONS

The nurse should use cephalosporins cautiously in patients with renal or hepatic impairment and in patients with bleeding disorders. Safety of cephalosporin administration has not been established in pregnancy or lactation; these drugs are assigned to Pregnancy Category B.

INTERACTIONS

The risk of nephrotoxicity increases when the cephalosporins are administered with the aminoglycosides.

محاضرة رقم -5-

Anti-Hypertenssive drugs

Hypertension is usually defined as a systolic pressure above 140 mm Hg and a diastolic pressure above 90 mm Hg . Hypertension is serious
because it causes the heart to work too hard and contributes to atherosclerosis. It increases the risk of heart disease, congestive heart failure, kidney disease, blindness, and stroke. Most cases of hypertension have no known cause. When there is no known cause of hypertension, the term **essential hypertension** is used. Essential hypertension has been linked to certain risk factors, such as diet and lifestyle.
When a direct cause of the hypertension can be identified, the condition is described as **secondary hypertension.** Among the known causes of secondary hypertension, kidney disease ranks first, with tumors or other abnormalities of the adrenal glands following. In **malignant hypertension** the diastolic pressure usually exceeds 130 mm Hg.
The types of drugs used for the treatment of hypertension include:

• Vasodilating drugs—for example, hydralazine
(Apresoline) and minoxidil (Loniten)
• B_-adrenergic blocking drugs—for example, atenolol (Tenormin), metoprolol (Lopressor), and propranolol (Inderal)
• Antiadrenergic drugs (centrally acting)—for example, guanabenz (Wytensin) and guanfacine (Tenex)
• Antiadrenergic drugs (peripherally acting)—for example, guanadrel (Hylorel) and guanethidine (Ismelin)
• Alpha (_)-adrenergic blocking drugs—for example, doxazosin (Cardura) and prazosin (Minipress)
• Calcium channel blocking drugs—for example, amlodipine (Norvasc) and diltiazem (Cardizem)
Angiotensin-converting enzyme (ACE) inhibitors— for example, captopril (Capoten), enalapril (Vasotec), and lisinopril (Prinivil)
• Angiotensin II receptor antagonists—for example, irbesartan (Avapro), losartan (Cozaar), and valsartan (Diovan)
• Diuretics—for example, furosemide (Lasix) and hydrochlorothiazide (HydroDIURIL)

ACTIONS

Many antihypertensive drugs lower the blood pressure by dilating or increasing the size of the arterial blood vessels **(vasodilatation).** Vasodilatation creates an increase in the **lumen** (the space or opening within an artery) of the arterial blood vessels, which in turn increases the amount of space available for the blood to circulate. Because blood volume (the amount of blood) remains relatively constant, an increase in the space in which the blood circulates (ie, the blood vessels) lowers the pressure of the fluid (measured as blood pressure) in the blood vessels

Antihypertensive drugs that have vasodilating activity include:

- Adrenergic blocking drugs
- Antiadrenergic blocking drugs
- Calcium channel blocking drugs
- Vasodilating drugs

Another type of antihypertensive drug is the diuretic, The mechanism by which the diuretics reduce elevated blood pressure is to their ability to increase the excretion of sodium from the body.

The mechanism of action of the ACE inhibitors is not fully understood. It is believed that these drugs may prevent (or inhibit) the activity of **angiotensin-converting enzyme,** which converts angiotensin I to angiotensin II, a powerful vasoconstrictor.

USES

Antihypertensives are used in the treatment of hypertension. Some antihypertensive drugs are used only in severe cases of hypertension and when other less potent drugs have failed to lower the blood pressure. At times, two antihypertensive drugs may be given together to achieve a better response.

Diazoxide (Hyperstat IV) and nitroprusside (Nitropress) are examples of intravenous (IV) drugs that may be used to treat hypertensive emergencies.

ADVERSE REACTIONS

When any antihypertensive drug is given, postural or orthostatic hypotension may be seen in some patients, especially early in therapy. **Postural hypotension** is the occurrence of dizziness and light-headedness when the individual rises suddenly from a lying or sitting position. **Orthostatic hypotension** occurs when the individual has been standing in one place for a long time. These reactions can be avoided or minimized by having the patient rise slowly from a lying or sitting position and by avoiding standing in one place for a prolonged period.

CONTRAINDICATIONS

Antihypertensive drugs are contraindicated in patients with known hypersensitivity to the individual drugs.

Use of the angiotensin II receptor antagonists during the second and third trimester of pregnancy is contraindicated because use may cause fetal and neonatal injury or death.

PRECAUTIONS

Antihypertensive drugs are used cautiously in patients with renal or hepatic impairment or electrolyte imbalances, during lactation and pregnancy

INTERACTIONS

The hypotensive effects of most antihypertensive drugs are increased when administered with diuretics and other antihypertensives

محاضرة رقم -4-

Anti-angina drugs

Angina is a disorder characterized by atherosclerotic plaque formation in the coronary arteries, which causes decreased oxygen supply to the heart muscle and results in chest pain or pressure. Any activity that increases the work load of the heart, such as exercise or simply climbing stairs, can precipitate an angina attack. Antianginal drugs relieve chest pain or pressure by dilating coronary arteries, increasing the blood supply to the myocardium. The antianginal drugs include the nitrates and the calcium channel blockers.

ACTIONS

Nitrates

The nitrates, such as isosorbide (Isordil) and nitroglycerin, have a direct relaxing effect on the smooth muscle layer of blood vessels. The result of this effect is an increase in the lumen of the artery or arteriole and an increase in the amount of blood flowing through these vessels. An increased blood flow results in an increase in the oxygen supply to surrounding tissues.

Calcium Channel Blockers

Systemic and coronary arteries are influenced by movement of calcium across cell membranes of vascular smooth muscle. The contractions of cardiac and vascular smooth muscle depend on movement of extracellular calcium ions into these walls through specific ion channels. Calcium channel blockers, such as amlodipine (Norvasc), diltiazem (Cardizem), nicardipine (Cardene), nifedipine (Procardia), and verapamil (Calan), inhibit the movement of calcium ions across cell membranes. This results in less calcium available for the transmission of nerve impulses. This drug action of the calcium channel blockers (also known as slow channel blockers) has several effects on the heart, including an effect on the smooth muscle of arteries and arterioles. These drugs dilate coronary arteries and arterioles, which in turn deliver more oxygen to cardiac muscle. Dilation of peripheral arteries reduces the workload of the heart.

USES

Nitrates

The nitrates are used to treat angina pectoris. Some of these drugs, such as isosorbide dinitrate (Isordil), are used for **prophylaxis** (prevention) and long-term treatment of angina, whereas others, such as sublingual nitroglycerin (Nitrostat),

are used to relieve the pain of acute angina attacks when they occur. Antianginal Drugs for additional uses of the nitrates.

Calcium Channel Blockers

Calcium channel blockers are primarily used to prevent anginal pain associated with certain forms of angina, such as vasospastic (Prinzmetal's variant) angina and chronic stable angina. They are not used to abort (stop) anginal pain once it has occurred. When angina is caused by coronary artery spasm, these drugs are recommended when the patient cannot tolerate therapy with the beta -adrenergic blocking drugs or the nitrates. Calcium channel blockers used as antianginals are listed in the Summary Drug Table: Antianginal Drugs. Some calcium channel blocking drugs have additional uses. Verapamil affects the conduction system of the heart and may be used to treat cardiac arrhythmias. Diltiazem, nicardipine, nifedipine, and verapamil also are used in the treatment of essential hypertension.

ADVERSE REACTIONS

Nitrates

A common adverse reaction seen with these drugs is headache, especially early in therapy. Hypotension, dizziness, vertigo, and weakness may also be associated with headache. Flushing caused by dilatation of small capillaries near the surface of the skin may also be seen.

Calcium Channel Blockers

Adverse reactions to the calcium channel blocking drugs usually are not serious and rarely require discontinuation of the drug therapy.

CONTRAINDICATIONS, PRECAUTIONS, AND INTERACTIONS

Nitrates

The nitrates are contraindicated in patients with known hypersensitivity to the drugs allergy to adhesive (transdermal system), The nitrates are used cautiously in patients with severe hepatic or renal disease, and during pregnancy or lactation. Increased nitrate serum concentrations may occur when the nitrates are administered with aspirin.

Calcium Channel Blockers

Calcium channel blockers are contraindicated in patients who are hypersensitive to the drugs .The calcium channel blockers are used cautiously during pregnancy and

lactation and in patients with congestive heart failure (CHF), hypotension, or renal or hepatic impairment.