THE BASICS OF PHARMACOLOGY FOR NURSES
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ABSTRACT

There are two distinct sets of responsibilities a registered nurse must fulfill: a social responsibility and a scientific responsibility. Drug administration falls squarely at the intersection of these two responsibilities. Not only do nurses need to understand the scientific elements of pharmacology—the science of how drugs are administered and processed by the body—but also the social component: nurses need to build relationships in order to glean important information from their patients and serve as educators for both the patient and the patient’s family. The information that nurses obtain from their patients is critical for avoiding drug-drug interactions and drug-food interactions, allergic reactions, and other adverse effects. But, without a strong background in the scientific elements of pharmacokinetics and pharmacodynamics, this information is meaningless. This course will help nurses navigate the relationship between these social and scientific roles.
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Statement of Need

Online pharmacology continuous learning has become a highly satisfying method for nurses to increase and maintain proficiency in medication administration. Pharmacology knowledge-based learning outcomes tailored to nursing learning needs are expected to lead to improved sharing of expertise and collaborative practice throughout all levels of acute and outpatient health care settings.

Course Purpose

This course will provide learning for nurses at all levels of experience in basic pharmacology knowledge of medication and administration skills.
Learning Objectives

1. Differentiate between pharmacokinetics and pharmacodynamics.
2. List the four stages of pharmacokinetics.
3. Categorize drugs into their corresponding schedules.
4. Identify the drug regulation and marketing processes.
5. Identify the roles of gender, race, and ethnicity in dosage calculation.
6. Explain therapeutic effects, side effects/adverse effects for common analgesics.
7. Recognize contraindications for drugs.
8. Describe patient teaching and preparation prior to drug administration.
9. Identify the three common methods of drug administration.
10. Describe circumstances that may require an infusion pump.
11. Describe drugs used in the treatment of each of the following disorders and disease categories: a) nervous system, b) cardiovascular, c) respiratory, d) HIV, e) nausea/vomiting, f) diabetes mellitus, g) reproductive and h) glaucoma.
12. Describe appropriate intervention responses to an adverse drug interaction.

Target Audience

Advanced Practice Registered Nurses, Registered Nurses/Licensed Practical Nurses

Course Author & Director Disclosures

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INTRODUCTION

There are two distinct sets of responsibilities that a registered nurse must fulfill: a social responsibility and a scientific responsibility. Drug administration falls squarely at the intersection of these two responsibilities. Not only do nurses need to understand the scientific elements of pharmacology but also the social component: nurses need to build relationships in order to glean important information from their patients and serve as educators for both the patient and the patient’s family.

Drugs are the most vital and extensively researched field of the medical sciences. The advent of drugs started ages ago and we now have a seemingly unlimited variety. The rapid advancement in drugs and medicines has brought forward new cures, therapies and treatments for the diseases and medical conditions that had previously been not possible to cure. These are due to advancements in pharmacology - the study of actions of drugs on living organisms. The medical staff including doctors, nurses and clinicians don’t only need to be aware of older medications, but should also have knowledge of advancements that are occurring and the way they affect the practice of medicine. A medication suitable for one patient might not necessarily be suitable to another even if that patient is exhibiting a similar condition.

The information that nurses obtain from their patients is critical for avoiding drug-drug interactions and drug-food interactions, allergic reactions, and other adverse effects. But without a strong background in the scientific elements of pharmacokinetics and pharmacodynamics, this information is not as useful. Hence, we cannot neglect the importance of drug administration and knowledge in the profession of modern nursing.

The study of drugs and their mechanisms of action (MOAs) should not be neglected in nursing practice as there are a number of benefits nurses can derive from it. Pharmacology provides comprehensive understanding regarding drug usage and precautionary measures that need to be considered while giving patients different drugs so that the drug benefits can be maximized and its harmful side effects minimized.
The science of pharmacology has existed for millennia. The application and usage of pharmacologic products to relieve adverse conditions and suffering has been norm throughout this time in almost every country. Modern trends and advancement in medical science have greatly enhanced pharmacology [1].

Drugs have been a fundamental component of the treatment of various diseases from the earliest existence of humankind, using various materials found in nature (e.g. tree bark, roots herbs, animal parts, plant seeds etc.) The MOA was unknown and as such, usages of these substances were based solely on the observed therapeutic benefits or the lack thereof. With the passage of time, through trial and error, knowledge was developed to distinguish between harmful and beneficial substances to be used as medicines [1].

Modern pharmacology started in the mid 19th century through scientific study of the chemical separation of particular active agents from their complicated and complex mixtures, often plant extracts. It began with scientists predicting the impacts of the medicine on the human patient [2]. This developed into further investigations of the effects of specific agents on isolated organs; an example among many of this development in modern pharmacology is the studied effect of ergometrine on strips of uterine muscle.

The origin of experimental pharmacology is usually linked with the work of the French physiologist, Francois Magendie, at the start of 19th century. Magendie’s research was based on strychnine-containing plants that clearly established the action site of these substances. The sites of action were the motor neurons of the spinal cord. This work provided proof for the view that poisons and drugs must be dissolved in the blood and carried to the location of action before generating their effects.

The development and input of 20th century pharmacology have been huge, with more than twenty pharmacologists having won Nobel prizes. Their contributions comprised of discoveries of numerous vital drugs, second messengers and neurotransmitters and, a more complete understanding of many biochemical and physiological processes [3]. Pharmacology in general and the growth of highly useful new drugs in particular have
flourished during the preceding half of the 20th century. This extraordinary development has paralleled progress in associated disciplines upon which the field of pharmacology builds and is built, such as the following disciplines:

- molecular biology
- biochemistry
- physiology
- pathology
- anatomy

The growth of new analytical and investigational techniques and tools has aided in the development of the following fundamental characteristics of pharmacology [4].

- The association between dose and effect
- Pharmacodynamics - the events involved in the ingestion, absorption, distribution, alteration and excretion of drugs
- The localization of the action site
- The mechanism of drug action
- The association between biological action of substances and chemical structure

The past, present and future development of pharmacology aims to:

- Understand drugs and the way they affect living things
- Know the accurate dosage of drugs
- Identify and respond to drug interactions, reactions and side effects and treat accordingly
- Know when to apply drugs since some conditions do not require drug therapy
- Understand the procedure of drug ingestion, absorption, distribution, metabolism and removal.
- Identify the attributes of ideal drugs
- Know the implications of pharmacology in nursing, addressing the following five “Right” approaches: [5]
1) Use right drug
2) Give to the right patient
3) Give the right dose
4) Give by the right route
5) Give at the right time

The field of pharmacology has been divided broadly into two major classes of pharmacokinetics and pharmacodynamics [5], which will be discussed in more depth in the following sections.

Pharmacokinetics

Pharmacokinetics can be defined as the movement of drugs within the body’s cells, tissues and organs. This process can be referred to as the (L)ADME scheme, which is explained below:

- **Liberation:**
  The process of drug release. This may apply, depending on the drug formulation and delivery system (e.g. is the drug enteric coated to increase release in the small intestine versus the stomach);

- **Absorption:**
  The process of the diffusing or being actively transported into the blood and plasma.

- **Distribution:**
  The dissemination of the drug into the fluid spaces of the body (intracellular, extracellular, intracapsular, plasma).

- **Metabolism:**
  This process is also known as biotransformation and is the biochemical series of processes used to alter the drug into its metabolites.

- **Excretion:**
  This is the removal of the drug and its metabolites from the body fluids.
Pharmacodynamics

Pharmacodynamics can be defined as the effects and MOA (Mechanism of Action) of a drug on the body’s cells, tissues and organs. This will be discussed in further depth later on in this introductory section.

Pharmacokinetics

Pharmacokinetics is a combination of two Greek words, “Pharmakon”, meaning drug and “kineticos”, meaning to do with motion. Pharmacokinetics is a subdivision of pharmacology that determines the effects living organisms have on substances administered exogenously to that organism. The substances usually consist of: [6]

- Pharmaceutical agents
- Hormones
- Nutrients
- Toxins

This branch of pharmacology studies the drug disposition in the human body that is a vital and crucial part of the drug’s sensible use and development. In other words, it can be said that pharmacokinetics is the quantitative research of drug movement, in and out of the human body, tissues, cells and organs. The impact intensity of the drug upon the body is based on the drug concentration at the site of action, which, in turn, depends upon its pharmacokinetic attributes.

Pharmacokinetics helps explain how a particular drug affects the target tissue after application through the processes of absorption, distribution, metabolism and excretion, along with the effect(s) these substances are expected to have on the body [6].

Pharmacokinetics is an essential medical discipline that involves applied therapeutics. Patients must be prescribed suitable medicines for a particular medical condition. The medication is selected on the basis of the evidence-based approach to medical practice, standards of care and should be chosen to minimize interactions with any other alternative drug or therapies the patient might be taking [5].
The plan of a dosage regimen is reliant on a fundamental understanding of the drug use process (DUP). With a patient who shows particular medical symptoms, pharmacists should always ask a basic question of the patient, such as: *Are you feeling any adverse effect from a drug-related problem?* Once this problem is assessed and a clinical analysis is made, a pharmacist applies the DUP to make sure the patient is given a suitable medication treatment, which the patient understands and finds acceptable.

Pharmacists who use DUP consider the following: [7]

- Requirement for a drug
- Selection of a drug
- Goals of treatment
- Design of schedule
  - Route
  - Dose and rate
  - Duration
- Monitoring and appraisal
- Counseling

Once a specific drug is chosen, the principles of medical pharmacokinetics are essential to ensure that the correct formulation of a drug is selected for administration. On the basis of drug management parameters for a patient, which need an understanding of absorption, distribution, metabolism and excretion, the dose schedule for the drug in a particular patient may be developed. The pharmacist is then required to ensure that the suitable drug and protocol is prescribed to attain optimal efficacy and to minimize toxicity.

Pharmacokinetics has given medicine a theoretical and mathematical basis to review the time course of drugs along with their impacts on the body. It allows the following four processes to be quantified (see diagram: The Pharmacokinetics Process): [8]

1. Absorption
2. Distribution
3. Metabolism
4. Excretion

The Pharmacokinetics Process

Indirect measurement of various parameters can be used to monitor the actions of some drugs [9].

Direct measurements of drug concentrations in the plasma or blood, saliva, urine, and other sampled fluids are often obtained and more clinically useful. Kinetic homogeneity, which is the relatively predictable relationship between plasma concentrations and the site of action or drug receptor cite, assumes that the plasma concentration is directly related to the tissue concentration, and may often be used to explain the effects of the specific drug.
Variation in the plasma drug concentration may reflect variations in a drug concentration at the receptor sites, along with tissue variations and drug metabolism. As the drug concentration in plasma increases, the drug concentration in most tissues will be increasing proportionally. Similarly, if the concentration of a drug is reduced in plasma then the concentration in tissues is likely to decrease, as is represented below:

Absorption
Absorption of a drug represents its shift from the site of administration to the blood. Most drugs are absorbed in the body via passive diffusion, which is the mechanism whereby drugs disperse across membranes along the concentration gradient [9].
Factors affecting absorption

Drug properties

Drug properties are described in terms of lipid solubility, molecular weight (molar mass) and polarity and affect the absorption of the drug. Drugs that are of low polarity and therefore higher lipid solubility, and, which are easily ionized, diffuse more through the membrane. The extent of the drug's ionization depends upon their surrounding pH. In addition, the routes of administration are also important [10].

Routes of administration and bioavailability:

The following are examples and definitions of drug administration routes and bioavailability:

Topical:

Topical applications are based on lipid solubility (lipophilicity) of a drug. These drugs, either alone or with the aid of a carrier, are those that are able to directly pass through the epidermal and dermal layers of the skin. Examples include nitroglycerin, Fentanyl and estradiol. The mucus membranes of the mouth, vagina, rectum, etc. allow for the diffusion of lipophillic drugs [10].

Subcutaneous and intramuscular:

Here, drugs are injected in the vicinity of blood capillaries, and bypass the capillary endothelium by passing through large paracellular pores. The subcutaneous (SQ) and intramuscular (IM) routes tend to provide greater predictability and are generally absorbed more quickly than by oral absorption.

Oral:

Oral preparations of drugs can be either water or lipid soluble and undergo first pass metabolism in the liver or absorption by the intestines (following liver metabolism) before they reach systemic circulation. As a consequence, the drug concentration in plasma may be decreased.
Bioavailability:
Bioavailability may be defined as the rate of drug absorption as verified by its excretion through urine or a concentration-time curve in the blood. It is assessed as the Area Under the Curve or AUC, which is directly proportional to the total amount of unmetabolized drug that reaches the systemic circulation.

It is the measure of the fraction (F) of the administered drug dosage that arrives at the systematic circulation in unmetabolized or active form. By definition, a drug that is injected has a bioavailability of 100%. However, bioavailability is frequently decreased following oral ingestion because of the following factors: [11]

- The drug might be incompletely absorbed by the intestines; and,
- The drug absorbed passes through the portal circulation and undergoes first pass metabolism with a percentage excreted in the bile.

Distribution
The distribution of a drug describes the drug route from blood circulation to the tissues and to active sites. The distribution rate of drugs is based on blood flow, which is the drugs’ degree of ionization, lipid solubility, and the degree of binding to tissue proteins and plasma as well as variations in regional differences in diseases such as uremia, congestive heart failure (CHF), and liver disease. The drug also is distributed throughout the body based on the equilibrium between drug distribution in tissue fluids and plasma (partition characteristics) [10].

Volume of distribution:
The volume of distribution is the volume needed to achieve the same drug concentration as exists in the plasma. It is measured in liters using the following formula: [11]

\[
V = \frac{\text{Dose administration IV}}{\text{Plasma concentration}}
\]

For example, if the total drug in body is 1000 mg and the drug concentration in plasma is 50 mg/L, then the volume will be:

\[
V= \frac{1000mg}{50 \text{ mg/L}} = 20 \text{ L}
\]
Drugs may be distributed into any or all of the following compartments:

- Plasma
- Interstitial fluid
- Intracellular fluid

The composition of standard total body fluid (42 L approx.) is stated below as:

- Plasma (4 Liters)
- Interstitial fluid (10 Liters)
- Intracellular fluid (28 Liters)

**Factors influencing distribution**

**Lipid solubility:**
Lipid soluble drugs can more readily pass through the plasma membrane and fatty tissues.

**Plasma protein binding**
Many drugs bind to plasma proteins. Basic drugs bind to alpha 1- Glycoprotiens and acidic ones bind to plasma albumin. The degree of binding is based on the physiochemical properties of the individual compound. Increasing drug concentrations can saturate the binding locations [11].

The drugs having high affinity to plasma proteins are able to replace other drugs and endogenous compounds. For example, aspirin and sulfanomides are drugs that can replace warfarin, bilirubin, etc. Higher level of binding proteins can make drugs have a
longer lasting action since the bound fraction is not fully accessible for liver metabolism, unless it is significantly excreted by the kidneys or the intestines.

*Tissue storage*
Drugs also get accumulated in particular organs and show tropism, or an affinity, to specific tissue elements. Some of the examples are given below:

<table>
<thead>
<tr>
<th>Organ</th>
<th>Accumulated drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart &amp; skeletal muscle</td>
<td>Digoxin (to muscle proteins)</td>
</tr>
<tr>
<td>Thyroid gland</td>
<td>Iodine</td>
</tr>
<tr>
<td>Bones &amp; teeth</td>
<td>Tetracyclines</td>
</tr>
</tbody>
</table>

**Metabolism**
Metabolism is the process of chemical transformations undergone by a drug in the body tissues and organs. Overall, drugs undergo Phase I, II and III metabolism in the liver to convert, for example, non-polar and lipid soluble drugs into polar water soluble compounds in order to promote excretion by the kidney [12].

Many hydrophilic (water soluble) drugs undergo less biotransformation and many are eliminated in the same form, e.g. streptomycin. Phase I, II and III metabolism by the liver is essential for protecting body against both endogenous and exogenous toxic metabolites.

**Results of metabolism**
The results of metabolism include conversion of the following:

- The active drug into inactive metabolites
- The nonactive drug into active product
- The nonactive drug (*prodrug*) into the active form.
- Non-toxic or low toxicity into a more toxic metabolite
Phases of metabolism
The three phases of drug and xenobiotic detoxifying metabolism primarily occur in the liver, and are listed as follows:

- **Phase I** or Nonsynthetic reactions) where, in general, drugs or xenobiotics are made more water soluble by the introduction of polar and/or reactive groups
- **Phase II** or conjugation reactions, which, in general, increase solubility, decrease reactivity and allow for more efficient excretion
- **Phase III** — excretion

**Phase I Reactions**
Phase I reactions can be broadly divided into three classes with additional reactions including cyclization and decyclization.

- Oxidation
- Reduction
- Hydrolysis

These reactions can occur in many different tissues but the most important aspect of Phase I metabolism generally takes place in the liver. Many substances (e.g. barbiturates) become less toxic in Phase I reactions, but some (e.g.acetaminophen) may become more toxic. It is important to note here than many drug interactions with foods, other drugs and supplements occur due to Phase I metabolism by the induction or inhibition of specific enzymes. If, for example, Drug X is metabolized by a specific enzyme that is inhibited by Drug Y, then the plasma concentration of Drug X will be increased. If the same Drug X is metabolized by a specific enzyme that is induced by Drug Y, the plasma concentration of Drug X will be decreased.

**Oxidation**
Oxidation, which always occurs with an accompanying reduction, is the primary drug metabolizing reaction in which oxygen or a negatively charged radical is added or hydrogen or positively charged radical is removed from the compound. Barbiturates, acetaminophen, nicotine, paracetamol, and steroids are examples of drugs that are
primarily oxidized [12]. The Cytochrome P450 family of enzymes are primarily responsible for these Phase I reactions.

Some substances are oxidized by non-microsomal enzymes (cytoplasmic and mitochondrial). Examples of these substances include alcohol and adrenaline.

**Reduction:**
Reduction always occurs with oxidation and involves CYP 450 enzymes as well. Drugs that are reduced include levodopa, halothane, chloral hydrate and warfarin.

![DOPA-decarboxylase](image)

**Hydrolysis:**
Hydrolysis is the cleavage of a molecule by water and can take place in the liver, plasma, intestines and other tissues [13]. For example, choline esters, procaine, oxytocin, aspirin, amides and many anesthetics are hydrolyzed.

![Ester + H₂O → Acid + Alcohol](image)

**Cyclization:**
Cyclization is the creation of a ring structure from a straight chain compound. For example, the anti-malarial drug proguanil is cyclicized to the active metabolite, cycloguanil.

**Decyclization:**
Decyclization is the opening up of ring structure of the cyclic molecule, as occurs with phenytoin and barbiturates.
**Phase II reactions:**

Phase II reactions are conjugation reactions, or the forming of two chemical compounds. Substances may be conjugated to glucuronic acid and/or specific groups including acetyl, carboxyl, amino, hydroxyl and sulfhydryl groups. Other conjugations involve glutathione, sulfates and glycine. Overall, water solubility is further increased. Molecular size is also increased, leading to less diffusion and the potential for active transport across the cell membrane and excretion by the kidneys and gastrointestinal (GI) tract.

**Glucoronide conjugation (Glucuronidation):**

Compounds with carboxylic or hydroxyl acid groups are conjugated with glucoronic acid, which is derived from glucose. Aspirin, nicotine, morphine, acetaminophen, lorazepam, and thyroxine are examples of drugs that represent glucoronide conjugation [14].

It is important to note that some glucoronidated drugs, excreted in bile, may then be hydrolyzed in the gut by bacteria or endogenous beta glucuronidases, generating beta glucuronides, potentially increasing toxicity and decreasing excretion.

**Acetylation**

Compounds having hydrazine residues or amino groups are conjugated (acetylated) with the cofactor AcetylCoA. Examples of acetylated drugs include sulfonamides such as dapsone, isoniazid, hydralazine and procainamide [14].

Genetic variations in these enzymes can cause an individual to be a *fast acetylator* where the drug in question is reduced in efficacy by that individual and *slow acetylators* where the drug in question may cause toxicity and drug interactions because it is inefficiently excreted.

**Sulfation**

The phenolic compounds and steroids are sulfated by sulfokinases. Examples include the adrenal and sex steroids and diflunisal. Sulfation is highly pH dependent and is reversible.
**Methylation**

The phenols and amines can be methylated. S-adenosyl methionine (SAMe) is the most common methyl donor. Examples of methylated drugs include adrenaline and nicotinic acid. Methylation is also reversible.

Factors affecting metabolism are listed below as: [15]

- Genetic Polymorphisms
- Concurrent usage of drugs: Induction & Inhibition
- Pollutant exposure from industry or the environment
- Pathological status
- Age

**Excretion**

The final phase of drug metabolism is excretion. In the transport process, the drug or its metabolite is excreted via the kidney, feces, respiratory system, or by the skin [16].

Hydrophilic (water-soluble) compounds can be easily excreted. The routes include:

- Kidney
- Bile
- Saliva and sweat
- Milk
- Exhalation via the pulmonary system

**Hepatic excretion**

Drugs can be excreted in the bile, and then by the feces, especially if they are conjugated with glucoronic acid. The process is as follows:

- The drug is absorbed and is glucoronicidated or sulfatated in the liver and secreted through the bile and into the feces.
- If the sulfate or glucoronic acid is cleaved off by bacteria in the GI tract, the drug may be reabsorbed. This can occur with steroid hormones and amoxicillin.
Renal excretion

Renal excretion depends on the following factors, as listed and explained below:

- Glomerular filtration
- Tubular reabsorption
- Tubular secretion

Glomerular filtration

Glomerular capillaries contain non-diaphragm fenestrated pores that are among the largest in the body. The kidney is responsible for the excretion of water-soluble substances including the drug metabolites resulting from Phase I and Phase II metabolism. Non-protein bound drugs (lipid soluble or insoluble) presented to the glomerulus are filtered and potentially excreted as well. This filtration is based on their plasma protein binding and characteristics of renal blood flow. Protein bound drugs are not filtered by the normal kidneys because the size of the protein-drug complex is too large [15].

Tubular Re-absorption

Tubular re-absorption is the re-entry or back diffusion of (lipid soluble) drugs. It depends upon the degree of ionization and such factors as the pH of the urine. Water soluble and ionized drugs are excreted intact, and examples include aminoglycoside and tobramycin. Changes in urinary pH can affect the excretion patterns of ionized drugs, which are explained below.

- Weak bases are ionized more in acidic urine and the renal excretion of these weak bases is increased.
- Weak acids are ionized more in alkaline (basic) and the renal excretion of these weak acids is increased.

Tubular secretion

This is the energy dependent active transport process that decreases the free drug concentration in the plasma. Increased drug dissociation from plasma binding proteins
allows increased secretion by the tubules and therefore increased excretion. In general, drug dissociation occurs in such physiological conditions, as follows:

- **Acidic urine**
  - Alkaline drugs eliminated
  - Acidic drugs reabsorbed

- **Alkaline urine**
  - Acidic drugs eliminated
  - Alkaline drugs reabsorbed

**Kinetics of elimination**

**Clearance:**

The clearance of a drug (CL) is the theoretical volume of plasma from which the drug is entirely removed in a unit of time. It is calculated as: [16]

\[
CL = \frac{\text{Rate of Elimination (ROE)}}{\text{Concentration}}
\]

For example, if a drug is 20 mcg/mL and the ROE is 100 mcg/min, the clearance will be:

\[
CL = \frac{100 \text{ mcg/min}}{20 \text{ mcg/mL}} = 5 \text{ mL/min}
\]

**Zero order kinetics (Linear)**

In zero order kinetics, the elimination rate is independent of the drug concentration but the half life \( (t_{1/2}) \) depends on the initial drug concentration. Alcohol is eliminated by zero-order kinetics. A plot of concentration versus time gives a straight line.

**First order kinetics (Exponential)**

Here, the elimination rate is directly proportional to the drug’s concentration and depends on the initial drug concentration, provided there is no physiologic process that affects the clearance. In other words, a constant fraction of drug is eliminated per unit time. \( T_{1/2} \) is independent of the concentration and a plot of concentration versus time gives a curved line. (See diagram below: a plot of the log of the concentration versus time will give a straight line and is very often used).
**Plasma half-life**

This is the time required for the plasma concentration to be reduced to half of its original value. It is calculated as:

\[ T_{1/2} = \ln 2 / k \]

Where 2 = natural logarithm of 2 (0.693); and, \( k = \text{Elimination constant} = \frac{\text{CL}}{V} \)
(Clearance of the drug/Volume of Distribution), it is found that

\[ T_{1/2} = 0.693 \times \left( \frac{V}{\text{CL}} \right) \]

**The plateau principle**

If a drug is infused continuously, the plasma concentration will increase over time until a steady state or equilibrium between the rate of infusion and the rate of elimination is achieved. This is the plateau or steady state concentration. A plateau can be achieved using other delivery systems as well, but the mathematics is more complicated. The plateau is used, along with the information on the most effective dose for a specific drug, to determine dose and the timing of dose.

**Monitoring of plasma concentration**

Monitoring plasma levels is useful in the following situations:

- Monitoring drugs with narrow therapeutic windows or narrow safety margin drugs, like digoxin and aminoglycosides.
• Where there is a large individual variation in the response to drugs like with antidepressants or lithium.
• In renal dysfunction and renal failure
• In poisoning cases

However, monitoring of plasma levels is *not* useful in:
• Determining the response to drugs whose plasma levels can be directly measured (e.g. diuretics)
• Prodrugs activated in body (e.g. levodopa)
• Monitoring MAO inhibitors
• Drugs with irreversible action (e.g. Orgnophosphorus compounds)

### Pharmacodynamics

Pharmacodynamics is the field that studies the physiological and biochemical effects of drugs on the body, parasites or on pathogenic microorganisms. It is also concerned with the drug’s action and the association between the drug effect and its concentration. In basic terms, it can be said that it studies what the drug does to the body [4].

Two important characteristics in the study of pharmacodynamics are:
• Drug concentration
• Drug effect on the site of action

This leads to drug-receptor relationship, an equilibrium, which is presented as: [17]

\[ L + R \rightleftharpoons L \cdot R \]

Where, the \( L = \) Ligand (drug) and \( R = \) Receptor (attachment site); and, the equilibrium constant, \( K_d \) is defined as \( \frac{[L][R]}{[L \cdot R]} \)

*The Receptor Theory*

The presence of receptors was initially inferred from observations of the physiological and chemical specificity of the effects of certain drugs [14]. To date, numerous drug
receptors have been described and the genes encoding receptor proteins have been replicated and sequenced.

Receptors establish the quantitative association between drug dose and its pharmacologic effect. They are responsible for the specificity of drug action and mediate the actions of pharmacologic agonists and antagonists. Drugs which act as agonists activate the receptor to its function and result in a biological response, based on the function of the receptor. A drug may be a full or partial agonist. Drugs which act as antagonists bind to the receptors and inhibit their function as well as block any further binding. A drug may be a full or partial antagonist and may fully or partially block the receptors and its natural ligand.

_The relationship between drug concentration and response_

The association between drug quantity and the clinically observed response is often quite complex. However, in controlled _in vitro_ pharmacologic studies, the association between the drug’s concentration and its result is less complex and can be explained with some mathematical precision [4].

Note that the first graph represents percent (%) maximal effect versus the drug concentration and the second graph represents the logarithmic conversion. This is a first order reaction.
Drug potency and efficacy

**Efficacy** is the greatest possible effect (Effect\textsubscript{max}) of a drug while **potency**, a more relative measure, refers to the different doses of two drugs required to generate the similar effect.

Usually data is plotted as effect versus the log of the drug concentration [Drug]. This makes it simpler to determine the half maximal effective concentration EC\textsubscript{50} and to contrast drug efficacy and potency [11].

In this graph, Drugs A and B have similar efficacy, but drug A has more potency.
than B or C since the dose of B or C must be higher to generate a similar effect as drug A. Although drug C has lesser efficacy than B, it is higher potency than B at lower drug concentrations.

*General Classes of Antagonists*

*Chemical Antagonists*

One drug might antagonize the binding of a second drug by binding to and inactivating the second drug. For example, protamine (a positively charged protein at physiologic pH) binds to (sequesters) heparin (a negatively charged anticoagulant), thus, blocking further interactions with proteins involved in the formation of blood clots and decreasing heparin’s anticoagulant activity [10].

*Physiological Antagonists*

Physicians often recommend drugs that take advantage of the feedback mechanisms between endogenous regulatory pathways. For example, the catabolic actions of glucocorticoids result in an increase in blood sugar - an outcome opposed by insulin. While glucocorticoids and insulin act on fairly diverse pathways, insulin is sometimes used to antagonize the hyperglycemic action of high levels of glucocorticoid hormones – resulting from either augmented endogenous synthesis (e.g. a tumor of the adrenal cortex) or due to glucocorticoid therapy [10].

*Pharmacological Antagonists*

Drugs may bind to receptors without changing receptor function but acting instead as competitive inhibitors. These antagonists might block endogenous agonists from binding to the receptor by competing for the similar receptor site or might bind to another site on the receptor that obstructs the action of the agonist. In both cases, the natural actions of the agonist are prevented [10]. In addition, pharmacological antagonists can inhibit the function of the receptor.

*Competitive and Irreversible Antagonists*

Receptor antagonists bind to the receptor but do not turn it on. Often, the impact of these antagonists is due to preventing agonists from binding to and activating the
receptors. Antagonists might be competitive (reversibly displaced by agonists) or noncompetitive (not reversibly displaced by agonists) [4].

**Implications for nurses and clinicians**

The degree of inhibition is based on the concentration of the antagonist. Thus the degree and duration of an antagonists’ action depends upon its concentration in the plasma which in turn is subject to the rate of its metabolic excretion or clearance. For example, different patients getting a fixed dosage of propranolol (a competitive β-adrenoreceptor antagonist) shows a broad range of plasma levels due to variations in drug clearance. Thus, the result of this competitive antagonist of norepinephrine and therefore the efficacy of the propranolol might differ extensively in different patients. The dosage must be adjusted accordingly in order to achieve the best results [17].

The degree of inhibition is based on the concentration of the competing agonist, for example, when propranolol is given in a high enough dose to decrease the effects of basal levels of the neurotransmitter norepinephrine, which causes the resting heart rate to be diminished. However, if norepinephrine levels rise from exercise, emotional stress or postural changes, the levels might be sufficient to overcome the competitive antagonism caused by propranolol and boost the heart rate. Thus the prescriber needs to take other medications, life issues, stressors and postural changes into consideration when determining the choice of an agent or agents in manipulating the therapeutic response to a particular drug.

**Noncompetitive antagonists**

Some receptor antagonists attach to the receptor at sites distant to the agonist binding site. Binding of this antagonist is not altered by changes in the concentration of an agonist.

In addition, the number of residual unoccupied receptors might be too low for
even high concentrations of agonist to elicit a maximal response [15].

**Benefits of irreversible inhibitors**

Once the receptor is irreversibly bound to a drug antagonist, there is no longer a requirement for more to inhibit the effects of an agonist. Thus the period of action of such an inhibitor is comparatively autonomous of its rate of elimination and more reliant on the turnover rate of the receptor, allowing less drug to be used. (The turnover rate is the rate of new receptor synthesis by the cell).

**Disadvantages of irreversible inhibitors**

Phenoxybenzamine, an irreversible α–adrenoreceptor antagonist, is used to manage hypertension due to high catecholamines caused by tumors of the adrenal medulla (pheochromocytomas) [8]. This inhibition can be maintained even through periodic bursts of catecholamine discharge, typical of pheochromocytomas. However, if an overdose occurs, the α–adrenoreceptor inhibition cannot be controlled by an agonist — in other words, there is no effective antidote. Instead, the effects may be antagonized physiologically via a pressor agent that does not act via α–adrenoreceptors (e.g. angiotensin II, vasopressin) or by a strong agonist such as levarterenol [9].

**Partial and Full Agonists**

Agonists might vary in how firmly they bind to their receptors (potency) and in the result they create (efficacy). Some drugs might bind extremely tightly (are highly potent) but create just a modest result (low efficacy).

Low efficacy drugs are called “partial agonists” while the structurally similar drugs which create a more complete effect are termed as “full agonists” [15].
Quantal Dose-Effect Curves

It is not always feasible to construct graded dose-response curves if the pharmacological reaction is an either/or (quantal) event like the prevention of arrhythmia, convulsions or death. (A quantal event is one which has only two possible states).

The clinical significance of a quantitative association in a single patient is limited for application to other patients owing to the huge potential variation among patients in severity of disease and response to drugs [10]. One solution is to find out the amount of drug necessary to create a particular scale of effect in a huge number of patients (or animals). The cumulative frequency distribution of response is then plotted versus a log of the drug dose. The quantal effect might be selected based on clinical significance (e.g. relief of headache), low frequency of adverse effects (e.g. low frequency of a cardiac stimulant producing a boost in heart rate of 20 beats/min) or decreased mortality and morbidity overall [14].

The quantal dose effect curve is typified by the median effective dose ($ED_{50}$) - the dose at which 50% of patients show the particular quantal effect.

The dose that is essential to create a particular toxic result in 50% of animals is termed as the median toxic dose ($TD_{50}$). If the toxic result is death of the animal, a median lethal dose ($LD_{50}$) might be defined.

**Therapeutic Index**

Quantal dose effect curves allow a study of the margin of safety (or selectivity in response) for a particular drug. In animal studies, the therapeutic index is characterized as the ratio of the $TD_{50}$ to $ED_{50}$ [13]. Therefore if $TD_{50} = 500$ mg and
ED_{50} = 5 \text{ mg}, the drug is 100-fold more selective for the preferred response and the therapeutic index is 100.

The therapeutic index for humans is rarely identified with great accuracy. Drug trials and past clinical experience point toward a variety of effective doses and a diverse (but sometimes overlapping) series of possibly toxic doses [17].

Clinically satisfactory risk depends on the severity of the disease being treated. For example, the dosage range of a medicine for relief from headache will be much higher than the dose series that generates toxicity even if just a small percentage of individuals exhibit toxic effect. With a lethal disease such as Hodgkin's lymphoma, the tolerable difference between therapeutic and toxic doses is likely to be much smaller.

**DRUG INFORMATION**

**Drug Classes/Schedules**

The Controlled Substances Act (CSA) was approved as Title II of the Comprehensive Drug Abuse Prevention and Control Act of 1970. The CSA is the centralized U.S. drug plan under which the production, import, control, use, and supply of certain substances is controlled and regulated [18].

The legislation formulated five Schedules (classifications) with different requisites for a substance to be added in each. Two federal agencies, the Food and Drug Administration (FDA) and the Drug Enforcement Administration (DEA), determine which substances are to be included or excluded from the schedules. Congress has often scheduled other substances through other legislations [19].

**Schedule I**

Schedule I has the following characteristics: [20]

- The drug has a high potential for mistreatment.
- The drug has no presently accepted medical application in treatment in the United States.
• There is a lack of established safety for utilization of the drug under health supervision

Except as specially authorized, it is unlawful for any person to do the following:
• produce, dispense, or possess with intention to produce or issue a controlled substance; or,
• make, distribute, or dispense, or possess with intention to distribute or issue a counterfeit substance.

Drugs listed in DEA Schedule I include the following: [20]
• Bath Salts (3,4-methylenedioxypyrovalerone or MDPV)
• Ecstasy (MDMA or 3,4-Methylenedioxyamphetamine)
• GHB (gamma-hydroxybutyric acid)
• Heroin (diacetylmorphine)
• Khat (Cathinone)
• LSD (Lysergic acid diethylamide)
• Marijuana (cannabis, THC)
• MDMA (3,4-methylenedioxymethamphetamine or “ecstasy”)  
• Mescaline (Peyote)
• Methaqualone (Quaalude)
• Psilocybin

Special licensing processes must be followed to utilize these or other Schedule I drugs or substances.

Schedule II

Schedule II drugs have the following characteristics: [23]
• The drug has a high potential for abuse;
• The drug, at present, has an accepted medical application in the United States, or has an accepted medical utilization with strict restrictions;
• Abuse of the drug might lead to severe physical or psychological dependence.
Schedule II drugs are those that have a high potential for abuse or dependence but that also has valid legal medical uses. They are only prescribed under certain medical conditions with strict regulations and monitoring [31].

Schedule II drug prescriptions are usually only given for one month at a time. Federal law does not permit refills to be issued. If the doctor considers it essential, such as for a cancer patient in chronic pain, he/she can write three split 30-day prescriptions for his/her patient.

Drugs in schedule II include the following: [24]

- Amphetamines and Dextroamphetamine (Dexedrine)
- Cocaine (used as a contemporary anesthetic)
- Dexamfetamine (Focalin) and Methylphenidate (Ritalin)
- Dextromethamphetamine (Desoxyn) and Methamphetamine
- Fentanyl and strong pure opioid agonists, i.e. opium, levorphanol
- Heroin
- Hydromorphone
- Lisdexamfetamine (Vyvanse) and mixed amphetamine salts (Adderall)
- Methadone
- Morphine
- Nabilone (Cesamet)
- Opium and opium tincture (Laudanum)
- Oxycodone
- Oxymorphone
- Pethidine
- Phencyclidine (PCP)
- Pure codeine
- Pure hydrocodone
- Secobarbital (Seconal)
- Short-acting barbiturates, like pentobarbital, Nembutal;
- Tapentadol (Nucynta)
Schedule III

Schedule III drugs have the following characteristics: [25, 34]

- The drug has a potential for abuse, however, the potential is less than that of schedules I and II drugs;
- The drug has at present an accepted medical usage in treatment in the United States;
- Abuse of the drug cause low to moderate physical dependence or a high psychological dependence.

Schedule III drugs have less potential for addiction or abuse than schedule I and II drugs and have legitimate medical uses. Written or oral prescriptions must be written for all Schedule III drugs. Some states require electronic filing or only written prescriptions on special, security-based prescription pads. Such prescriptions cannot be filled or refilled six months after the date written or be refilled more than five times following the date of the prescription [34].

Drugs in schedule III include: [25]

- Anabolic steroids, including prohormones like androstenedione
- Benzphetamine HCl (Didrex)
- Buprenorphine
- Dihydrocodeine
- Ergine (lysergic acid amide)
- Fast-Acting barbiturates like pentobarbital (Nembutal) and secobarbital (Seconal)
- Hydrocodone / codeine,
- Intermediate-acting barbiturates, like butalbital or talbutal
- Ketamine
- Marinol
- Paregoric
- Phendimetrazine Tartrate
- Xyrem
Schedule IV

Schedule IV drugs have the following characteristics: [26, 32]

- The drug has less potential for abuse as compared to schedule III drugs;
- The drug has at present a accepted medical use in treatment in the United States;
- Abuse of the drug may cause limited psychological dependence or physical dependence as compared to schedule III drugs.

Control processes are similar to Schedule III drugs. Prescriptions for Schedule IV drugs can be refilled up to five times within a six-month time.

Drugs in schedule IV include: [30]

- Benzodiazepines, like chlordiazepoxide (Librium), alprazolam (Xanax), clonazepam (Klonopin) and diazepam (Valium)
- Carisoprodol (Soma)
- Chlora hydrate
- Difenoxin,
- Diphenoxylate with chlordiazepoxide, atropine sulfate, diazepam, diethylpropion
- Flunitrazepam (Rohypnol)
- Cloral hydrate
- Long-acting barbiturates like phenobarbital;
- Meprobamate
- Partial agonist opioid analgesics, like pentazocine (Talwin)
- Phenobarbital
- Temazepam (Restoril)
- The benzodiazepine-like Z-drugs such as zolpidem (Ambien), eszopiclone (Lunesta), zopiclone (Imovane) and zaleplon (Sonata)
- Tramadol (Ultram)

Schedule V

Schedule V drugs have the following characteristics: [29]
• The drug has a low potential for abuse compared to relative schedule IV drugs;
• The drug has at present, an accepted medical application in treatment in the United States;
• Abuse of the drug might cause limited psychological dependence or physical dependence compared to the drugs in schedule IV.

No drug in schedule V can be distributed or issued other than for a medical use.

Drugs in schedule V include: [28]

• Anticonvulsants like lacosamide (Vimpat), pregabalin (Lyrica) and retigabine (Potiga/Trobalt)
• Antidiarrheals, like diphenoxylate
• Cough suppressants having little amounts of codeine, like promethazine+codeine
• Opium or diphenoxylate
• Pyrovalerone

Regulation and Approval

The drugs that have been classified under these five schedules are regulated by The Controlled Substances Act (CSA). It is the federal drug regulatory policy that monitors, evaluates and controls the manufacturing, import, distribution, usage, possession and supply of the drugs. The same act also regulates narcotic drugs [35].

The drugs that have been classified into 5 categories are further controlled by the Department of Justice’s Drug Enforcement Administration (DEA) and the Food and Drug Administration (FDA). The DEA also addresses petitions regarding inclusion and exclusion of specific drugs from interested parties. Once the petition regarding any drug belonging to any schedule is filed, the DEA begins an investigation of the particular drug [36].

The DEA’s investigation of drugs is based on a number of factors. Usually the investigation is begun with the information collected from local and state law enforcement agencies, laboratories, regulatory agencies and other relevant sources.
Once the information is collected, the deputy administrator of the DEA and a committee of experts may request a medical and scientific appraisal and recommendations from the Department of Health and Human Services (HHS) regarding whether the particular drug should be removed or controlled. Once the DEA gets the medical and scientific evaluation from HHS, the DEA Administrator and relevant committees will assess all existing data and make a recommendation determining the schedule the drug should be listed under [37].

The Controlled Substances Act (CSA) is one of the most important documents for practitioners and nurses to comply with. In addition, it is also important for clinicians and nurses to stay current regarding any changes that may be made in the schedules in order to ensure enhanced public safety and health [38].

**Dosage Calculations**

Dosage calculation is used to determine the accurate dose of a drug. There can be a significant deal of variation in how different drugs are prescribed and it may be necessary at times to calculate the proper dose. For instance, an order might be written for Amoxicillin 500mg, but the drug that is available in the pharmacy is Amoxicillin 250 mg per tablet. The clinician can calculate that the patient requires 2 tablets to get the prescribed dosage of 500mg [39].

Some drugs, particularly those obtainable without a prescription or over the counter (OTC) preparations, have a wide therapeutic index (TI). This implies that broad ranges of doses can be utilized effectively and securely. For instance, the label on a bottle of aspirin might recommend taking two tablets for a mild headache. But a single tablet (half the dose) is usually enough to relieve symptoms for many people. While there is still potential for the abuse of OTC medications (e.g. laxative abuse), the wide TI does imply some greater degree of safety for the public using these OTC medications.

Most of the chemotherapy drugs, on the other hand, are toxins and have a fairly narrow range of effective and safe doses. Using too little may be insufficient for the desired therapeutic effect while using too much may prove toxic for the patient [40].
Depending on the drugs to be given, different ways are available to determine chemotherapy doses. Mostly, the chemotherapy drugs are calculated in milligrams (mg).

There are three special kinds of measurements that can be used when measuring medication dosages: [41]

- Household
- Apothecary
- Metric

<table>
<thead>
<tr>
<th>Type</th>
<th>Number</th>
<th>Solids</th>
<th>Liquids</th>
</tr>
</thead>
<tbody>
<tr>
<td>Household</td>
<td>Whole numbers and fractions before unit. Ex: 1 ½ T</td>
<td>Teaspoons (tsp, t)</td>
<td>Drop (gr)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tablespoons (Tbs, T)</td>
<td>Ounce (oz)</td>
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<tr>
<td></td>
<td></td>
<td>Pounds (lb)</td>
<td>Cup (c)</td>
</tr>
<tr>
<td>Apothecary</td>
<td>Whole numbers, fractions, and Roman Numerals after unit. Ex: gr 15 ½ or dr iss</td>
<td>Grains (gr)</td>
<td>Pint (pt)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Drams (dr or ʒ)</td>
<td>Quart (qt)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Glass</td>
</tr>
<tr>
<td>Metric</td>
<td>Whole numbers and decimals before unit (always put a 0 in front of the decimal. Ex: 0.15 mL</td>
<td>Grams (g)</td>
<td>Minum (m)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Meter (m)</td>
<td>Fluid Dram (dr or ʒ)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Liters (L)</td>
</tr>
</tbody>
</table>

The overall dose might be based on the body weight of an individual in kilograms (1 kilogram is equal to 2.2 pounds). For example, if the normal dose of a medicine is 10 milligrams per kilogram (10 mg/kg), an individual weighing 110 pounds (50 kilograms) would be given 500 mg (10 mg/kg x 50 kg) [41].

Several chemotherapeutic doses are determined on the basis of body surface area (BSA), based on a patient’s weight and height. BSA is calculated in meters squared (m²). Dosages for adults and children differ, even after BSA is considered. This is because the bodies of children process drugs less efficiently or more slowly than adults.
Children might have varied levels of sensitivity to the drugs as well. For similar reasons, dosages of certain drugs can also be attuned for the following individuals: [42]

- Elderly
- Those with a poor nutritional status
- Those that are obese
- Having already used or are currently using other medicines
- Having already passed through or currently passing through radiation therapy
- Having anemia, kidney or liver disorders

The dosage calculation is also based on the schedule to which a particular drug belongs. For example, Schedule I drugs are not generally prescribed as these medications have no acceptable medical usage, except sometimes, in experimental therapies.

Schedule II drugs are usually only prescribed in sufficient quantities for 30 days. Except when issued directly by a practitioner, no drug in Schedules III or IV can be issued without an oral or written prescription in compliance with legal regulations. Such prescriptions may not be filled or refilled after six months past the date written or be refilled more than five times following the date of the prescription unless changed by the practitioner. Prescriptions for Schedule IV drugs might be refilled up to five times within a six-month time [43].

**Monitoring requirements for nurses**

The provider prescribing a drug is liable for the appropriate, safe use of that drug. However, the licensed individual administering a drug in a hospital setting or at home (the nurses) also have a moral, ethical and legal responsibility to ensure that the drug is safe, therapeutic and being applied as per the schedule.

Nurses must keep in mind that every drug is given on a specific schedule that is carefully set up to get the maximum benefits of it and to minimize its side effects. If more than one medicine is given, the treatment plan will indicate how often and when every drug should be given. This is one of the major aspects of nurses’ monitoring requirements. They should observe if there are any side effects or adverse effects. If a
patient has been given more than one drug, they also need to observe if there are any significant drug interactions \[44\].

**The key principles**

Drug management activities carried out by nurses may differ, and are dependent upon the patient’s condition, the health care environment, its protocols and policies in place and the extent of the nurse’s professional standards of care and scope of their nursing practice or nursing specialty.

The major factors that must be considered when finding out the scope of nursing practice are also applicable to drug management. These include the following: \[45\]

- Competence
- Accountability and independence
- Continuing professional development
- Support for specialized nursing practice
- Delegation
- Emergency situations

**Standards of Care**

Each nurse is required to learn and maintain capability with regard to all facets of drug management, making sure that her/his skills, knowledge and clinical practice are up to date. Drug management practice makes every nurse accountable to the patient, the public, the nursing profession, her/his agency and any pertinent supervisory authority. This relates to both omissions and to actions \[46\].

**Supportive guidance**

It is the duty of the nurse to ensure the continuation of their sustained professional development, which is essential for the continuance of competence, mainly with regard to medicinal products. The nurse should look for aid and support where needed from professional associations, the health service provider and state regulatory boards regarding professional development \[46\].
The five rights of drug administration

There are certain principles for drug management that every nurse should adhere to in their delivery of service related to all therapeutic products [47]. The medication prescription should be confirmed that it is approved prior to administration of the medical product. Explanation of any questions concerning the prescription should be carried out at this time with the suitable health care expert. The cessation date of the drug should be checked before administration. Expired or improperly stored drugs must not be administered.

The five rights of drug administration are listed and elaborated on below [48]:

- Right medication
- Right Patient
- Right Dosage
- Right Form
- Right Time

1. The right medication:
   - Matching the prescription against the label of the dispensed drug
   - Being conscious of similar looking and similar sounding drugs
   - Using best practice by utilizing the generic names of drugs whenever possible

2. The right patient:
   - Ensuring the identity of the patient who is getting the medication
   - Checking the medical record number and/or recognition band
   - Asking the patient to state her/his name
   - Confirming that the age and name are correct
   - Maintaining a photograph of the individual on the drug administration record

3. The right dosage:
   - Considering if the dose is suitable based on size, age, vital symptoms or other variables
- If it is essential to calculate the dose (e.g., liquid form) the suitable equipment should be utilized

4. **The right form:**
   - Ensuring that the right form, route of delivery and management method of the drug are as prescribed
   - If this information is not shown on the prescription or on the label of the drug, it should be explained by the prescriber, as numerous drugs can be given by a range of routes

5. **The right time:**
   - Ensure accurate timing, frequency and period of the prescription
   - The timing of medications dosages can be important for maintaining particular therapeutic blood-drug levels (such as antibiotics) and avoiding mixing with other drugs
   - Document precisely and accurately the drug administration times

**Adverse effects**

An adverse effect or side effect of a drug is the non-therapeutic effect related to the use of a given drug or set of drugs at the usual dosage and during normal application. It is the harm or unfavorable effect on the body that arises due to drug use \[49].

From the most commonly used to the most complicated prescription medicine on the market, nearly all drugs carry a range of side effects. Many of these are minor side effects, while some can be significant for individual patients or for many patients. Other side effects are severe and can be life threatening, particularly when interacting with other medications.

Perhaps the most common adverse effects of drugs taken internally involves the GI system. Almost any drug can lead to nausea or an upset stomach, though it might only occur to a handful of patients. For drugs applied externally, skin irritation and non-specific rashes are a common complaint.
**Allergic reactions:**

Allergic reactions can occur with any medicine and can range from rashes and burning to severe anaphylactic reaction. A number of drugs activate side effects due to the similarity of their chemical structure with natural, endogenous substances [49]. One example is the general allergy drug diphenhydramine. Though it relieves allergy symptoms, it also represses the activity of acetylcholine, causing drowsiness along with some other side effects, including dry mouth.

Some drugs have few side effects when given properly. For instance, Warfarin (Coumadin, Jantoven), used to inhibit clot formation, is generally well tolerated; however serious internal blood loss may occur.

Side effects might only arise when drugs interact with other medications, foods, herbs or alcohol. Drinking alcohol along with narcotic painkillers is increasingly becoming a source of accidental overdose casualties. Consuming significant amounts of grapefruit juice, in some patients, can decrease the blood levels of numerous drugs, including the heart medicine Digoxin [48]. Often, these interactions occur because of either the inhibition or the induction of CYP450 Liver enzymes. (See Section on Phase I/Phase II Liver detoxification pathways).

For more serious or life-threatening side effects, details can be found on the packaging of OTC medicines and the inserts given with prescription drugs. Since the inserts can be a long list of potential bad effects, it is extremely useful to also speak to the provider or another nurse for any questions regarding a side effect of a drug.

**Contraindications**

A contraindication is a particular situation in which a medicine, process, or surgical treatment should not be used because it might be damaging to the patient. In other words, it is the reason to withhold or postpone a certain medical therapy [38].

Some contraindications are unconditional, meaning that there are no situations where the use is acceptable. For instance, teenagers and children with viral infections should never use aspirin due to the potential risk of Reye's syndrome, and a patient with a food
allergy must avoid the food to which they are allergic. Similarly, a person diagnosed with hemochromatosis must not be given iron supplements.

**Types of Contraindications**

There are two kinds of contraindications: [49]

1. The phrase *relative contraindication* implies that caution should be taken when two procedures or drugs are used at the same time. (It may be determined however, that the benefits offset the risk).

2. The phrase *absolute contraindication* states that combining substances or events could lead to a life-threatening situation. A medication or procedure that falls under this class must be avoided.

Some treatments might cause dangerous or unwanted reactions in patients with allergies, high blood pressure, or pregnancy. For instance, isotretinoin, a medicine given to treat acne, is absolutely contraindicated during pregnancy due to the danger of birth defects. Some decongestants are absolutely contraindicated in patients with high blood pressure and must be avoided.

Many drugs should not be given together. For example, a person who uses warfarin to reduce clotting should avoid taking aspirin, which is also a blood thinner. This is an example of a relative contraindication.

**DRUG ADMINISTRATION**

Due to the risks that are connected with drug administration, patients have the right to the following:

- To be educated and knowledgeable regarding the name, reason, action and possible side effects of drugs
- To refuse a medication after they have been informed of the possible consequences

The same as medical providers, nurses are responsible to ensure that patients are provided with necessary information prior to administration of medication. This includes
the anatomy, physiology, pharmacology, potential risks and benefits, as well as any legal issues [12].

**Communication prior to administration**

Before administration of any drug, a nurse needs to know and examine the data about the patient that includes his /her age, medical condition, previous medical records, drug history, and most importantly, the current medical chart. All of this data needs to be reviewed in advance to prepare clinicians to communicate information about a drug to the patient, in terms of the correct drug administration and safety profile [45].

Medication charts are basically legal documents that must be completed correctly and accurately in order to ensure that patients receive safe and effective drug therapy. Medication charts must be legible and in accordance the prescriber’s written or electronic entry; and, generally comprise the patient’s surname, first name, ward/clinic, medical record number (MRN), and patient ID, the drug name (generic/brand), dose form, strength and quantity required.

Nurses should verify that the medical chart has the prescriber’s printed name, signature and date of prescription. These requirements must be complete with each drug prescription. The patient’s weight should also be included for use to calculate any drug dosed by weight [48].

It can’t be emphasized enough that every nurse is lawfully accountable for the right administration of drugs, and, as already described, this includes the five “rights” of administration. [46]

**Allergies**

Prior to administration of medication, the nurse should determine if the patient has experienced any of the following:

1. Any recognized drug allergies
2. Any earlier adverse drug reaction
In evaluating a patient for an allergic reaction to a drug, the nurse must also determine the following in a timely way:

- Whether the drug had the needed effect
- Whether there has been little or no change
- Any adverse reactions occurring, if any

**Types of administration**

*Percutaneous administration*

Percutaneous drug administration involves drugs given to and absorbed through a patient’s skin or mucous membranes [50]. The drug is absorbed through the skin at a slow but steady rate. However, the rate of absorption across a mucous membrane is generally faster.

The method of administration via percutaneous route is as follows:
1. Clean the administration site
2. Administer medication
3. Leave medication on the spot for the necessary length of time.
4. Monitor the patient for wanted or unfavorable effects.

*Enteral administration*

Enteral administration involves any drug delivered and absorbed through the gastrointestinal tract. There are various forms of enteral administration, which may be divided into three diverse categories - oral, gastric, and rectal. Gastric administration involves the utilization of a tube by means of nasal route or a tube in the esophagus leading straight to the stomach [51].

The following chart outlines some basic pharmacology administration routes and forms, such as oral (solid/liquid) and rectal medication:
### Parenteral administration

Parenteral administration of a drug is other than by mouth or by rectal suppository [52]. Types of parenteral drug containers are listed and illustrated below:

- Glass ampules
- Single and multi-dose vials
- Non-constituted syringes
- Prefilled syringes
- Intravenous medication fluids

<table>
<thead>
<tr>
<th>Oral administration</th>
<th>Rectal administration</th>
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<tbody>
<tr>
<td>Solids</td>
<td>Liquids</td>
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<tr>
<td>Pill</td>
<td>Solution</td>
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<tr>
<td>Tablet</td>
<td>Soft gel</td>
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<tr>
<td><strong>Time release</strong></td>
<td><strong>Technology</strong></td>
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<tr>
<td><strong>Osmotic controlled</strong></td>
<td><strong>release capsule</strong></td>
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<tr>
<td>Suspension</td>
<td>Emulsion</td>
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<td>Syrup</td>
<td>Nutrient enema</td>
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<tr>
<td>Elixir</td>
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<tr>
<td>Tincture</td>
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</tbody>
</table>
Important standard safety measures that nurses must observe prior to administering any drug include checking drug labels for the following:

- Name of drug
- Expiration date
- Total dosage and concentration

Obtaining drug from a glass ampule includes the following steps, and, as illustrated to the right:
1. Hold the ampule erect and tap its top to remove any trapped solution.
2. Place gauze around the slim neck.
3. Snap it off using your thumb.
4. Draw up the drug.

Obtaining drug from a vial is outlined and illustrated below:

1. Confirm the vial label.
2. Set up the syringe and hypodermic needle.
3. Place in the hypodermic needle into the rubber top and insert the air from the syringe into the vial.
4. Non-reconstituted medicine consists of two vials, one having a powdered drug and one having a liquid mixing solution.
5. Remove all solution from the vial containing the mixing solution.
6. Swab the top of the vial having the powdered medicine with alcohol and insert the solution.
7. Agitate the vial to make sure that the mixture is completely even.
8. Prepare a fresh syringe and hypodermic needle.
9. Withdraw the suitable volume of drug.
Parenteral administration

Parenteral administration includes the following methods [54]:
1. Intradermal injection
2. Subcutaneous injection
3. Intramuscular injection
4. Intravenous access
5. Intraosseous infusion*

Properly placed Intraosseous cannulation (Photo courtesy of Medscape)
*Intraosseous (IO) infusion can be used in emergency situations for patients who are in shock and/or have vascular collapse, where peripheral IV access is difficult or impossible. The marrow of long bones offer a vast vascular system that drain into a central venous canal that ultimately makes its way into the central circulation. While IO can be used in patients of all ages, it is often employed in children younger than six years of age.

**Blood and blood components**

Just as in the reporting of unfavorable or adverse drug reactions, the nurse should be conscious of the need for the reporting of adverse reactions and events related to blood and blood components. Hemovigilance is defined as follows [58]:

*A collection of surveillance processes, from the set of blood and its components to the follow-up of recipients, to gather and review information on unanticipated or unwanted effects resulting from the remedial utilization of labile blood products and to stop their occurrence or reappearance.* (Irish Blood Transfusion Service).

Nurses are usually referred to the Guidelines for the Administration of Blood that are issued by the Red Cross and their own clinical laboratory departments for particular information and direction on the issue of blood supervision, monitoring and coverage of unfavorable events and reactions [63].

**Medical Devices**

Medical devices play an important role in helping the health care professionals in the provision of patient care. As nurses are frequently frontline users of health devices and *in vitro* diagnostic testing devices, they play a major role in the recognition and communication of any unfavorable incidents involving these medical devices [59].

The reporting of unfavorable incidents can help in enhancing patient safety, and helps to develop improved safety of a medical device by suggesting a modification in its design or usage. The FDA is the elected authority to which a nurse should communicate unfavorable incidents related to medical devices. There is no obligatory reporting structure for users; though, users are expected to communicate severe incidents. The
FDA offers guidance for all health care professionals in the reporting of adverse incidents. The producer of the device must also be notified of the event. Information on the alert system for therapeutic devices, including the duties of the medical device producer and the medical device incident user report form, are accessible from the FDA medical devices department [62].

The health care service provider and health care professional and regulatory organizations, especially nurses, have accountability to the patient to promise safe and efficient drug management practices. Drug management practices must be audited on a frequent basis to ensure useful and safe patient care [60].

**Communication during monitoring**

The appraisal and evaluation of the administered drug or medical product should include the observation and communication of the following information [55].

- Vital symptoms and laboratory values before the administration (as applicable)
- Effectiveness of drug administration technique (e.g., is the route selected suitable?)
- Awareness and inspection for drug allergies, potential side effects, unfavorable reactions, toxicity, contraindications and interactions of therapeutic products administered
- Monitoring the usefulness of the administered drug or medical products

Monitoring, documentation and communication of observations to the patient and to the prescribing provider are key responsibilities and duties for nurses in drug management; they include the activities of appraisal, planning, execution and evaluation. These duties require successful and well-organized communication between the clinician and the patient [56].

Education must be given to the patient in relation to the utilization of medication. It should be clarified to the patient in a way that is understandable. Consideration must be given to the suitable timing of education, including the patient’s willingness to learn.
Best practice specifies that education a patient on medication therapy should contain the following [57]:

- The projected system of action of the therapeutic product
- Possible side effects
- Signs and symptoms of possible adverse effects and measures required, if needed
- Potential interactions of the therapeutic product with other medicines, specific foods or other substances
- Precautions or directions to follow, including time, process of administration, route, and storage of drug
- Importance of adherence to given therapy (duration and incidence)
- Suggestions for follow-up and coverage of possible side effects or unfavorable reactions.

**DRUGS AFFECTING THE NERVOUS SYSTEM**

Generally, drugs are classified in many ways. For instance, they might be classified on the basis of the following:

- Uses
- Impact on the body (the particular impact on the central nervous system)
- Source of the drug (synthetic or natural)
- Chemical structure
- Legal status (legal/prohibited)
- Risk status (risky/safe)

One of the most general and helpful ways of categorizing a drug is by the impact that it creates on the patient’s central nervous system. The brain is the main component of the central nervous system, and this is where psychoactive drugs have their key effect. Psychoactive drug types and examples of each type are discussed below.
Psychoactive drugs

Stimulants
Stimulants tend to boost the functioning of an individual’s central nervous system (CNS) including the brain. These drugs generally result in the patient feeling more attentive and energetic.

Examples:
- Amphetamines
- Cocaine
- Pseudoephedrine (found in drugs such as Codral Cold and Sudafed)
- Nicotine
- Caffeine

Depressants (also called relaxants)
Depressants or relaxants tend to slow down the function of the CNS, which results in the patient feeling less pain, more sleepy and relaxed. These symptoms might be very pronounced when a drug is taken in excess amounts.

It is significant to note that the word depressant is used to explain the impact on the CNS, not on an individual’s mood. CNS depressants most probably result in euphoria more than depression, particularly in moderate use.

Examples:
- Alcohol
- Major tranquilizers
- Benzodiazepines (such as Valium, Temazepam)
- Opioids (heroin, morphine)
- Volatile substances (glue, petrol, and paint)

Hallucinogens
Hallucinogens have the ability to change a patient’s sensory perceptions by altering messages carried along the CNS pathways. An example would be the effect of LSD as a hallucinogen, and its effect to change perceptions and consciousness states.
Examples:

- LSD
- Psilocybin (magic mushrooms)
- Mescaline (peyote cactus)

Other Drugs

Other drugs include psychoactive drugs that do not fit perfectly into one of the other classifications, but are obviously psychoactive, like antidepressants (e.g. Zoloft) and mood stabilizers (e.g. Lithium).

Examples:

- MDMA (ecstasy)
- Cannabis
- Volatile substances (petrol, glue, paint)

Sleep disorders

Sleep can be considered one of the barometers used to measure overall health. In most cases, individuals in good health tend to sleep well, while those suffering from frequent sleeping problems may face an underlying health or mental health problem, varying in significance. Sleeping well is necessary to one's emotional well-being and physical health and unfortunately, even a relatively small amount of sleep loss can impact mood, efficiency, energy, and the ability to handle stress. Ignoring sleep issues and disorders can cause poor health, impair job performance, increase the risk of accidents and place relationships under stress [64].

Common symptoms of a sleep disorder are described below [65]:

- Difficulty in sleeping at night or getting back to sleep after awaking during the night
- Waking up frequently during the night
- Insufficient deep sleep
- Sleepiness, fatigue and a lack of energy during the day
Drugs causing sleep problems

Many recommended and OTC medicines can result in sleep problems. The degree of sleep problems resulting from medications will differ from person to person [66]. Prescription drugs that might cause sleep problems are:

- High blood pressure drugs
- Hormones like oral contraceptives
- Steroids including prednisone
- Respiratory medicines
- Diet pills
- Attention deficit/hyperactivity disorder drugs
- Some antidepressants

The following non-prescription drugs can cause sleep problems [66]:

- Pseudoephedrine
- Medicines containing caffeine as well as cold and cough medicines
- Illegal (or illicit) medications such as heroin, cocaine, marijuana, amphetamines, and methamphetamines
- Nicotine can disturb sleep and decrease total sleep time. (Smokers show more daytime drowsiness and an increased frequency of minor accidents than do non-smokers, particularly in younger age groups).

Alcohol and sleep

Alcohol is usually considered a calming or sedative drug. While alcohol may stimulate sleep, the quality of sleep is usually disturbed during the second half sleep. Alcohol boosts the number of awakenings in the second half of the night when the relaxing effect of alcohol wears off. Alcohol prevents a profound sleep and inhibits rapid eye movement (REM) sleep [67].

Sustained consumption prior to sleep can cause daytime fatigue and drowsiness. The elderly are at particular risk for alcohol-based sleep disorders since the elderly experience higher levels of alcohol in the brain and blood than do younger adults with
similar doses. Bedtime alcohol use among older adults may cause increased instability with a greater risk of falls upon awakening [68].

Sleep disorder medications are briefly outlined below (69, 70, 71, 72):

- **Ambien CR:****n
  Ambien (Zolpidem) is the drug that is used to treat insomnia (sleep disorder) in adults. It induces more rapid sleep and decreases the frequency of waking.

- **Butabarbital:**
  Butabarbital is used for short term (not more than 2 weeks) insomnia relief, and is also an anxiolytic.

- **Doral:**
  Doral is used for the temporary treatment of patients having trouble sleeping. It is usually used for 7-10 days.

- **Nuvigil**
  Nuvigil (Armodafinil) reduces extreme sleepiness because of narcolepsy and other sleep disorders such as respiratory irregularities during sleep.

- **Seconal Sodium**
  This medicine is used for a short time (not to exceed 2 weeks) to treat insomnia.

- **Sodium Oxybate**
  This drug is used to treat narcolepsy, a disorder with extreme daytime sleepiness and intermittent, uncontrollable sleep during the day.

- **Zaleplon**
  This drug is used for short term treatment of patients with insomnia. It can also be used to treat other sleep disorders.

- **Temazepam**
  This medicine is used for the temporary treatment of patients with insomnia. It is usually used for 7-10 days. It allows patients to fall asleep faster and reduces the number of awake periods.

**Parkinson’s disease**

Parkinson's disease (PD) is a progressive and degenerative movement disorder involving dopaminergic neurons, primarily in the basal ganglia and the substantia nigra.
with resulting extrapyramidal effects [73]. In PD, dopamine, a neurotransmitter, is decreased with resultant loss of coordination and control of movement. As PD progresses, the quantity of dopamine formed in the brain decreases further, leaving a person incapable to managing movement normally. Depression, cognitive and other mental and emotional issues become common [74].

**Drugs affecting PD**

Certain drugs worsen PD in patients. Therefore, it is necessary to know these drugs. Any drug or treatment that slows down or inhibits the action of dopamine (called a dopamine antagonist) can cause Parkinson-like symptoms. Drugs that are prescribed for treating schizophrenia and other psychotic conditions, such as a behavior disorder in an individual with Alzheimer's disease, are known as *neuroleptic* drugs. These drugs are the main source of *drug-induced* Parkinson-like disorders, which can occur as an adverse effect of a variety of neuroleptics [75].

In general, except for those drugs listed below, on page 57, the following should be avoided in a patient with PD:

- Typical and atypical anti-psychotics
- Nausea/GI drugs: Prochlorromethazine (Compazine), metoclopramide (Reglan), promethazine (Phenergan), droperidol (Inapsine)
- Anti-depressants such as amoapine (Asendin)

Some medications should be taken with caution in a patient taking an MAO-B inhibitor such as selegiline or rasagiline (Azilect). In such cases, meperidine (Demerol), tramadol, methadone, propoxyphene (Darvon), cyclobenzaprine (Flexaril) and halothane should be avoided.

The atypical antipsychotic quetiapine (Seroquel), the neuroleptic clozapine (Clozaril) and to a lesser degree risperidone (Risperdal) and olanzapine (Zyprexa) seem to have fewer occurrences of extrapyramidal side effects. These medications are still usually avoided for patients with Parkinson’s, though some might be used to treat hallucinations that may occur in Parkinson’s [76].
For patients with PD, anti-nausea medications like ondansetron (Zofran) or domperidone (Motilium) are the medicines of choice for vomiting and nausea. Along with neuroleptics, a few other drugs can lead to drug-induced Parkinsonism. These are drugs used for nausea and dizziness like prochlorperazine (Stemetil); and metoclopramide (Maxalon), which is provided to treat nausea and indigestion [77].

Calcium channel blocking medicines used for treating high blood pressure, irregular heart rhythm, panic attacks, angina pectoris, migraine and manic depression may rarely lead to drug-induced Parkinsonism. Calcium channel blocking medicines are, however, extensively used to treat high blood pressure and angina, and it is significant to note that most general agents in clinical use do not have this side effect. These medicines should not be stopped suddenly without consulting with the physician [77].

There are certain other agents that have been reported to cause drug-induced Parkinsonism, however, clear evidence of cause and effect is still lacking. Amiodarone, given to treat heart conditions causes tremor and in some patients, has been reported to induce Parkinson-like symptoms.

Sodium valproate, recommended to treat epilepsy, and lithium, for depression, both frequently cause tremor which might be mistaken for PD. Usually, most people will get better within two months, and within hours or days, of stopping the interacting drug. However, some patients might take as long as two years to fully recover [78].

*Medication for treating PD*

Parkinson's disease is not curable, but a number of medications can facilitate control of the symptoms, often considerably. In some later stages, surgery might also be advised [79].

Medications can facilitate problems with coordination, movement, walking, and tremor by boosting the level of dopamine. Dopamine can't be given directly, as it cannot cross the blood-brain barrier. Instead, analogs or dopamine agonists are used.
**Carbidopa-levodopa (Parcopa)**

Levodopa, which is considered to be the most effective Parkinson's disease drug, is derived from tyrosine and is converted to dopamine in the brain. Levodopa is often combined with carbidopa, which inhibits the conversion of levodopa outside the CNS and which helps prevent nausea [81].

**Dopamine agonists**

Unlike levodopa, dopamine agonists can’t be converted into dopamine. Rather, they imitate the dopaminergic affects in the brain. In general, they aren't as effective as levodopa [84] though, they are longer acting and might be used along with levodopa to stabilize levodopa effects.

Dopamine agonists include ropinirole (Requip) and pramipexole (Mirapex). A short-acting injectable dopamine agonist is apomorphine (Apokyn), which is used for acute relief [81].

**Catechol O-methyltransferase (COMT) inhibitors**

Entacapone (Comtan) is the classic example of this class. This drug mildly prolongs the result of levodopa treatment by inhibiting COMT, an enzyme that metabolizes levodopa [82].

**Anticholinergics**

These drugs were used historically to help manage the tremor related to Parkinson's disease. A number of anticholinergic drugs are available, including trihexyphenidyl and benztropine (Cogentin) [83].

**Amantadine**

Physicians might prescribe amantadine only to offer immediate relief of signs of mild, early-stage Parkinson's disease. It also might be included to carbidopa-levodopa treatment for people in the advanced stages of Parkinson's disease, to help manage involuntary movements (dyskinesia) caused by carbidopa-levodopa [85].
Mood and Anxiety Disorders

It is important to remember that anxiety disorders are not mood disorders. However, anxiety disorders can lead or predispose to mood disorders.

Anxiety impacts mood. Anxiety can lead to hopelessness, panic, and quite a lot of other emotions. But, it is not regarded as a mood disorder since, while anxiety affects mood, it isn't directly related to mood. Mood problems along with anxiety are secondary to the state.

Mood disorders usually refer to the following conditions: [81]

- Major Depressive Disorder
- Depressive disorders including atypical depression, post-partum depression, Seasonal Affective Disorder (SAD), recurrent brief depression and minor depression
- Substance-induced mood disorders
- Cyclothymia
- Bipolar disorder

Mood and anxiety disorders are related to the levels of brain neurotransmitters. The patient can experience both mood disorders and anxiety and there are a number of medications that can be useful in the treatment of mood disorders, anxiety or both [81].

Drugs affecting mood and anxiety disorders

Psychoactive drugs, such as cannabis, ecstasy, alcohol, and heroin, have the capability to impact mood. They can stimulate definite emotions or inhibit others. This may be the reason individuals with a mood disorder or anxiety self-medicate with these agents [82].

Drug-induced anxiety disorders

Various drugs can induce panic attacks. These are events accompanied by severe anxiety, an increased heart rate, trembling, shortness of breath, sweats and
overwhelming fears. The individual might also feel like their surroundings are weird or imaginary, or they are losing individual identity and a sense of reality [82].

**Drug-induced mood disorders**

These may appear as episodes of feeling dejected, sad, irritable, restless, fatigued, or as a loss of enjoyment. These may also appear as elevated moods, periods of over-excitement, fantasy, impulsive behavior or weird thoughts. This can be caused by drugs like cocaine, amphetamines, methadone, and heroin.

**Medications for treating mood and anxiety disorders**

Remember that drugs generally take four to eight weeks to achieve stable plasma levels. It is also very important to remember that, many of these drugs should not be used in patients younger than 25 years old.

Some of the most generally used drugs used to relieve mood and anxiety disorders include: [83]

- **Selective serotonin reuptake inhibitors (SSRIs)**
  - Citalopram (Celexa)
  - Escitalopram (Lexapro)
  - Fluoxetine (Prozac)
  - Fluvoxamine (Luvox)
  - Paroxetine (Paxil)
  - Sertraline (Zoloft)

- **Selective serotonin and norepinephrine inhibitors (SNRIs)**
  - Desvenlafaxine (Pristiq)
  - Duloxetine (Cymbalta)
  - Milnacipran (Savella)
  - Venlafaxine (Effexor)

- **Tri- and Heterocyclic antidepressants**
  - Amitriptyline
  - Desipramine (Norpramin)
- Doxepin (Zonalon)
- Imipramine (Tofranil)
- Nortriptyline (Aventyl, Pamelnor)
- Protriptyline (Vivactil)
- Trimipramine maleate (Surmontil)
- Heterocyclic Anti-depressants
  - Amoxapine
  - Maprotiline
- Tetracyclic Anti-depressants
  - Mirtazapine (Remeron)
- Older tricyclic antidepressants
  - Amitriptyline (Elavil)
  - Doxipin (Sinequan)
- Atypical anti-depressants
  - Bupropion (Wellbutrin)
- Monoamine oxidase inhibitors (MAOIs)
  - Phenelzine (Nardil)
  - Selegiline (Emsam)
  - Tranylcypromine (Parnate)

Some of the potential side effects of separate drug categories are listed below:

- Tricyclic antidepressants:
  Dry mouth, blurry vision, increased weight, fatigue and sleepiness, muscle
tremors, constipation, urine retention, dizziness, tachycardia, sexual dysfunction.
- MAOIs:
  Headache, palpitations, chest pain, stiffness of the neck, nausea and vomiting.
- SSRIs:
  Sexual problems: low sex drive, inability to have an orgasm; and,
dizziness/lightheadedness, headaches, nausea, insomnia, strange dreams and
feeling jittery, drowsiness, blurred vision, constipation, fever/chills, increased or
decreased appetite, tremor, and dry mouth. Cymbalta can cause increase sweating and hypertension.

- Bupropion:
  Weight loss, loss of appetite, restlessness, insomnia, anxiety, constipation/diarrhea, dry mouth, dizziness and seizures.

**Psychoses**

Psychoses are mental disorders characterized by significant personality changes, improper functioning, false beliefs or delusions and a loss of connection with reality. It might be a sign of bipolar disorder, schizophrenia, or brain tumor. Psychoses can include schizophrenia, schizoaffective disorder, delusional disorder and chronic hallucinatory psychosis. Symptoms resembling psychoses can be seen in schizotypal disorder, some personality disorders (particularly during stressful times), post-traumatic stress disorder (PTSD) and in obsessive-compulsive disorder (OCD).

Psychoses can be caused by the following: [84]

- Psychological conditions
- General medical conditions
- Substances, like alcohol or drugs
- Unknown factors (genetic predispositions exist)

*Drugs affecting psychoses*

Drug and alcohol misuse can trigger a psychotic occurrence. A psychotic occurrence can also be produced if an individual abruptly stops taking a medicine or drinking alcohol after utilizing it for a long time. Drugs which are known to prompt psychotic episodes include: [85]

- Cocaine
- Methamphetamine (crystal meth)
- Mephedrone (MCAT or miaow)
- Amphetamine (speed)
- MDMA (ecstasy)
• Cannabis
• LSD (acid)
• Psilocybins (magic mushrooms)
• Ketamine

In exceptional situations, psychosis can also take place as a side effect of several types of drugs, or as the result of an overdose of that drug. One example is levodopa, a drug used to treat Parkinson’s disease. However, potentially any drug that acts on the brain can lead to psychosis if taken in excess amount [84].

Treatment for psychoses is based on a mixture of antipsychotic drugs, psychological therapies and social support.

*Drugs for treating psychoses*

When treating psychoses, numerous drug options are on hand. Some of the most generally used are phenothiazines and include: [86]

- Chlorpromazine (Thorazine)
- Fluphenazine (Prolixin)
- Haloperidol (Haldol)

The phenothiazines are considered to be dopamine-2 receptor antagonists and are considered typical anti-psychotics.

Side effects for the atypical anti-psychotics include: sensitivity to light, jaundice, blood disorders, extrapyramidal effects, weight gain, tremors, and muscular cramping/stiffness.

Atypical anti-psychotics that may be used include:

- Aripiprazole (Abilify, Aripiprex)
- Clozapine (Clozaril, FazaClo)
- Olanzapine (Zyprexa)
- Quetiapine (Seroquel)
- Risperidone (Risperdal)
Side effects for the atypical anti-psychotics include: weight gain, diabetes, hyperlipidemia, EKG changes, myocarditis, sexual dysfunction, and extrapyramidal effects.

**Seizure Disorders**

A seizure occurs when a sudden *explosion of electrical impulses* in the brain occurs. They can spread to neighboring parts and create an unrestrained storm of electrical activity. The electrical impulses can be transmitted to the muscles, resulting in convulsions, spasms or twitching [87]. Seizures may be partial (focal) or generalized. Generalized seizures can be Grand-mal (generalized tonic-clonic), absence, myoclonic, clonic, tonic or atonic. Partial seizures can be simple (where awareness is maintained) or complex (with impaired awareness).

Although the fundamental causes of seizures, including epilepsy, are generally not known, they are often associated with traumatic head injuries, brain tumors, infections of the central nervous system and strokes. In addition, certain factors can provoke seizures in patients with epilepsy. Avoiding the triggers listed below can help avoid seizures [88]:

- Missing drug doses
- Heavy alcohol consumption
- Cocaine or other medicine use (e.g. ecstasy)
- Lack of sleep
- Other medications that affect other seizure medications adversely
- Cyclic hormonal changes in women

*Drugs causing seizure disorders*

Alcohol can be hazardous when mixed with sedative drugs, like phenobarbital, and can lead to coma, or even death. Most of the illegal drugs, principally stimulants like cocaine, PCP, crack, and speed, may lead to seizures. Some of the additives or impurities in illegal drugs can be a source of seizures, and illegal drugs might have hazardous interactions with prescription medicines [88].
Drugs for treating seizure disorders are listed below [89, 90, 91, 92, 93, 94, 95]:

- **Tegretol or Carbatrol (carbamazepine)**
  - This is the drug-of-choice for partial, general tonic-clonic and mixed seizures
  - Adverse effects: fatigue, nausea, vision changes, dizziness, and rash.

- **Zarontin (ethosuximide)**
  - Primarily used for absence seizures
  - Adverse effects: nausea, decreased appetite, vomiting, and weight loss.

- **Felbatol (felbamate)**
  - Used for treating partial and some general seizures
  - Adverse effects: decreased hunger, inability to sleep, weight loss, headache, and depression.
  - Although rare, the medicine may lead to liver or bone marrow or failure. Therefore, the utilization of the drug is restricted and patients taking it should have blood cell counts and liver tests recurrently during therapy.

- **Gabitril (tiagabine)**
  - Given as other antiepileptics for treating partial and some generalized seizures
  - Adverse effects: dizziness, irritability, anxiety, fatigue, weakness, and confusion.

- **Keppra (levetiracetam)**
  - Given along with other epilepsy medications to treat partial seizures
  - Adverse effects: tiredness, behavioral changes and weakness

- **Lamictal (lamotrigine)**
  - It is used to treat partial and some general seizures
  - Adverse effects: insomnia, dizziness, or rash.

- **Lyrica (pregabalin)**
  - Given for partial seizures
- Adverse effects: dizziness, dry mouth, sleepiness (somnolence), blurred vision, peripheral edema, weight gain, and complicatedness with concentration/attention.

• Neurontin (Gabapentin)
  - It is used in combination with other epilepsy drugs for treating partial and some general seizures
  - Adverse effects: sleepiness and dizziness.

• Dilantin (Phenytoin)
  - It controls partial and general tonic-clonic seizures; also can be applied IV (intravenously) to quickly treat active seizures, though if the medicine is being delivered by iv, Cerebyx (fosphenytoin) is generally used.
  - Adverse effects: dizziness, slurred speech, fatigue, acne, increased hair (hirsutism) and rash. Over the long term, the medicine may result in bone thinning.

• Topamax
  - It is combined with other drugs for treating partial or general tonic-clonic seizures
  - Adverse effects: sleepiness, speech problems, dizziness, nervousness, visions problems, memory problems, weight loss.

Pain

Pain is an unpleasant or disturbing feeling resulting from some damage to the external or internal body structure. It ranges from minor to severe and can be stable and constant, in which case it might be an ache, a throbbing or pulsating pain or it may be a pinching, stabbing or stitching feeling. Pain is one of the most common reasons for doctor visits and can be acute or chronic.

While there are a number of medications available for pain, chronic pain is still a difficult management problem. It should also be remembered that chronic pain can lead to depression and a number of emotional issues [96].
Drugs affecting pain

Caffeine-containing drugs (including Midol, Excedrin, Anacin):
If a patient is experiencing headaches and is also using a caffeine-containing drugs more than two or three times for each week, headaches can be caused by these over-the-counter (OTC) drugs [97].

Use of these drugs may result in rebound headaches since the brain becomes tolerant and requires higher concentration for the same results. So, what once was an incident of headaches as a young individual could result in a lifetime of headaches due to routine consumption of these products. The consumption of these medications should be limited [98].

Non-steroidal Anti-inflammatory drugs (NSAIDs: Advil, Ibuprofen, Aleve):
These OTC anti-inflammatory drugs can also lead to stomach pain and can cause bleeding ulcers. Chronic use of NSAIDs should be discouraged [98].

Opioids (hydrocodone, oxycodone, hydromorphone, morphine):
Opioids have both addictive and tolerance characteristics. In addition, these drugs, when not carefully controlled, managed and monitored can also result in pain. If a patient has been medicating with opioid drugs for long-term pain, they may experience opioid-induced hyperalgesia (OIH).

OIH closely resembles tolerance, however, tolerance can be overcome with increased opioid dose and in OIH the same dose increase results in worsened pain. Also, in OIH, pain is resolved with the discontinuance of the opioid. It must be noted, however, that there is also hyperalgesia during opioid therapy. In OIH, the pain tends to be more diffuse, harder to pinpoint and the individual responds to noxious stimuli with more pain than is normally expected (nociceptive sensitization) [100].

It is also important to note the differences between tolerance and addiction. Tolerance is due to neuroadaptation with receptor down-regulation and is a physiological process. It does not indicate addiction or dependence. Addiction involves the psychological
dependence on a drug, often accompanied by physical withdrawal symptoms. The withdrawal symptoms tend to encourage continued abuse.

Opioids bind to three main classes of opioid receptors (mu, kappa and delta) and subtypes as well as the opioid-receptor-like receptor 1 (ORL-1) which plays a role in the development of tolerance. Each individual opioid drug will bind to a specific receptor or receptors, giving each opioid a distinct effect profile.

**Chemotherapy**

Many physicians who recommend chemotherapy are cognizant of the fact that these drugs may cause nerve harm in the form of a peripheral neuropathy. In fact, the onset of peripheral neuropathy can be the main preventive factor for the quantity and period of the chemotherapy. Chemotherapy may be life-saving, but an aching neuropathy is not simple to live with. Acetyl-L-Carnitine (1000 mg three times every day) can protect nerves while undergoing chemotherapy [99]. Severe post-chemotherapeutic pain is often treated with opiates.

**Hypercholesterolemia**

Statins are often recommended to lower cholesterol levels. A significant proportion of these people will also experience chronic muscle pain and fatigue as a consequence of these medications. Muscle aches and weakness is usually considered as a side-effect of these cholesterol-lowering drugs, but can also be mistaken for fibromyalgia and not an adverse effect of the statins. If the patient is on statins and experiencing significant pain, aches and fatigue, the prescribing physician should be notified [98].

**DRUGS AFFECTING THE CARDIOVASCULAR SYSTEM**

**Cardiovascular Disease**

Cardiovascular disease includes coronary artery disease, cerebrovascular disease (stroke), raised blood pressure (hypertension), rheumatic heart disease, peripheral artery and venous diseases, congenital heart disease and heart failure. The main causes of cardiovascular disease include: [103]
• Tobacco use
• Physical inactivity
• Unhealthy diet
• Obesity
• Age
• Congenital defects
• Harmful consumption of alcohol

The function of cardiovascular system is to transport nutrients throughout the body and to carry wastes to the various eliminating organs. This system consists of the heart and the circulatory system. The lymphatic system is also considered to be a part of the cardiovascular system [101].

Cardiovascular disorders result from a number of factors, both internal and external. Among external factors, drugs and medications that patients consume are important to consider [102].

*Acid Reflux drugs*

If taken frequently, PPIs (Proton Pump Inhibitors) can cause a range of cardiovascular problems with time, including a weakened heart and hypertension. The PPIs are used to treat ulcers, Gastroesophageal Reflux Disease (GERD) and Zollinger-Ellison syndrome [104].

PPIs are taken as inert prodrugs. After oral ingestion, they are activated by acid content in the stomach. Once activated, the PPIs irreversibly block the H⁺/K⁺ ATPase and inhibit proton movements into the stomach, decreasing the acid levels [105]. Common examples are:

• Nexium (esomeprazole)
• Prevacid (lansoprazole).
• Prilosec (omeprazole)
Antipsychotic drugs

A number of antipsychotic medications have been correlated with cardiovascular disease, hyperlipidemia, hyperglycemia, and weight gain \[109\]. Researchers noted that people who are mentally ill receiving these drugs are at an increased risk for heart disease, diabetes and hypertension \[108\]. The highest rates of cardiovascular adverse effects, including weight gain, diabetes, hyperlipidemia, EKG changes and myocarditis have been associated with the atypical anti-psychotics that include:

- Aripiprazole (Abilify, Aripiprex)
- Clozapine (Clozaril, FazaClo)
- Olanzapine (Zyprexa)
- Quetiapine (Seroquel)
- Risperidone (Risperdal)

Marijuana, Cocaine and Other similar Drugs

Cocaine consumption can damage the heart and leads to many deaths. A number of cardiovascular complications are directly related to cocaine intake. They include heart attacks, chest pain syndromes, strokes, aortic dissection, heart failure, and fatal and nonfatal arrhythmias \[107\].

Cocaine is unsafe for pregnant women. Data is accumulating that cocaine consumption can cause birth defects in the child in addition to cardiovascular complications in the mother \[108\].

Marijuana smoking and cannabis can lead to variations in blood pressure and heart rate that are linked to an increased stroke risk, primarily because of an increased risk of atrial fibrillation. Significantly, it can also lead to heart palpitations and anxiety \[110\].

Side effects of commonly prescribed cardiovascular drugs are listed below:

- Furosemide (Lasix)
  - Dehydration
  - Electrolyte imbalance
- Muscle cramps/weakness
- Arrhythmia
- Dizziness
- Anuria
- Fatigue

- Clopidogrel (Plavix)
  - Severe abdominal pain
  - Uncontrolled bleeding
  - Tarry stools/bloody stools
  - Confusion
  - Purpura
  - Sudden, severe headaches
  - Changes in vision
  - Tachycardia
  - Bloody vomit (coffee grounds vomit)
  - Jaundice
  - Slurred speech

- Cavedilol (Coreg)
  - Dizziness
  - Interactions with hypoglycemic

- Nifedipine (Procardia)
  - Edema
  - Mood changes
  - Vision changes
  - Arrhythmias
  - Difficulty breathing
  - Allergic reactions
  - Rash
- Diltiazem (Cardizem)
  - Arrhythmias
  - Edema
  - Shortness of breath
  - Mood changes
  - Fainting/Dizziness

- Nitroglycerin
  - Dizziness/fainting/lightheadedness
  - Arrhythmia
  - Rash
  - Shortness of breath

- Dabigatran (Pradaxa)
  - Purpura
  - Uncontrolled bleeding

- Sotalol
  - QT prolongation in the EKG
  - Torsade de pointes

- Warfarin/Coumadin
  - Heavy bleeding

**Metabolic Syndrome**

Metabolic syndrome is a combination of characteristics that increases the risk for cardiovascular disease and diabetes. Metabolic syndrome has been variously called Syndrome X, cardiometabolic syndrome and insulin resistance syndrome. It can be defined as the presence of high triglycerides, reduced HDL cholesterol, hypertension and a raised fasting glucose level. It is most often associated with central obesity, high
levels of the inflammatory marker, C-Reactive protein (CRP) and is often associated with liver dysfunction [111].

Drugs affecting metabolic disorder are discussed in the section below.

*Bipolar disorder drugs*

Bipolar disorder is a state with signs including extremes of mood, vacillating between depression and mania. Many medications prescribed for treating bipolar disorder can put people at risk for metabolic syndrome [112].

Many of the medications used to manage bipolar disorder are considered to contribute to the danger of metabolic syndrome and type 2 diabetes. Not all medications used for bipolar disorder lead to metabolic symptoms, however the drugs listed here are prone to cause insulin resistance, weight gain, hyperglycemia (high blood glucose levels) and other symptoms linked with metabolic syndrome [112].

Examples of bipolar disorder drugs that can increase the risk for metabolic syndrome are listed below: [113]

- Clozapine (clozaril)
- Lithium
- Olanzapine (Zyprexa)
- Quetiapine (Seroquel)
- Risperidone (Risperdal)
- Valproic acid (Depakote) and Sodium valproate

*Drugs for treating metabolic syndrome*

Harmful cholesterol levels are treated with drugs including fibrates, statins, or niacin (Vitamin B₃). High blood pressure is controlled with medications like ACE inhibitors or diuretics [130]. High blood sugar is treated with oral drugs (like metformin), insulin injections, or both [114].
Low-dose aspirin can help in decreasing the risk of blood clots. This is particularly the case for patients having a higher risk of heart disease [131].

There is no cure for metabolic syndrome [132]. Hypoglycemics, statins and anti-hypertensives may be used to control symptoms though the first line of therapy is dietary and lifestyle-based [114].

**Hypertension**

Hypertension, also called high blood pressure, is a chronic condition with increased arterial pressure. Hypertension may be primary (essential) hypertension with no known cause or secondary hypertension, cause by renal, arterial, cardiac or endocrine disorders [133, 115].

Blood pressure is a measurement of the force of the blood against the blood vessel walls. The higher the pressure the more work will be required of the heart, predisposing to myocardial infarcts, strokes, heart failure, peripheral artery disease and chronic kidney disease [116].

**Drugs affecting hypertension**

The term “Drug-induced hypertension” is high blood pressure that results from a chemical substance or a drug [129]. Drugs that can result in hypertension include: [117]

- Alcohol, ecstasy (MDMA and derivatives), amphetamines, and cocaine
- Corticosteroids
- Cyclosporine
- Erythropoietin
- Estrogens (including birth control pills) and other hormones
- Many over-the-counter medications like cough/cold and asthma drugs, mainly when the cough/cold drug is taken with some antidepressants such as tricyclics or tranylcypromine [118,134]
- Migraine medications
- Nasal decongestants
Rebound hypertension takes place when blood pressure increases after the patient stops taking or decreases the dose of a drug, usually an anti-hypertensive [119].

**Drugs for treating hypertension**

Medical providers can decide from a number of classes of antihypertensive drugs including those listed below: [120]

- Diuretics
- Anti-adrenergics (α and β blockers)
- Direct-acting vasodilators
- Calcium-channel blockers
- Angiotensin-converting–enzyme (ACE) inhibitors
- Angiotensin-receptor blockers (ARBs)

In addition, there have been three newer classes of drugs that may be used in the control of hypertension: [121]

- Direct renin inhibitors
- Endothelin-receptor antagonists
- Vasopeptidase inhibitors

Drugs that may be used to control hypertension are listed and represented in the corresponding tables below, including the class, generic name and potential side effects [122, 123, 124, 125, 126, 127, 128].

**Diuretics**

<table>
<thead>
<tr>
<th>Class</th>
<th>Generic name</th>
<th>Side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thiazide diuretics</td>
<td>Chlorothiazide&lt;br&gt;chlorthalidone&lt;br&gt;hydrochlorothiazide&lt;br&gt;indapamide&lt;br&gt;metolazone</td>
<td>Weakness, gout, fatigue, thirst, frequent urination, confusion, potassium depletion, lightheadedness, diarrhea or constipation, increased sensitivity to sunlight, allergic reactions in people allergic to sulfa medicines, muscle cramps, impotence.</td>
</tr>
<tr>
<td>Loop diuretics</td>
<td>Bumetanide</td>
<td>Ethacrynic acid</td>
</tr>
<tr>
<td>---------------</td>
<td>------------</td>
<td>----------------</td>
</tr>
<tr>
<td>Potassium-sparing diuretics/aldosterone-receptor blockers*</td>
<td>Amiloride</td>
<td>Spironolactone</td>
</tr>
</tbody>
</table>

**Anti-adrenergics**

<table>
<thead>
<tr>
<th>Class</th>
<th>Generic name</th>
<th>Side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta blockers (cardioselective)</td>
<td>Atenolol</td>
<td>Wheezing, depression, impotence, fatigue, dizziness, insomnia, decreased HDL cholesterol levels, reduced exercise tolerance.</td>
</tr>
<tr>
<td>Beta blockers (nonselective)</td>
<td>Nadolol</td>
<td>Decreased blood pressure upon standing up, weakness, heart palpitations, fainting, headache, nasal congestion and dry mouth.</td>
</tr>
<tr>
<td>Alpha-1 blockers</td>
<td>Doxazosin</td>
<td>Decreased blood pressure upon standing up, weakness, heart palpitations, fainting, headache, nasal congestion and dry mouth.</td>
</tr>
<tr>
<td>Alpha and beta blockers</td>
<td>Carvedilol</td>
<td>Wheezing, insomnia, diarrhea, lightheadedness, dizziness, depression, unusual weariness or weakness, drying of the eyes, headache, dry mouth, nasal congestion, erectile dysfunction, decreased HDL cholesterol levels, lower work out tolerance, decrease in blood pressure upon standing up, heart palpitations and fainting, weight gain</td>
</tr>
<tr>
<td>Centrally acting agents</td>
<td>Clonidine</td>
<td>A drop in blood pressure upon standing up, sedation, dry mouth, fatigue, drowsiness, erectile dysfunction, depression, dizziness.</td>
</tr>
<tr>
<td>Peripheral nerve–acting agents</td>
<td>Guanethidine Reserpine</td>
<td>A drop in blood pressure upon standing up, nasal stuffiness, depression, nightmares.</td>
</tr>
</tbody>
</table>
**Direct-acting vasodilators**

<table>
<thead>
<tr>
<th>Generic name</th>
<th>Side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydralazine</td>
<td>Headaches, weakness, flushing, palpitations, nausea. Minoxidil use can result in increased hair growth, fluid retention, and higher levels of blood sugar.</td>
</tr>
<tr>
<td>Minoxidil</td>
<td></td>
</tr>
</tbody>
</table>

**Calcium-channel blockers**

<table>
<thead>
<tr>
<th>Generic name</th>
<th>Side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amlodipine</td>
<td>Headache, edema, dizziness, and heartburn. Nifedipine can result in palpitations. Diltiazem and verapamil can lead to constipation and a slowed heartbeat.</td>
</tr>
<tr>
<td>Diltiazem</td>
<td></td>
</tr>
<tr>
<td>Felodipine</td>
<td></td>
</tr>
<tr>
<td>Isradipine</td>
<td></td>
</tr>
<tr>
<td>Nicardipine</td>
<td></td>
</tr>
<tr>
<td>Nifedipine</td>
<td></td>
</tr>
<tr>
<td>Verapamil</td>
<td></td>
</tr>
</tbody>
</table>

**ACE inhibitors**

<table>
<thead>
<tr>
<th>Generic name</th>
<th>Side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benazepril</td>
<td>Cough, rash, increased potassium levels, fluid retention and loss of taste. Might cause low blood pressure and weakness. Can worsen kidney injury if renal arteries involved. May cause fetal abnormalities.</td>
</tr>
<tr>
<td>Captopril</td>
<td></td>
</tr>
<tr>
<td>Enalapril</td>
<td></td>
</tr>
<tr>
<td>Fosinopril</td>
<td></td>
</tr>
<tr>
<td>Lisinopril</td>
<td></td>
</tr>
<tr>
<td>Quinapril</td>
<td></td>
</tr>
<tr>
<td>Ramipril</td>
<td></td>
</tr>
</tbody>
</table>

**Angiotensin-receptor blockers (ARB)**

<table>
<thead>
<tr>
<th>Generic name</th>
<th>Side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Candesartan</td>
<td>Muscle cramps, dizziness.</td>
</tr>
<tr>
<td>Eprosartan</td>
<td></td>
</tr>
<tr>
<td>Irbesartan</td>
<td></td>
</tr>
<tr>
<td>Losartan</td>
<td></td>
</tr>
<tr>
<td>Olmesartan</td>
<td></td>
</tr>
<tr>
<td>Telmisartan</td>
<td></td>
</tr>
<tr>
<td>Valsartan</td>
<td></td>
</tr>
</tbody>
</table>
## Combination antihypertensive drugs

<table>
<thead>
<tr>
<th>Class</th>
<th>Generic name</th>
<th>Brand name</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Potassium-sparing and thiazide diuretics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>amiloride + HCTZ*</td>
<td>Moduretic</td>
</tr>
<tr>
<td></td>
<td>spironolactone + HCTZ</td>
<td>Aldactazide, Spironazide, Spirozide</td>
</tr>
<tr>
<td></td>
<td>triamterene + HCTZ</td>
<td>Dyazide, Maxzide</td>
</tr>
<tr>
<td><strong>Alpha blocker and diuretic</strong></td>
<td>prazosin + polythiazide</td>
<td>Minizide</td>
</tr>
<tr>
<td><strong>Beta blocker and diuretic</strong></td>
<td>atenolol + chlorthalidone</td>
<td>Tenoretic</td>
</tr>
<tr>
<td></td>
<td>bisoprolol + HCTZ</td>
<td>Ziac</td>
</tr>
<tr>
<td></td>
<td>metoprolol + HCTZ</td>
<td>Lopressor HCT</td>
</tr>
<tr>
<td></td>
<td>nadolol + bendroflumethiazide</td>
<td>Corzide</td>
</tr>
<tr>
<td></td>
<td>propranolol + HCTZ</td>
<td>Inderide, Inderide LA</td>
</tr>
<tr>
<td></td>
<td>timolol + HCTZ</td>
<td>Timolide</td>
</tr>
<tr>
<td><strong>ACE inhibitor and diuretic</strong></td>
<td>benazepril +HCTZ</td>
<td>Lotensin HCT</td>
</tr>
<tr>
<td></td>
<td>captopril + HCTZ</td>
<td>Capozide</td>
</tr>
<tr>
<td></td>
<td>enalapril + HCTZ</td>
<td>Vaseretic</td>
</tr>
<tr>
<td></td>
<td>fosinopril + HCTZ</td>
<td>Monopril HCT</td>
</tr>
<tr>
<td></td>
<td>lisinopril + HCTZ</td>
<td>Prinzide, Zestoretic</td>
</tr>
<tr>
<td></td>
<td>moexipril + HCTZ</td>
<td>Uniretic</td>
</tr>
<tr>
<td></td>
<td>quinapril + HCTZ</td>
<td>Accuretic</td>
</tr>
<tr>
<td><strong>ARB and diuretic</strong></td>
<td>candesartan + HCTZ</td>
<td>Atacand HCT</td>
</tr>
<tr>
<td></td>
<td>eprosartan + HCTZ</td>
<td>Teveten HCT</td>
</tr>
<tr>
<td></td>
<td>irbesartan + HCTZ</td>
<td>Avalide</td>
</tr>
<tr>
<td></td>
<td>losartan + HCTZ</td>
<td>Hyzaar</td>
</tr>
<tr>
<td></td>
<td>telmisartan + HCTZ</td>
<td>Micardis HCT</td>
</tr>
<tr>
<td></td>
<td>valsartan + HCTZ</td>
<td>Diovan HCT</td>
</tr>
<tr>
<td><strong>Calcium-channel blocker and</strong></td>
<td>amlodipine + benazeprini</td>
<td>Lotrel</td>
</tr>
</tbody>
</table>
ACE inhibitor
- diltiazem + enalapril (Teczem)
- felodipine + enalapril (Lexxel)
- verapamil + trandolapril (Tarka)

Other combinations
- methyldopa + HCTZ (Aldoril)
- reserpine + chlorothiazide (Diupres)
- reserpine + HCTZ (Hydropres)
- aliskiren + HCTZ (Tekturna HCT)

Calcium-channel blocker and ARB
- amlodipine + valsartan (Exforge)
- amlodipine + olmesartan (Azor)

*HCTZ=hydrochlorothiazide

**Dysrhythmias**

Cardiac dysrhythmia is also called arrhythmia or an irregular heartbeat. It is any of a set of conditions that are characterized by the electrical activity of the heart when it is irregular or is unusually faster or slower than normal. The heartbeat might be tachycardic (more than 100 beats every minute) or bradycardic (less than 60 beats every minute), and can be regular or unequal [135].

Some types of arrhythmias are serious medical emergencies and may lead to cardiac arrest. Cardiac arrhythmias are one of the most widespread causes of mortality casualty enroute to a hospital. Other symptoms can be an awareness of an irregular heart beat (palpitations) and might be just uncomfortable. These palpitations are often associated with anatomic anomalies in the conduction system, atrial/ventricular fibrillation, and other mechanical or technical issues in the cardiac pacemaker. Still others might not be linked with any indications at all, but might increase the patient’s risk to a potentially life threatening embolism or stroke [136].

Drugs and agents causing dysrhythmias are listed below: [137]
- Alcohol abuse
- Diabetes
- Drug abuse
- High coffee consumption
- Heart disease
- Hypertension
- Hyperthyroidism (overactive thyroid gland)
- Mental stress
- Structural and functional anomalies of the heart; often the consequence of a heart attack
- Smoking
- Supplements containing cola (kola) nut, ephedra or guarana
- High levels of mineral supplements
- Some medications

Drugs for treating dysrhythmias

Many tachycardias react well to anti-arrhythmic drugs. Though these medications don’t cure the dysfunction, they can decrease the frequency of tachycardia. Some drugs can slow down the heart so much that the patient might become bradycardic. It is extremely important that a patient takes any anti-arrhythmic drug exactly as directed by their medical provider in order to minimize complications [138].

If the patient is experiencing atrial fibrillation, the clinician will probably recommend blood-thinning medication — like aspirin, warfarin (Coumadin) or rivaroxaban (Xarelto) or dabigatran (Pradaxa) — to keep hazardous clots from forming. Its important to be observant of the fact that these drugs can lead to severe bleeding. Dabigatran isn’t recommended for the treatment of atrial fibrillation in anyone who possesses heart valve replacements [139].

Some commonly recommended antiarrhythmic medications include: [140]
- Amiodarone (Cordarone, Pacerone)
Bepridil Hydrochloride (Vascor)
Disopyramide (Norpace)
Dofetilide (Tikosyn)
Dronedarone (Multaq)
Flecainide (Tambocor)
Ibutilide (Corvert)
Lidocaine (Xylocaine)
Procainamide (Procan, Procanbid)
Propafenone (Rythmol)
Propranolol (Inderal)
Quinidine (several trade names)
Sotalol (Betapace)
Tocainide (Tonocard)

Vascular Disease

Vascular disease is a kind of cardiovascular disease which impacts the blood vessels and the circulatory system. Vascular disease includes peripheral artery disease (PAD), aneurysm, renal artery disease, peripheral venous disease, Reynaud’s disease, Buerger’s disease, deep vein thrombosis (DVT), chronic venous insufficiency, clotting disorders and lymphedema. Some conditions, like myocardial ischemia and angina, can be better understood as both heart and vascular diseases [141].

The vascular system is the body’s network that consists of blood vessels. It includes the veins, arteries and capillaries transporting blood to and from the heart. Issues of the vascular system are widespread and can be severe [154]. The endothelial cells within the arteries and arterioles can become inflamed with characteristic plaque formation, a condition called atherosclerosis. Blood clots can form, creating in situ thrombi or distant emboli, and have the tendency to clog vessels and lump blood flow to the brain or heart. Damaged blood vessels may burst, causing bleeding within the body [142].
Risk for vascular disease increases with a family history of either vascular or heart disease, pregnancy, trauma, a sedentary lifestyle, smoking, obesity or conditions affecting the vasculature (including diabetes, hypercholesterolemia, metabolic syndrome and autoimmune diseases).

Drugs for treating vascular disease are discussed in this section [143, 144, 155]. While changes in lifestyle including increased exercise and dietary modifications might be sufficient for some patients with peripheral artery or venous disease, others might need medication. Examples of drugs used to treat vascular disease include: [144]

- Anticlotting or antiplatelet agents
- Cholesterol-lowering medications like statins
- Drugs that boost blood supply to the extremities like cilostazol (Pletal) and pentoxifylline (Trental)

The types of medications used to control vascular disorders, specifically plaques and clots are defined as:

- **Antiplatelet medications** (clopidogrel [Plavix] and aspirin):
  These inhibit the blood platelets "stickiness". Aspirin in low dosage (81 to 325 mg/day) is usually recommended since it is also useful in preventing heart attacks and strokes in patients having peripheral artery disease [145].

  Clopidogrel (Plavix) is a substitute to aspirin for patients who are allergic or unable to tolerate aspirin. Antiplatelet drugs also help stop occlusion of blood vessels following bypass surgery or angioplasty [146].

- **Anticoagulant medications**
  Help to prevent blood clotting. Both warfarin (Coumadin) and heparin are anticoagulant drugs [153]. Anticoagulants are often given to patients with peripheral artery/venous disease if they are at higher risk for blood clot formation; these agents are utilized much less often than anti platelet agents in patients having peripheral artery disease [147].
• **Cholesterol-lowering medications**
  Drugs belonging to the statin category have been utilized in several large clinical trials to prevent strokes and heart attack and extend survival among patients having atherosclerosis [152]. Statins also slow the development of peripheral artery disorder, reduces artherosclerosis in the arteries, and the development of claudication symptoms such as Buerger's disease [148].

• **Cilostazol (Pletal)** is a drug that can boost physical activity (by decreasing the frequency or intensity of claudication pain). Cilostazol functions by dilation of the arteries and an augmented blood flow to the extremities. Cilostazol is suggested for some patients with intermittent claudication when lifestyle changes and exercise are unsuccessful [149].

Cilostazol is recommended to be given to patient in an empty stomach either a half an hour prior to or two hours following meals. Fatty meals, grapefruit juice, and some medications like diltiazem (Cardizem) and omeprazole (Prilosec) can enhance the absorption, and therefore the blood levels of cilostazol [150]. The side effects are usually mild and include diarrhea, headache, and dizziness. Cilostazol should not be used in patients with heart failure due to the concern over increased mortality in heart failure patients using drugs similar to cilostazol [151].

• **Pentoxifylline** (Pentoxyl, Trental) enhances blood flow to the extremities by reducing the viscosity ("tackiness") of blood, enabling more proficient blood flow. Side effects are less than with cilostazol, but its effects are weaker and have not been decisively confirmed by all studies [155].

**Heart Failure**

Heart failure is a state in which the heart is unable to pump sufficient blood [156]. It can affect one or both sides of the heart [157]. The deterioration of the heart’s pumping capability causes the following conditions and symptoms: [158]

• fluid and blood to back up into the lungs
• The accumulation of fluid in the legs, ankles and feet - edema
• shortness of breath and exhaustion

General causes of heart failure include high blood pressure, coronary artery disease, and diabetes [159].

**Drugs causing heart failure**

High doses of certain normally used pain medicines can lead to a coronary event. This includes the drug ibuprofen, which has been found to increase the risk of strokes, heart attacks and related deaths [160].

Drugs used in the treatment of heart failure may be prescribed as monotherapy or to augment a treatment improved symptom control, as explained below [161]. Medical providers generally treat heart failure with a blend of medications. Depending on patient’s symptoms, one or more types of drugs may be recommended; these are discussed below: [162]

- **Angiotensin-converting enzyme (ACE) inhibitors**
  These medicines help patients with systolic heart failure live longer and have a higher quality of life (QOL) [172]. ACE inhibitors are vasodilators, drugs that increases the diameter of blood vessels to decrease blood pressure, develop greater blood flow and reduce the workload on the heart [174]. Examples of ACE inhibitors are lisinopril (Prinivil, Zestril), enalapril (Vasotec) and captopril (Capoten) [163].

- **Angiotensin II receptor blockers**
  Also vasodilators, these medications include valsartan (Diovan) and losartan (Cozaar) and have similar benefits as ACE inhibitors [173]. They might be a substitute for people who are unable to tolerate ACE inhibitors [164].

- **Digoxin (Lanoxin)**
  This drug, also called digitalis, increases the power of heart muscle contractions [175]. It also slows down the heartbeat. Digoxin decreases heart failure signs in systolic heart failure [165].
• **Beta blockers**
  This category of drugs decreases the heart rate and decreases blood pressure, and it also reverses or limits some of the injuries to patients with systolic heart failure [171]. Examples are metoprolol (Lopressor), carvedilol (Coreg) and bisoprolol (Zebeta). These medicines decrease the danger of some irregular heart rhythms and diminish the possibility of dying suddenly. Beta blockers might decrease symptoms and signs of heart failure, improve heart function, and decrease mortality [168].

• **Diuretics**
  This was covered in the earlier section that discussed drugs commonly used for patient’s with hypertension, however is worthy of discussion here. Diuretics, often referred to as water pills, increase the frequency of urination, preventing fluids from collecting in the body. Examples, like furosemide (Lasix), also reduce fluid levels in the lungs to assist patients to retain respiratory function. Because diuretics increase urinary loss of magnesium and potassium, the medical provider also might recommend Mg and K supplements. If a patient is on a non-potassium sparing diuretic, it is important to monitor the levels of potassium and magnesium in the blood by regular blood tests [167].

• **Aldosterone antagonists**
  These medicines include eplerenone (Inspra) and spironolactone (Aldactone). They are basically potassium-sparing diuretics, but also have extra properties that might reverse scarring of the heart and assist patient’s diagnosed with severe systolic heart failure [170]. Unlike certain other diuretics, spironolactone can increase the levels of potassium in the patient’s blood to hazardous levels, therefore, these must be monitored as well [68].

• **Inotropes**
  These are intravenous medications used in severe heart failure patients to improve heart pumping function and maintain blood pressure [169].
Diuresis

Osmotic diuresis is a condition of increased urination because of the presence of particular substances in the liquid filtered by the kidneys [170, 188]. These substances can increase the dilution and volume of urine [171].

Osmotic diuresis can result from the following preexisting factors: [172]

- High blood sugar
- Use of some medications, like Mannitol

Drugs causing diuresis are discussed below in terms of their therapeutic classification and desired actions in clinical conditions where fluid overload is a concern [173, 187].

Drugs for incontinence

Some drugs typically used for hypertension, referred to as alpha blockers or alpha-adrenergic antagonists, are used to treat incontinence. Examples of these drugs include Minipress, Cardura and Hytrin, which function by dilating blood vessels and decreasing blood pressure [174]. In fact, they are frequently recommended for men to assist with problems with urination. In men with an enlarged prostate, or benign prostatic hyperplasia (BPH), alpha blockers can relax the muscles in the bladder neck, enabling flow and improving signs of BPH [175].

Antidepressants

While certain antidepressants aid urinary incontinence, such as Tofranil and Elavil, most can deteriorate symptoms in some patients [176, 186]. Antidepressants can damage the capability of the bladder to contract, deteriorating symptoms of urinary flood and stress incontinence, since the bladder can’t be emptied completely. Other antidepressants might reduce a person’s consciousness of the need to urinate [177]. If an antidepressant is causing adverse side effects, the prescribing provider will need to discontinue and consider an alternative medication or therapy of the patient [178].
Diuretics

Generally called "water pills," these work drugs flush surplus salt and water out of the body. Hence, the patient will need to be taught to expect more frequent visits to the bathroom and a potential aggravation of incontinence symptoms [179].

Drugs for treating diuresis

Diuresis is treated using anti-diuretic drugs along with certain types of medicines for treating the underlying cause [181]. In patients with post obstructive diuresis the urine production needs to be directly monitored; urinary volume following resolution of an obstruction should be limited to 4 liters in a day. Extreme urination can lead to hypokalemia and plasma volume contraction in patients [180, 185].

If the body fluids are significantly decreased, fluids must be given immediately [183]. This will stop the plasma volume contraction. In cases of post obstructive diuresis, the diuresis treatment consists primarily of achieving a consistent fluid balance [182].

Diuresis, particularly post obstructive cases, generally resolves after a few days. In some cases, they may last up to a week and then dissipate [184].

DRUGS AFFECTING THE RESPIRATORY SYSTEM

The respiratory system consists of the lungs, trachea, mouth, nose, and ancillary musculature assisting in breathing [196]. The aim of respiration is to transport oxygen to the body and to eliminate carbon dioxide. The lungs, trachea, bronchi and diaphragm, are the parts of respiratory system and any problem may lead to respiratory disorders and diseases [197].

Upper respiratory disease

Upper respiratory disease often primarily involves an upper respiratory infection [198]. The upper respiratory tract consists of the nasal passages, sinuses, pharynx, and larynx. These structures control the air we breathe from the outside to the trachea and finally to the lungs [199]. We will focus here on upper respiratory infection, which is an infection of any of the components of the upper airway [200].
The widespread upper respiratory tract infections are: [201]
- the common cold
- tonsillitis (infection of the tissues at the back of the throat and tonsils)
- sinusitis (infection of the sinuses)
- laryngitis (infection of the larynx)
- influenza (viral)

Upper respiratory infection is usually caused by the attack of the inner lining (mucus membrane) of the upper airway by the offender bacteria or virus. In order for the pathogens (bacteria and virus) to attack the mucus membrane of the upper airways, they have to pass through a number of immunologic and physical barriers [202].

Drugs used to treat upper respiratory infections are outlined below: [203]

<table>
<thead>
<tr>
<th>Drug</th>
<th>Generic Name</th>
<th>Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxil</td>
<td>Amoxicillin</td>
<td>aminopenicillins</td>
</tr>
<tr>
<td>Augmentin</td>
<td>amoxicillin/clavulanate</td>
<td>beta-lactamase inhibitors</td>
</tr>
<tr>
<td>Azithromycin Dose Pack</td>
<td>Azithromycin</td>
<td>Macrolides</td>
</tr>
<tr>
<td>Bactrim</td>
<td>sulfamethoxazole/trimethoprim</td>
<td>miscellaneous</td>
</tr>
<tr>
<td>Bactrim DS</td>
<td>sulfamethoxazole/trimethoprim</td>
<td>miscellaneous</td>
</tr>
<tr>
<td>Biaxin</td>
<td>Clarithromycin</td>
<td>Macrolides</td>
</tr>
<tr>
<td>Ceftin</td>
<td>Cefuroxime</td>
<td>second generation cephalosporins</td>
</tr>
</tbody>
</table>

**Lower respiratory disease**

Lower respiratory diseases are those diseases that impact the lungs. One of the most fatal of these is called chronic obstructive pulmonary disease (COPD), which makes it difficult to breathe. COPD includes two major illnesses: [204]

*Emphysema*

In emphysema, the alveoli are damaged, most commonly due to cigarette smoking or persistent air pollution, decreasing the amount of oxygen exchanged to the blood and the CO₂ removed from the blood [205].

*Chronic bronchitis and other lower lung diseases*
If a patient has chronic bronchitis, the lining of the airways of the lungs becomes inflamed. After periods of prolonged inflammation, the airway walls thin and become congested with mucus. The most widespread lower respiratory tract infections and drug treatment options are identified below [206].

- Flu (this can impact either the lower or upper respiratory tract)
- Bronchitis (disease of the airways)
- Pneumonia (disease of the lungs)
- Bronchiolitis (an infection of the smaller airways that impacts children younger than two)
- Tuberculosis

The major symptom of a lower respiratory tract infection can also be a cough, although it is generally harsher and may be productive. Other potential symptoms are a tight chest, increased respiratory rate, wheezing and breathlessness [207].

Drugs that may be used in the treatment of a lower respiratory infection and disease are listed below: [205]

- Amoxicillin Oral
- Aamoxicillin-pot clavulanate Oral
- Aaztreonam in dextrose(iso-osm) IV
- Aaztreonam Inj
- Augmentin Oral
- Azactam in dextrose (iso-osm) IV
- Azactam Inj
- Cefaclor Oral
- Cefazolin in 0.9% sod chloride IV
- Cefazolin in dextrose (iso-os) IV
- Cefazolin in dextrose 5 % IV
- Cefazolin in sterile water IV
- Cefazolin IV
- Cefotaxime Inj
• Cefotaxime IV
• Cefotetan in dextrose, iso-osm IV
• Cefotetan Inj
• Cefotetan IV
• Ceftazidime in D5W IV
• Ceftazidime Inj
• Ceftazidime-dextrose (iso-osm) IV
• Ceftriaxone in dextrose, iso-os IV
• Ceftriaxone Inj
• Ceftriaxone IV
• Cefuroxime axetil Oral
• Ciprofloxacin in D5W IV
• Ciprofloxacin IV
• Ciprofloxacin Oral
• Cefazolin Inj
• Ceftin Oral
• Cipro in D5W IV
• Cipro Oral
• Claforan Inj
• Claforan IV
• Flagyl Oral
• Fortaz in dextrose 5 % IV
• Fortaz Inj
• Fortaz IV
• imipenem-cilastatin IV
• Metro I.V. IV
• Metronidazole in NaCl (iso-os) IV
• Metronidazole Oral
• Ofloxacin Oral
• Primaxin IV IV
• Rocephin Inj
• Tazicef

It should be mentioned that cigarette smoking is a major cause of this disease. If a person smokes, he/she is 12 times as likely to expire from an infection of the lower respiratory tract associated with chronic lung disease than those who have never smoked. Additionally, emphysema and chronic bronchitis are strongly connected with lung cancer [203]. All health care professionals should document smoking cessation education – date, time and methods used – offered to the patient. Helpful referrals and smoking cessation help lines are available as handouts for patients within their communities.

**DRUGS AFFECTING THE IMMUNE SYSTEM**

The immune system is the network of cells, and tissues, and organs that function together to protect the body against a number of attacks by invaders (parasites, bacteria, viruses and fungi). These are mainly microbes - minute organisms like bacteria, fungi, viruses - that can be a source of infections. The body offers a perfect host for a lot of microbes. It is the immune system’s task to prevent pathogens or any foreign substances from entering the body, or failing that, to destroy them [208].

The immune system, therefore, is referred to as the body's defense against contagious organisms and related invaders. Through a sequence of steps called the immune reaction or immune response, the immune system destroys invading organisms that attack body systems and lead to disease [209]. When the immune system attacks the wrong target, or over-reacts, however, it can set loose a flood of disorders, including arthritis, allergic diseases, and a type of diabetes. In short, a compromised immune system leads to various other sorts of diseases [210].

Most of the other immune disorders arise due to an extreme immune response or an autoimmune attack. Familial Mediterranean fever, asthma, allergies and Crohn's disease (inflammatory bowel) all result from an over-reaction of the system. Other immune system diseases, such as autoimmune polyglandular syndrome and certain
aspects of diabetes, occur due to an autoimmune response against 'self' cells and molecules [210].

Drugs used for the treatment of immune system disorders are discussed below primarily in terms of correlating dysfunctions and usage. The drugs in the treatment of immune system dysfunction resulting in persistent infections tend to involve long-term use of antifungal or antibiotic medications and defensive (prophylactic) treatments [211]. One drug, Interferon, is utilized to treat various viral infections and certain kinds of cancer. It is a natural cytokine and acts as an immunostimulant that makes a patient’s immune system work in a better way.

The following is a list of the available options for drug treatment for individuals with a disease of the immune system.

- A-Hydrocort Inj
- Aristospan Intralesional Inj
- Betamethasone Oral
- Celestone Oral
- Cortef Oral
- Cortisone Oral
- Depo-Medrol Inj
- Dexamethasone in 0.9 % NaCl IV
- Flo-Pred Oral
- Hydrocortisone Oral
- Kenalog Inj
- Medrol (Pak) Oral
- Medrol Oral
- Methylprednisolone
- Millipred DP Oral
- Orapred Oral
- Pediapred Oral
- Prednisolone acetate Oral
• Prednisolone Oral
• Prednisolone sodium phosphate Oral
• Prelone Oral
• Solu-Cortef (PF) Inj
• Solu-Medrol (PF) Inj
• Triamcinolone hexacetonide Inj
• Veripred 20 Oral

Sometimes combination therapy is needed. Individuals suffering from HIV or AIDS might take combinations of drugs to decrease the amount of viral load. Patients having hypogammaglobulinemia are treated by using IV immunoglobulin infusions. These infusions increase blood immunoglobulin levels and can provide passive defense against several infections [212]. The most common medications that are prescribed to patients with immune-based inflammatory conditions are steroids and NSAIDs [212].

**DRUGS AFFECTING THE GASTROINTESTINAL SYSTEM**

The gastrointestinal system, also called the digestive system, consists of a long tube running through the body, with particular areas specialized for the cleavage (digestion) of nutrients, selectively absorbing the nutrients and excreting waste products [213].

The entire system is controlled by the enteric nervous system, the CNS, the endocrine system and various local feedback systems. Digestion begins even before food enters the mouth with visual, olfactory stimuli playing a role in salivary secretion. Chewing begins the mechanical and chemical process of digestion along with the secretion of amylases. Acid secretion in the stomach denatures proteins.
Digestion continues with the secretion of pancreatic enzymes (including preoteases, lipases, amylases), and bile stored in the gall bladder emulsifies fats [217]. Diverse neuronal and endocrine systems control appetite, gut motility, absorption and secretion of acid and enzymes. Most absorption of nutrients takes place in the small intestine, including vitamins, minerals, glucose and others, while water balance is primarily controlled by the large intestine. In addition, the liver plays a role in the production of bile and the storage of glucose in the form of glycogen [214, 215].

The gut flora, or *microbiome*, is also recognized to play an important role in digestion, the synthesis of some vitamins (e.g. Vitamin K and B₁₂) and in both the adaptive and the acquired immune system [305].

The digestive system breaks down food and fluids into smaller, absorbable units. In this intricate process, blood transports nutrients all through the body to feed cells and supply energy [216]. It is important to recognize the role that a healthy digestive system plays in overall health. Any issue in any of the parts of the digestive tract lead to severe digestive problems can also affect the other body organs and systems [218].

**Oral Disorders**

Oral and maxillofacial pathology involves diseases of the mouth and jaw. The mouth is an important organ with diverse functions. It is also inclined to cause a number of health and dental disorders [219]. Common oral disorders include: [220]

- Oral hygiene
- Gingivitis
- Periodontitis
- Oral cancer
- Dental caries
- Trench mouth
- Mouth ulcers
- Tooth - abnormal colors
- Cleidocranial dysostosis
**Chemotherapeutic agents causing Oral Disorders**

The following cancer drugs are most likely to cause mouth ulcers [221].

- Alemtuzumab (Mabcampath)
- Bleomycin
- Capecitabine (Xeloda)
- Cetuximab (Erbitux)
- Docetaxel (Taxotere)
- Doxorubicin
- Epirubicin
- Erlotinib (Tarceva)
- Fluorouracil
- Methotrexate
- Sunitinib (Sutent)
- Vincristine

**Other Drugs causing oral disorders**

Following are some of the most common medications prescribed to patients that cause dry mouth, lesions in the oral mucus membranes and other adverse effects [221]:

- Divalproex Oral, Valproic acid (as sodium salt) Oral, Depakene Oral, Valproic acid (bulk)
- Lithium carbonate Oral, Lithium citrate Oral, Lithobid Oral
- Olanzepine oral/IM, Quetiapine Oral, Risperidone microspheres IM, Risperdal Consta IM, Seroquel XR Oral

**GERD/Peptic Ulcer Disease**

A peptic ulcer, also called peptic ulcer disease (PUD), is the most common defect in the mucosal surface of the esophagus, stomach and duodenum. It is characterized as mucosal erosions equivalent to or bigger than 0.5 cm (1/5"). Ulcers can also be worsened or caused by medicines such as ibuprofen, aspirin, and other NSAIDs [222].
The appearance of an ulcer can be either the typical concave, erosive, crater-like ulcer, or convex, resembling a colonic polyp. As a simplification, the erosive concave kind tends to be located in the stomach while the convex kind tends to be found in the areas of pylorus/duodenum [223]. The two most common causes of peptic ulcers are identified below: [224]

- Helicobacter pylori: is a bacteria that is often found in the stomach and has been associated with ulcer formation
- Nonsteroidal anti-inflammatory drugs (NSAIDS) like ibuprofen (and several others)

Furthermore, smoking and some other environmental and genetic factors (such as drugs) might influence the etiology of peptic ulcer disease. Psychological stressors and dietary factors were often thought to be the cause of ulcers, though these factors are no longer considered to have a main role, the role of stress in the formation of ulcers is still believed to be considerable [225].

Symptoms of GERD/PUD vary. Pain is the most common symptom, but may be variously reported as heartburn, chest pain, indigestion and vary in location from abdominal to epigastric. Other signs and symptoms can include blood in the stool (resulting in black, tarry stools), vomiting blood (coffee-ground vomit), generalized nausea and vomiting, unexplained weight loss and changes in appetite [226]. Smoking and various foods can trigger or worsen ulcer pain; these include beverages such as coffee, tea and alcohol and foods, such as tomatoes, wheat products, fatty foods and some others.

Drugs for treating GERD/PUD are discussed below in terms of the desired outcome [226]. In the setting of a positive H pylori test, treatment involves a blend of drugs to kill the bacteria and decrease the acid levels in the stomach. This allows the patient’s ulcer to heal and can decrease the possibility of recurrence.

If a patient has a peptic ulcer with an H. pylori infection, the normal treatment uses diverse combinations of the medications given below, for 5 - 14 days:
• Two types of antibiotics to destroy H. pylori, such as amoxicillin, clarithromycin (Biaxin), tetracycline, or metronidazole (Flagyl)
• Proton pump inhibitors such as lansoprazole (Prevacid), omeprazole (Prilosec), or esomeprazole (Nexium)
• Bismuth (the key ingredient in Pepto-Bismol) might be added to kill the bacteria
• If the patient has an ulcer with no H. pylori infection, or one that resulted by taking NSAIDs or aspirin, a proton pump inhibitor may be started and continued for about 8 weeks.

Patients remaining on certain drugs, such as NSAIDS or aspirin to treat a chronic health condition, may be required to be on a current dose of a proton pump inhibitor.

Specifically, medications that might be used for ulcer disease are identified as: [227]

• Proton pump inhibitors:
  Omeprazole (Prilosec), Lansoprazole (Prevacid), Esomeprazole (Nexium) and Pantoprazole (Protonix) Misoprostol, a synthetic prostaglandin may be used to help stop ulcers in patients who take NSAIDs on a frequent basis.
• Medications that defend the tissue lining (sucralfate)
• Histamine₂ (H₂) blockers such as Ranitidine (Zantac), Famotidine (Pepcid), Cimetidine (Tagamet) and Nizatidine (Axid) reduce the levels of acid in the stomach, relieving ulcer pain.

Nausea and Vomiting

Nausea and vomiting are the signs and symptoms of an underlying sickness and not a particular disease. Nausea and vomiting can lead to dehydration, and dehydration can aggravate nausea and vomiting. [228, 229]

There are many causes of nausea and vomiting. These signs and symptoms might be due to the following: [229]

• Acute gastritis (direct pain and inflammation in the stomach lining)
• CNS signals from the brain can lead to nausea and vomiting
• Other illnesses
- Medications
- Mechanical hindrance of the bowel

Drugs that cause nausea and vomiting are listed below, including some chemotherapeutic agents with the potential to cause worse nausea and vomiting more than other drugs [231, 230].

Many kinds of antiemetics can reduce the harshness of nausea, though most of them require a medical evaluation and a prescription. Medicines obtainable over-the-counter are mainly suggested for motion sickness and milder cases of nausea. Drugs used in the treatment of nausea and vomiting, antiemetics, are discussed below in terms of the desired effects [232].

- **Meclizine hydrochloride (Bonine)**
  Meclizine is an antihistamine that is effective in reducing nausea, vomiting, and faintness linked with motion sickness. Unless suggested by a physician, it should not be in use by patients with glaucoma, lung diseases, or those with trouble urinating due to an enlarged prostate. Meclizine can cause sleepiness and should not be used with other sedatives such as tranquilizers, alcohol, or sleeping pills. Meclizine is not recommended for children who are under age 12, or in nursing or pregnant women, unless suggested by a physician [233].

- **Dimenhydrinate (Dramamine)**
  Dimenhydrinate is also an antihistamine. It's utilization should be restricted to motion sickness. It can cause sleepiness and should be avoided in the similar situations as Meclizine. Quite a lot of diverse formulations of dimenhydrinate are obtainable, including a children’s liquid that should be applied according to the instructions of physician. Dramamine Less Drowsy Formula consists of meclizine, like Bonine, and might have fewer tranquilizer side effects. Both dimenhydrinate and meclizine are suggested to be taken about an hour prior to travel to stop motion sickness [233].
• **Emetrol**
  Emetrol is an oral solution intended to calm the stomach when nausea and vomiting are the result of a bacterial or viral infection or by overeating. Emetrol consists of phosphoric acid and sugar. Diabetics should not make use of Emetrol without health supervision since it contains concentrated sugar. According to its producer, Emetrol should not be taken for over five doses in one hour exclusive of a physician’s consultation [232].

• **Bismuth subsalicylate (Pepto-Bismol)**
  Bismuth is a product containing bismuth subsalicylate, a substance shown to be useful in relieving nausea and a disturbed stomach. This medicine has a direct effect on the stomach lining and has no recognized serious side effects. It might cause darkening of the stool color and of the tongue. Pregnant women should check with their physicians prior to using bismuth subsalicylate as part of the active ingredient (salicylate) is chemically similar to aspirin, which might harm infants and the fetus.

  Patients who are allergic to aspirin or associated drugs also should not use bismuth subsalicylate. Physician evaluation and instruction is needed if the patient is taking anticoagulants or has diabetes or gout since the salicylate might further amplify the anticoagulant effect [234].

**Diarrhea and Constipation**

Diarrhea is the medical condition specified by an increased frequency of bowel movements that are watery and loose. It is very common and generally not serious [235]. Many people will have diarrhea once or twice every year. It usually lasts two to three days and can be treated with over-the-counter (OTC) drugs. Some people face diarrhea frequently as part of an irritable bowel condition or other chronic diseases of the small or large intestine [236].

Diarrhea can be caused by the following factors and conditions: [237]
• Bacterial infection (the cause of most kinds of food poisoning)
• Infections by other organisms
• Eating foods that disturb the digestive system
• Sensitivities to some foods
• Medications
• Radiation therapy
• Diseases of the intestines (ulcerative colitis and Crohn's disease)
• Malabsorption (the body is unable absorbed certain nutrients from the diet)
• Hyperthyroidism
• Some cancers
• Laxative abuse
• Alcohol abuse
• Surgery
• Diabetes

Diarrhea might also follow constipation, particularly for people who are suffering from irritable bowel syndrome [237].

Constipation occurs when bowel movements turn out to be difficult or less frequent. The usual length of time between bowel movements ranges extensively from person to person [244]. Some people have bowel movements three times a day; others, just one or two times a week. Going more than three days with no bowel movement is generally considered too long. After three days, the stool becomes harder and more difficult to pass [238].

General causes of constipation are listed below: [239, 243]

• Inadequate water intake
• Inadequate fiber in the diet
• A disruption of regular diet or routine; traveling
• Inadequate activity or exercise or immobility
• Eating large amounts of dairy products
• Stress
• Resisting the urge to have a bowel movement, which is sometimes the result of pain from hemorrhoids
• Overuse of laxatives (stool softeners) which, over time, weaken the bowel muscles
• Hypothyroidism
• Neurological conditions such as Parkinson's disease or multiple sclerosis
• Antacid medicines containing calcium or aluminum
• Medicines (especially strong pain medicines, such as narcotics, antidepressants, or iron pills)
• Depression
• Eating disorders
• Irritable bowel syndrome
• Pregnancy
• Colon cancer

Constipation can be due to a drug side effect. The most general offending medications include are listed below: [240]
• Narcotic pain drugs, such as codeine (for instance, Tylenol #3), oxycodone (for instance, Percocet), and hydromorphone (for instance, Dilaudid);
• Antidepressants such as imipramine (Tofranil) and amitriptyline (Elavil, Endep)
• Anticonvulsants such as carbamazepine (Tegretol) and phenytoin (Dilantin)
• Iron supplements
• Calcium channel blocking medications such as diltiazem (Cardizem) and nifedipine (Procardia)
• Aluminum-containing antacids such as aluminum hydroxide suspension (Amphojel) and aluminum carbonate (Basaljel)

Drugs commonly used to treat diarrhea and constipation are listed below, and include the addition of probiotics to aid in the balance of gut flora [241, 242].
Drugs for treating diarrhea:

- Acidophilus
- Acidophilus
- Bacid
- Flora-Q
- Florastor
- Florastor Kids
- Fulyzaq
- Imodium
- Imodium A-D
- Kaopectate
- Lomotil
- Lonox
- Lotronex
- Mycifradin
- Paregoric
- Pepto-Bismol
- Pepto-Bismol Maximum Strength
- RisaQuad
- Xifaxan

Drugs for treating constipation

- Amitiza
- Citrucel
- Colace
- Doc-Q-Lace
- DOK
- DSS
- Dulcolax
- Dulcolax Laxative
- Dulcolax Stool Softener
- FiberCon
- Fleet Enema
- Glycerin Suppositories Maximum Strength
- GlycoLax
- Linzess
- Metamucil
- Milk of Magnesia
- MiraLax
- Phillips' Milk of Magnesia
- Senokot
- Surfak

DRUGS AFFECTING THE ENDOCRINE SYSTEM

The endocrine system is a set of ductless glands that generate hormones, which control development, overall metabolism and energy metabolism, sleep, mood, appetite and sexual growth and function. The hormones are discharged directly into the bloodstream and carried to organs and tissues all through the body [245]. Endocrine
disorders are often multifaceted, involving a varied picture of hyposcretion and/or hypersecretion due to the feedback mechanisms involved in the endocrine system.

This section discusses the most common and widespread endocrine diseases [246].

**Diabetes Mellitus**

Diabetes mellitus is a metabolic disease in which a patient has elevated blood sugar, either due insufficient insulin (because of autoimmune or non-immune destruction of pancreatic beta-cells), or because the cells have become insulin resistant [248]. This elevated level of blood sugar creates the classic symptoms of polyuria (recurrent urination), polydipsia (increased thirst) and polyphagia (increased hunger) [249]. Genetics, obesity, increasing age, female gender, poor diet and lack of physical activity are risk factors for diabetes. There are three kinds of diabetes, as discussed below.

*Type 1 Diabetes*

In Type 1 diabetes the body does not synthesize insulin because an autoimmune response destroys the pancreatic beta-cells responsible for insulin synthesis. Type 1
diabetes (T1D) is also referred to as insulin-dependent diabetes (IDDM), juvenile diabetes, or early-onset diabetes. People generally develop type 1 diabetes prior to their adult years, usually in early middle age or teen years.

Patients having type 1 diabetes require insulin injections for life. They must also maintain appropriate blood-glucose levels by going through regular blood tests and following specific dietary plans [250].

*Type 2 Diabetes*

In Type 2 diabetes (T2D) the pancreas generates insulin but the insulin levels may be inadequate or the cells in the body do not respond to insulin (insulin resistance). T2D is also known as non-insulin dependent diabetes mellitus (NIDDM).

Obesity is a major risk factor for developing T2D. Men with low testosterone levels also have a higher risk of developing type 2 diabetes [251].

*Gestational Diabetes*

This type of diabetes affects 3 -10% of previously undiagnosed females during pregnancy, particularly during the 3rd trimester. Insulin resistance characterizes gestational diabetes (GDM). Children born to women with GDM have a higher risk for obesity and diabetes as well [252].

*Drugs causing Diabetes Mellitus*

Many drugs that are used to decrease cardiovascular risk also influence the development of diabetes. These include beta-blockers, thiazide diuretics, and statins, as outlined below [252, 253, 254, 255].

- Thiazides:
  Thiazide diuretics were found to boost the risk of diabetes. This danger is greatly reduced by low-dose treatment.
- **Beta-blockers:**
  Beta-blockers can damage pancreatic beta cells, particularly agents that are not selective for the β1-receptor subtype. Numerous studies have indicated that chronic utilization of β-blockers increase the risk for the diabetes. The risk can be increased by the use of non-selective beta blockers along with a thiazide diuretic.

- **Statins:**
  Meta-analysis has revealed an excess danger of 9% of progression to diabetes in patients taking statin drugs to lower cholesterol.

- **Steroids:**
  Steroid drugs can lead to a type of iatrogenic Cushing's syndrome, and are almost certainly the most extensively used drugs which increase the risk of diabetes. It was found that 0.4% of childhood diabetes was due to medication according to one study, and 55 of 56 children in this group were on steroids. Monogenic diabetes was identified in just 0.2% of children. Anabolic steroids (artificial androgens mimicking testosterone or dihydrotestosterone) should not be confused with glucocorticoids. Though they have significant adverse effects, diabetes is not among them [254].

Drugs used in the treatment of diabetes mellitus depend upon the type of diabetes involved. Controlling elevated blood sugar helps prevent kidney damage, nerve problems, blindness, loss of limbs, and issues with sexual function. Proper management of diabetes can also lessen the risk of a stroke or heart attack.

Some of the most commonly prescribed drugs for diabetic patients include those discussed and listed in the table below [253, 254, 247].

- **Acarbose**
  Acarbose is used along with an appropriate diet and exercise programs to manage high blood sugar in patients with type 2 diabetes (non-insulin-dependent diabetes). Acarbose inhibits alpha glucosidase and decreases the amounts of
glucose released from dietary carbohydrates, so that blood sugar level does not increase as much after a meal.

- **Actoplus MET**
  This combination medication is used along with a good diet and exercise program to manage high blood sugar in patients with T2D. This drug should not be used to treat T1D.

<table>
<thead>
<tr>
<th>Injectable medications</th>
<th>Medications</th>
<th>Action</th>
<th>Possible side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Amylin mimetics</strong></td>
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<td></td>
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<tr>
<td></td>
<td>• Pramlintide (Symlin)</td>
<td>Increase insulin release; used along with insulin injections</td>
<td>Hypoglycemia; nausea/vomiting; headache; redness and irritation at injection site</td>
</tr>
<tr>
<td></td>
<td><strong>Incretin mimetics</strong></td>
<td>Increase insulin release; used along with metformin and sulfonylureas</td>
<td>Nausea/vomiting; headache; dizziness; kidney damage or failure</td>
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<tr>
<td></td>
<td>• Exenatide (Byetta)</td>
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<td></td>
<td>• Liraglutide (Victoza)</td>
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<tr>
<td>Medications</td>
<td>Action</td>
<td>Potential Adverse Effects</td>
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<tr>
<td>Meglitinides</td>
<td>Increase insulin release</td>
<td>Hypoglycemia; weight gain; nausea; back pain; headache</td>
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<tr>
<td>• Repaglinide (Prandin)</td>
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<td>• Nateglinide (Starlix)</td>
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<tr>
<td>Sulfonylureas</td>
<td>Increase insulin release</td>
<td>Hypoglycemia; weight gain; nausea; skin rash</td>
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<tr>
<td>• Glipizide (Glucotrol)</td>
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<td>• Glimepiride (Amaryl)</td>
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<tr>
<td>• Glyburide (DiaBeta, Glynase)</td>
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<tr>
<td>Dipeptidy peptidase-4 (DPP-4) inhibitors</td>
<td>Increase insulin release. Decrease hepatic glucose release.</td>
<td>Upper respiratory tract infection; sore throat; headache; Pancreatits (sitagliptin)</td>
<td></td>
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<tr>
<td>• Saxagliptin (Onglyza)</td>
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<tr>
<td>• Sitagliptin (Januvia)</td>
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<tr>
<td>• Linagliptin (Tradjenta)</td>
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<tr>
<td>Biguanides</td>
<td>Decrease hepatic glucose release. Increase insulin sensitivity.</td>
<td>Nausea; diarrhea; rarely, lactic acidosis</td>
<td></td>
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<tr>
<td>• Metformin (Fortamet, Glucophage, others)</td>
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<tr>
<td>Thiazolidinediones</td>
<td>Increase insulin sensitivity. Decrease hepatic glucose release.</td>
<td>Heart failure; heart attack; stroke; liver disease</td>
<td></td>
</tr>
<tr>
<td>• Rosiglitazone (Avandia)</td>
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<tr>
<td>• Pioglitazone (Actos)</td>
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<tr>
<td>Alpha-glucosidase inhibitors</td>
<td>Inhibit enzymatic cleavage of carbohydrates</td>
<td>Stomach pain; gas; diarrhea</td>
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<tr>
<td>• Acarbose (Precose)</td>
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<tr>
<td>• Miglitol (Glyset)</td>
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</table>

**Thyroid Disease**

The thyroid is a large gland situated below the skin and muscles at the base of the neck, just at the region where a bow tie would rest. It is brownish red, with right and left lobes that appear like a butterfly’s wings [255].

Thyroid hormones are secreted from the gland and go through the bloodstream to reach the tissues. Thyroid hormones function in controlling overall metabolism, sensitivity to other endocrine hormones, in musculoskeletal and neuronal development, sexual growth (puberty),
and regulation of body temperature. The production of the thyroid pro-hormone, T4 (thyroxine) is controlled by Thyroid Stimulating Hormone (TSH) from the anterior pituitary, which is in turn controlled by thyrotropin releasing hormone (TRH) from the hypothalamus. In tissue, T3 is converted to the active thyroid hormone T3 (triiodothyronine). High levels of T3/T4 feedback inhibit the production of TRH/TSH.

Thyroid disease occurs when the thyroid gland is unable to supply the appropriate quantity of hormones required. If the thyroid has become overactive, it releases high levels of thyroid hormone into a person’s bloodstream, leading to hyperthyroidism. Hyperthyroidism leads to an overall increase in metabolism.

On the other hand, if an underactive thyroid releases too little thyroid hormone, it leads to hypothyroidism. When the quantity of hormone released into the blood is below standard, the body utilizes energy more slowly, and chemical activity (metabolism) in the cells decreases. The two most widespread causes of hypothyroidism are iodine shortage and chronic thyroiditis, primarily due to autoimmune destruction (Hashimoto’s thyroiditis).

**Drugs causing thyroid disease**

Many different medications can lead to hypothyroidism by blocking the uptake of iodine, inhibiting the conversion of T4 to T3 and by directly damaging the cells of the thyroid. Goitrogens are substances that interfere with iodine uptake. Goitrogenic foods include the brassica foods (broccoli, bok choy, brussel sprouts, cabbage, and cauliflower).

While patients with a thyroid disease do not need to avoid these foods, they should be aware that in very large amounts, these foods can affect thyroid function.

**Drugs used to treat hyper- and hypothyroidism**

Drugs used to treat hyperthyroidism and Graves’ disease is discussed below in terms of symptom management and desired outcomes. The symptoms of Graves’ disease include exophthalmos, pretibial myxedema (non-pitting edema) in addition to
the generalized symptoms of hyperthyroidism, which include rapid heart rate, fatigue, increased sweating, thinning hair, tremor, weight loss and muscular weakness. Drugs recommended for Graves’ disease are also termed anti-thyroid medications, and include:

- Tapazole (methimazole)
- Propylthiouracil, or PTU

Other medications that are likely to be prescribed for hyperthyroidism include the following:

- Adrenal steroids such as prednisone and hydrocortisone, which treat inflammation
- Amiodarone, a heart medicine
- Lithium, used for psychiatric disorders
- Propranolol, a beta blocker

Patients with hyperthyroidism may also be prescribed a beta blocker — not to treat the thyroid disease, but to control its symptoms. Hyperthyroidism can lead to increased heart rate, nervousness, tremors, and anxiety. Beta blockers are usually prescribed to treat high blood pressure, but may manage these other symptoms as well, and include:

- Inderal (propranolol)
- Tenormin (atenolol)
- Lopressor (metoprolol)

Once the hyperthyroidism is well controlled, these medications may no longer be necessary.

Anti-thyroid drugs can be very helpful in treating hyperthyroidism, mainly Graves’ disease, which is an autoimmune illness with antibodies directed against the receptor for TSH. Up to 30 percent of patients having Graves' disease that take anti-thyroid drugs long-term (between 12 and 18 months) might find that the signs of this thyroid condition abate over time.
In *hypothyroidism* the disease may be primary (thyroid gland itself is affected), secondary (due to pituitary dysfunction) or tertiary (due to hypothalamic dysfunction). Symptoms of hypothyroidism include dry, itchy skin, weight gain, hair loss, edema, decreased reflexes, cold intolerance, heavy menstrual periods (or irregular), muscle weakness and fatigue, depression and constipation. Later signs include loss of the lateral third of the eyebrows, slowed or slurred speech, paresthesias, altered libido, goiter and low basal body temperature.

Drugs used in the treatment of hypothyroidism and Hashimoto’s Thyroiditis is discussed below: [260]

- **T4 Analog Drugs**

  Levothyroxine is the general name for the synthetic form of thyroxine, a thyroid hormone replacement drug. This medication is a T4 analog. Levothyroxine is the most commonly given thyroid hormone replacement medicine.

- **T3 Analog Drugs**

  There are numerous T3 drug choices including the synthetic T3 drug Cytomel. Synthroid, a synthetic T3, is one of the most commonly recommended medications for hypothyroidism.

Thyroid disease and replacement therapy must be carefully monitored and followed by the appropriate lab tests, particularly during times of stress or when medication is being adjusted.

**Corticosteroids**

Corticosteroids are synthetic drugs that structurally resemble cortisol, a hormone secreted by adrenal glands. Corticosteroids are frequently referred to by the term "steroids" [261]. Corticosteroids are distinct from the androgen-related steroid compounds misused or abused by some athletes [262, 263, 264]. Corticosteroids are involved in the stress response, the immune response, carbohydrate and protein metabolism,
maintaining electrolyte (mineral) levels and inflammation. Corticosteroids may be

glucocorticoids, mineralocorticoids or have both effects.

Corticosteroid drugs include prednisone, cortisone, and methylprednisolone.
Prednisone is the most generally used steroid to treat rheumatologic diseases.

Examples of steroid treatments can be joint injections, skin creams, eye drops and
eardrops. Systemic steroid treatments are drugs that are given orally, directly into a vein
(intravenously or IV) or muscle (intramuscularly or IM).

Steroids are utilized to treat a range of conditions in which inflammation or a
dysfunctional immune system plays a role. In some circumstances steroids may be
used when other measures have not been successful [265].

Steroids are used as the major treatment for inflammatory conditions, such as [266]:

- Systemic vasculitis (inflammation of blood vessels)
- Myositis (inflammation of muscle)
- Dermatitis
- Inflammatory bowel diseases
- Asthma
- Autoimmune diseases
- Adrenal failure or insufficiency (Addison’s disease and Addison’s-like diseases)
- Allergic disorders
- Rheumatoid arthritis (constant inflammatory arthritis taking place in joints on both
  sides of the body)
- Systemic lupus erythematosus (a widespread illness caused by irregular immune
  system function)
- Sjögren's condition (unceasing disorder that results in a dry mouth and dry eyes)

Under certain circumstances, steroids can be effective to minimize organ-damage. For
instance, steroids can be useful to prevent kidney inflammation, which could cause
kidney failure in patients who have lupus or vasculitis. For these kinds of patients, steroid therapy may abrogate the need for kidney dialysis or kidney transplantation\textsuperscript{[267]}. 

Low doses of steroids may offer relief from pain and rigidity for patients with rheumatoid arthritis. Temporary utilization of higher doses of steroids may help a person recover from a harsh flare-up of arthritis. 

The incidence of side effects depends on the quantity, kind of steroid, and duration of treatment. Some side effects are more severe than others. General side effects of systemic steroids include: \textsuperscript{[268]} 

- Increased appetite, weight gain 
- Unexpected mood swings 
- Muscle weakness 
- Blurred vision 
- Increased development of body hair 
- Easy bruising 
- Lower confrontation to infection 
- Swollen, \textit{puffy face} 
- Acne 
- Osteoporosis (bone weakening illness) 
- Worsening of diabetes 
- High blood pressure 
- Stomach irritation 
- Nervousness, restlessness 
- Having problems in sleeping 
- Cataracts or glaucoma 
- Water preservation, swelling 

To reduce the side effects of these steroids, the following guidelines are recommended in pursuing a treatment plan: \textsuperscript{[269]}
- Use steroids just when necessary.
- Monitor the patient personally to observe any severe side effects.
- If possible, make use of local steroids for local problems.
- Use the least dose required to get control of the disease.
- Reduce the amount slowly as long as the illness remains under control.
- Check blood pressure frequently and treat if needed.
- Recommend calcium supplements to help maintain patient’s bone density.

**Gonadal Hormones**

Gonadal hormones, also called sex steroids, or gonadal steroids, interact with vertebrate androgen or estrogen receptors [270]. The production of sex hormones is regulated by classic cascade pathways. The hypothalamus makes a neurohormone called "gonadotropin-releasing hormone" (GnRH), which functions on the anterior pituitary, causing it to secrete two hormones, follicle-stimulating hormone (FSH) and luteinizing hormone (LH) [271].

Sex hormones serve numerous functions, including growth and development, reproductive cycles, growth, and sexual behavior. Gonads produce three main categories of steroid hormones: [272]

- **Androgens** (primarily testosterone) are synthesized by the testes. Androgens are responsible for the secondary male sexual characteristics of male hair growth pattern, and increased muscle and bone mass.

- **Estrogens** (estriol, estradiol and estrone) are produced primarily by the ovaries, but also by the adrenal glands and liver. Estrogens promote secondary female sexual characteristics, play a role in overall metabolism, bone reabsorption and fat metabolism, increase endometrial and uterine growth and vaginal structure. Estrogens also play a role in fluid balance, coagulation, ovulation, sexual function and fetal development.
• Progesterones are produced by the corpus luteum and the placenta and function to prepare the uterus for implantation, inhibit the maternal immune response, decrease uterine contractility, signals insulin release, controls body temperature during ovulation and can affect mood.

Gonadal hormone disorders

Gonadal hormone disorders are discussed in this section. During the phase of puberty, secondary sexual characteristics emerge, the rate of linear growth boosts, and menstruation and spermatogenesis take place [273].

In the following section some of the most common gonadal hormone disorders are discussed.

Hypogonadism:

Hypogonadism is a hormonal state that happens when the gonads become underactive. Hypogonadism disorders are more widespread among males than females.

Primary hypogonadism happens when the gonads are directly affected. General causes of primary hypogonadism that exist in males include undescended testicles, Klinefelter's syndrome, mumps orchitis, testicular injury, hemochromatosis, and cancer treatment. General causes of primary hypogonadism in females can be cancer treatment and injuries to the ovaries [277].

Secondary hypogonadism occurs when the hypothalamus and pituitary do not secrete sufficient amounts of GnRH. General causes of secondary hypogonadism in males and females are Kallman syndrome, drugs called opiates, inflammatory diseases (like sarcoidosis), and obesity.

Menopause/Andropause:

Males and females encounter a natural diminution in their sex hormones with age. Menopause treatment is a complex topic and the efficacy of specific hormone replacement therapy is still uncertain.
Addison's disease:
Addison's disease, termed as adrenal insufficiency or hypocortisolism, is an uncommon hormonal disorder that is typified by weight loss, fatigue, low blood pressure, muscle weakness, and infrequent darkening of the skin.

Addison's disease results when the adrenal glands are unable to make sufficient cortisol. Some patients having this disease might also have low levels of aldosterone. When aldosterone secretion falls too low, the kidneys are not able to control the salt and water equilibrium, subsequently leading the blood pressure and blood volume to drop [274].

Cushing's syndrome:
Cushing's syndrome, also called hypercortisolism, is a state that is characterized by a hump between the shoulders (buffalo hump), a round face (moon face), and pink or violet stretch marks on the skin [275].

High cortisol levels might be caused by parameters outside of the body (exogenous), such as drugs. It might also be caused by factors inside the body (endogenous) [276].

Hyperglycemia:
Hyperglycemia is a hormonal problem that occurs when there is excessive sugar in the blood. Blood sugar level increases when there is not adequate insulin in the blood, or if the body is unable to properly utilize insulin [278].

**DRUGS AFFECTING THE MUSCULOSKELETAL SYSTEM**

The musculoskeletal system consists of the muscles, bones, ligaments and tendons [279]. The purpose of the musculoskeletal system is as follows [280]:

- Defend and support the interior structures and organs of the body
- Allow movement
- Provide shape to the body
- Manufacture blood cells
- Store up calcium and phosphorus
- Produce heat

All of the bones, muscles, joints, cartilage, tendons and ligaments in a person’s body make up what is known as the musculoskeletal system. The bones provide the body with a framework, giving it shape and support; they also serve as protection for internal organs such as the lungs and liver [281]. Muscles are those fibers that assist to make purposeful movement of a body part or instinctive movement within an internal organ. Some people view this organization as two distinct systems that work extremely closely together, with one being the muscular system and the other being the skeletal system.

**Musculoskeletal disorders**

Musculoskeletal disorders are one of the most widespread of human afflictions. They impact all age groups and often cause disability, handicaps and impairments. They consist of a range of diverse diseases that cause pain or uneasiness in the bones, muscles, joints, or surrounding structures, and they can be chronic or acute, focal, or dispersed. The occurrence of musculoskeletal disorders usually increases with age, with the majority of persons aged seventy-five and over having some sort of musculoskeletal disorder, particularly arthritis [282].

Musculoskeletal disorders are extremely prevalent, and, due to their connection with aging, they are likely to turn out to be more widespread as the population ages. All racial groups face an impact. While much of the considerable cost of these disorders is because of the medications and medical care and other treatments necessary for patients, the preponderance of costs is because of the work loss, which is a direct result of these disorders [278].

The causes of musculoskeletal disorders are varied. Muscle tissue can be injured with the wear and tear of everyday activities. Trauma to a region (jerking movements, falls, fractures, sprains, auto accidents, dislocations, and straight blows to the muscle) also can lead to musculoskeletal pain. Other causes of pain are postural strain, overuse, repetitive movements, and protracted immobilization. Changes in position or poor body
mechanics might bring about spinal position problems and muscle shortening, thus causing other muscles to be distorted and that turn out to be painful.

Drugs used in the treatment of musculoskeletal disorders are listed below in terms of decreasing symptoms and the intended effects: [282]

- **Corticosteroids**
  - Betamethasone
  - Dexamethasone
  - Hydrocortisone
  - Methylprednisolone
  - Prednisolone
  - Triamcinolone

- **Non-biologic Anti-rheumatic drugs also known as Disease-modifying antirheumatic drugs (DMARDs)**
  - Auranofin
  - Azathioprine
  - Chloroquine
  - Ciclosporin
  - Cyclophosphamide
  - Hydroxychloroquine
  - Leflunomide
  - Methotrexate
  - Penicillamine
  - Sodium aurothiomalate
  - Sulfasalazine

- **Biologic DMARDs**
  - Abatacept (Orencia)
  - Adalimumab
  - Anakinra
Canakinumab (Ilaris) for: Polyarticular Juvenile Idiopathic Arthritis
- Etanercept
- Infliximab (Remicade)
- OnabotulinumtoxinA (Botox)
- Rituximab
- Tocilizumab for: systemic juvenile idiopathic arthritis and rheumatoid arthritis

- NSAIDs
  - Diclofenac (Arthrotec, Pennsaid)
  - Etodolac (Lodine XL)
  - Ibuprofen (Advil, Motrin)
  - Indomethacin (Indocin)
  - Nabumetone (Relafen)
  - Naproxen (Naprosyn)
  - Piroxicam (Feldene)

- COX-2 Inhibitors
  - Celecoxib (Celebrex) (Other COX-2 inhibitors were taken off the US market because of the risk of heart attacks and strokes with long term use)

- Muscle Relaxants
  - Baclofen
  - Botulinum toxin
  - Carisoprodol (Soma)
  - Cyclobenzaprine (Flexeril)
  - Dantrolene (Dantrium)
  - Diazepam (Valium)
  - Quinine
  - Tizanidine (Zanaflex)
• Anti-Gout
  o Colchicine Colcrys
  o Pegloticase (Krystexxa)

• Multiple Sclerosis Drugs
  o Dalfampridine (Ampyra)
  o Fingolimod (Gilenya)
  o Interferon beta-1b (Extavia)
  o Teriflunomide (Aubagio)

• SSRIs
  o Milnacipran (Savella): fibromyalgia

• Other
  o Pregabalin (Lyrica): For fibromyalgia
  o Rotigotine (Neupro) (Transdermal System)

• Drugs to treat osteoporosis
  o Alendronate sodium (Fosamax)
  o Alora
  o Calcitonin-salmon (Miacalcin) (Nasal Spray)
  o Conjugated estrogens (Premarin)
  o Conjugated estrogens/medroxyprogesterone acetate tablets (Prempro & Premphase)
  o Denosumab (Prolia)
  o Estradiol transdermal system (Vivelle-Dot)
  o Estradiol/Norethindrone Acetate (Activella)
  o Estratab
  o Iblandronate (Boniva)
  o Raloxifene hydrochloride (Evista)
  o Zoledronic acid (Reclast)
DRUGS AFFECTING THE REPRODUCTIVE AND GENITOURINARY DISORDERS

This section will start with a brief discussion on disease processes affecting the reproductive and genitourinary systems. Renal failure, the inability of the kidneys to function normally, can be acute or chronic. This state has a range of etiologies like medical diseases (diabetes, hypertension), primary renal diseases, and urinary impediment (prostate swelling or cancer). These conditions might be reversible or permanent [288]. In the latter, also termed as end-stage renal disease, the kidneys do not function well enough to preserve life. In this state, renal transplant or treatment with dialysis may be essential.

Kidney stones, where solid mineral or acid salts are deposited in the bladder, kidney, and/or ureter, is a widespread problem in many industrialized countries. Stones may be produced due to genetic abnormalities, dehydration, dietary factors, metabolic abnormalities, and urinary tract infections. Simple nutritional and behavioral modifications, along with medications, can reduce the possibility of recurring stones [289]. Therefore, metabolic assessment might help to stop stone formation and reduce morbidity. Pain medication and hydration is often sufficient to pass urinary tract stones and most can be eliminated without surgery.

Testicular cancer, a most common condition in young men, occurs between the ages 20 and 35 years. In contrast, the maximum occurrence of kidney cancer and bladder cancer has been found to be in adults between 60 and 70 years of age. Prostate cancer is the most common genitourinary malignancy in men and is the second leading causes of cancer death in men. The occurrence of prostate cancer is associated with age, African ancestry, family history, obesity and a diet high in red meat and dairy products. Higher levels of prostate-specific antigen (PSA) in the blood has been found to be correlated with prostate cancer, as cancer cells secrete more PSA into the blood than do normal cells. Current data recommend that yearly prostate cancer screening for PSA and digital rectal exam might translate into a reduced mortality rate from prostate cancer in the future [288].
Kidney cancer is a relatively rare tumor and accounts for 3 percent of all adult malignancies. Certain types of kidney cancer are associated with inborn defects in specific genes, such as kidney cancers in patients with Von Hippel-Lindau syndrome. Epidemiological studies have implicated tobacco as an etiologic agent. No other definite environmental or occupational factors have been identified [287].

Bladder cancer is almost three times more widespread among men than women, and it is considered as the fourth most widespread cause of cancer in men. It is approximately two times as frequent in white men as it is in black men. Genetic and ecological factors play a significant role in the growth of bladder cancer. Cigarette smoking is the most important risk factor, and smokers face a fourfold higher risk. This danger correlates with the period and extent of smoking.

Aniline dyes, other related chemicals, particularly aromatic amines, have been linked with bladder cancer. Occupations that involve exposure with these kinds of chemicals, such as car manufacturing and painting, have an increased risk of bladder cancer. Other etiologic factors for bladder cancer are chronic bladder infections, pelvic irradiation, analgesic abuse, and chemotherapy. Information of these risk factors might aid in the avoidance and recognition of bladder cancer [283].

*Drugs affecting the reproductive and genitourinary systems*

The term genitourinary system combines the urinary and reproductive systems and is often discussed as a single system [283]. The kidneys function to process waste, and the ureters drain the kidneys into the bladder. From the bladder, urine passes through the urethra [284].

Dysfunction in the urinary system can affect the internal and external genitalia. The reverse is also true. Swelling or inflammation of the prostate gland can cause urinary dysfunction in men, for example. Bladder disease such as cystitis in a woman can lead to pain during intercourse (dyspareunia), or infection with a sexually transmitted infection (STI) can affect the urinary tract. Finally, severe dysfunction of the kidneys in men or women can affect many other organs and systems, often relating to the build-up of waste products normally excreted by the kidneys [287].
Drugs for treating Reproductive and Genitourinary disorders

Every reproductive and genitourinary disorder has its own remedies and drugs prescribed. However, following are some of the related general facts that might of great help for treating patients more safely [290].

The efficiency of a drug strongly depends on the right diagnosis and the phase of the disease development. Among the classes of drugs used to treat a reproductive and genitourinary condition or disease the following can be distinguished:

- Androgens given to treat male hormone deficiencies (Testosterone)
- Contraceptives preparations utilized to stop unwanted pregnancies
- Drugs for the treatment of erectile dysfunction (phosphodiesterase type 5 inhibitors or PDE5 inhibitors to inhibit the degradation of a second messenger (cGMP) in smooth muscle cells)
  - Tadalafil (Adcirca, Cialis)
  - Alprostadil (Caverject, Edex)
  - Verdenafil (Levitra)
  - Sildenafil (Viagra, Revatio)
- Estrogens and progesterones mostly used to treat female hormone deficiencies. Note that the term progestin indicates a synthetic progesterone while progesterone is used to indicate a bioidentical hormone preparation.
- Prostate gland medicines used in cure of prostate related disorders
- Spasmolytic preparations utilized to treat urinary incontinence. (in addition to behavioral techniques, devices, surgery and physical therapy)
  - Botulinum toxin type A
  - Duloxetine (Cymbalta)
  - Imipramine (Tofranil)
- Urogenital antibiotics preparations utilized to treat urogenital infections
  - Amoxicillin (Augmentin, Amoxil)
  - Ampicillin
  - Ciprofloxacin (Cipro)
  - Levofloxacin (Levaquin)
Nitrofurantoin (Furadantin, Macrodantin)
- Sulfamethoxazole-trimethoprim (Bactrim, Septra)
- Urogenital antiseptics utilized in prophylaxis or subsidiary treatments of urogenital infections

**DRUGS AFFECTING THE EYES AND EARS**

This section will briefly review conditions and discuss the drug therapy for the eyes and ears.

The eye is a somewhat asymmetrical globe, nearly an inch in diameter. The front piece of the eye includes: [291]

- The iris (the pigmented component)
- The cornea (a clear dome over the iris)
- The pupil (the black round opening in the iris that enables light in)
- The sclera (the white part)
- The conjunctiva (an invisible, lucid layer of tissue covering the front of the eye, except the cornea)

![Eye Diagram](image)

**Eye disorders and conditions**

The eyes are such a critical and sensitive part of the human body and serve a number of purposes. Therefore any problem in the eyes can be source of significant problems. Following are some of the most common eye disorders [292, 293, 294].
- Macular degeneration with age:
  In this state a central vision is lost in one or both eyes.
- Amblyopia (lazy eye):
  One eye can see things better than the other; a difficulty arises because of issues in childhood development. The weaker eye might or might not "wander." The weaker eye is termed as a "lazy eye."
- Astigmatism:
  A fault that causes an inability to correctly focus light onto the retina; Astigmatism results in a blurry vision that can be rectified with glasses or contact lenses.
- Black eye:
  Swelling and staining around the eye because of the injury to the face.
- Blepharitis:
  Inflammation of the eyelids close to the eyelashes. Blepharitis is a common cause of itching or a reaction to grit or debris in the eyes.
- Cataract:
  A clouding of the lens, which obstructs the path of light through the lens.
- Chalazion (meibomian gland lipogranuloma):
  An inflammatory cyst of a blocked oil-secreting meibomian gland. Often confused with styes, chalazion cysts are not due to infections, but to inflammations caused by a blockage in the duct.
- Conjunctivitis:
  Also called "pinkeye," conjunctivitis is a disease or inflammation of the conjunctiva, the clear layer that cover the front of the eye. It is typically caused by allergies, a bacterial infection or a virus.
- Corneal abrasion:
  A scrape on the clear part of the front of the eye. Pain, light sensitivity, or feelings of sand in the eye are common symptoms.
- Diabetic retinopathy:
  High blood sugar damages blood vessels in the eye. Eventually, damaged blood vessels might overgrow the retina or bleed, affecting vision.
• Diplopia (double vision):
   Seeing double caused by a lot of serious conditions. Diplopia requires emergency medical attention.
• Dry eye:
   Either the eyes don't make sufficient tears, or the tears are not of adequate quality. Dry eye can result from medical problems such as scleroderma, lupus, and Sjogren's syndrome.
• Glaucoma:
   Increased pressure inside the eye gradually reduces vision. Peripheral vision is lost initially, often going unnoticed for years.
• Hyperopia (farsightedness):
   Inability to see near objects clearly. The eye is “too short” for the lens, or specific ocular muscles have become damaged.
• Hyphema:
   Bleeding into the front of the eye, at the back of the cornea. Hyphema is generally caused by trauma.
• Keratitis:
   Inflammation of the cornea. Keratitis usually occurs after germs enter a corneal abrasion.
• Myopia (nearsightedness):
   Inability to see at a distance. The eye is “too long” for the lens, so light is not focused correctly on the retina.
• Optic neuritis:
   The optic nerve gets inflamed, frequently from an overactive immune system.
• Pterygium:
   A non-malignant growth on the conjunctiva, generally on the nasal side of the eye. It might cover a fraction of the cornea, causing vision difficulties.
• Retinal detachment:
   The retina comes loose from the back of the eye. Trauma and diabetes are general causes of this emergency.
• **Retinitis:**
  Inflammation of the retina. Retinitis might be a long-standing genetic condition or consequence of a viral infection.

• **Scotoma:**
  A blind or dim spot in the visual field.

• **Strabismus:**
  The eyes do not focus in the same direction. The brain might then compensate using one eye, causing reduced vision (amblyopia) in the other eye.

• **Stye:**
  An inflamed oil gland. May be tender and may get infected.

• **Uveitis (iritis):** The pigmented part of the eye gets inflamed or contaminated. An overactive immune system, viruses or bacteria can be accountable.

**Drugs causing eye related problems and diseases**

A number of eye related problems and diseases are drug induced, which are discussed below [295].

The eyelids and conjunctiva (a thin membrane covering the internal part of the eyelid and the external part of the cornea) are common targets for drug toxicity. For example, a number of drugs might result in erythema multiforme, a type of immune mediated hypersensitivity response of the skin (including the eyelid) that creates a range of skin lesions ranging from bumps to plaques to blisters. In its more severe forms, it is known as Stevens - Johnson syndrome (SJS) and as Toxic Epidermal Necrolysis (TEN). The main treatment is to discontinue using the drug that is resulting in the response.

Following is the list of generally used medicines that are strongly linked with inducing eye disorders [296].

<table>
<thead>
<tr>
<th>Disease</th>
<th>Generic Name</th>
<th>Brand Name</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Eyelid and Conjunctival Diseases</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Erythema multiforme</td>
<td>Acetaminophen</td>
<td>TYLENOL</td>
</tr>
<tr>
<td></td>
<td>Allopurinol</td>
<td>ZYLOPRIM</td>
</tr>
<tr>
<td>Stevens-Johnson Syndrome</td>
<td>Same as erythema multiforme</td>
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<tr>
<td>--------------------------</td>
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<td></td>
</tr>
<tr>
<td>Red eye</td>
<td>Drugs containing benzalkonium chloride</td>
<td>Certain drugs used in the eye</td>
</tr>
<tr>
<td></td>
<td>Drugs containing thimerosol</td>
<td>Certain drugs used in the eye</td>
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<tr>
<td></td>
<td>Morphine</td>
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<tr>
<td>Eyelid droop</td>
<td>botulinum toxin</td>
<td>BOTOX</td>
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**Uveal Tract Diseases**

<table>
<thead>
<tr>
<th>Eye surgery complications</th>
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<tr>
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<td>Doxazosin</td>
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<td>Sildenafil</td>
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<td>LEVITRA</td>
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<td>betamethasone</td>
<td>ALPHATREX, DIPROLENE, DIPROSONE</td>
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<tr>
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<td>---------------------------------</td>
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<td>Open-angle glaucoma</td>
<td>desoximetasone</td>
<td>TOPICORT</td>
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<tr>
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<td>dexamethasone</td>
<td>DECADRON, HEXADROL, MYMETHASONE</td>
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<td></td>
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<td>SYNALAR</td>
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<td>Fluocinonide</td>
<td>LIDEX-E, LIDEX</td>
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<tr>
<td></td>
<td>hydrocortisone (oral)</td>
<td>CORTEF, HYDROCORTONE</td>
</tr>
<tr>
<td></td>
<td>hydrocortisone (topical)</td>
<td>ALA-CORT, HI-COR, HYTONE, NEACLEAR LIQUID OXYGEN SCAR, PENECORT, SYNACORT</td>
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<td></td>
<td>Methylprednisolone</td>
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<td>Prednisone</td>
<td>DELTASONE</td>
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<td>triamcinolone (topical)</td>
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<td>Angle-closure glaucoma</td>
<td>Cimetidine</td>
<td>TAGAMET</td>
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<td>Ephedrine</td>
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<td>Epinephrine</td>
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<td>Fluoxetine</td>
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<td>Paroxetine</td>
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<td>Ranitidine</td>
<td>ZANTAC</td>
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<td>sulfamethoxazole (with)</td>
<td>BACTRIM, COTRIM, SEPTRA</td>
</tr>
<tr>
<td>Drug</td>
<td>Brand Name(s)</td>
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<tr>
<td>Trimethoprim</td>
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<td>Sulfisoxazole</td>
<td>GANTRISIN</td>
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<td>Topiramate</td>
<td>TOPAMAX</td>
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<tr>
<td>Venlafaxine</td>
<td>EFFEXOR, EFFEXOR XR</td>
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**Cataracts**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Brand Name(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Betamethasone</td>
<td>ALPHATREX, DIPROLENE, DIPROSONE</td>
</tr>
<tr>
<td>Busulfan</td>
<td>BUSULFEX, MYLERAN</td>
</tr>
<tr>
<td>Chlorpromazine</td>
<td>THORAZINE</td>
</tr>
<tr>
<td>Desoximetasone</td>
<td>TOPICORT</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>DECADRON, HEXADROL, MYMETHASONE</td>
</tr>
<tr>
<td>Fluocinolone</td>
<td>SYNALAR</td>
</tr>
<tr>
<td>Fluocinonide</td>
<td>LIDEX-E, LIDEX</td>
</tr>
<tr>
<td>Hydrocortisone (oral)</td>
<td>CORTEF, HYDROCORTONE</td>
</tr>
<tr>
<td>Hydrocortisone (topical)</td>
<td>ALA-CORT, HI-COR, HYTONE, NEACLEAR LIQUID OXYGEN SCAR, PENECORT, SYNACORT</td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td>MEDROL</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>PRELONE</td>
</tr>
<tr>
<td>Prednisone</td>
<td>DELTASONE</td>
</tr>
<tr>
<td>Thioridazine</td>
<td>MELLARIL</td>
</tr>
<tr>
<td>Triamcinolone (injectable)</td>
<td>ARISTOCORT, KENALOG, TRIACET, TRIDERM</td>
</tr>
<tr>
<td>Triamcinolone (topical)</td>
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</table>

**Retinal Abnormalities**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Brand Name(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acitretin</td>
<td>SORITANE</td>
</tr>
<tr>
<td>Chloroquine</td>
<td>ARALEN</td>
</tr>
<tr>
<td>Chlorpromazine</td>
<td>THORAZINE</td>
</tr>
</tbody>
</table>
Over - the - Counter Drugs

- **Antihistamines**
  Antihistamines are prescription and non-prescription capsules, pills, liquids, and fizzy tablets (like Alka-Seltzer). They might be sold as individual drug or in blended with other medications like decongestants, pain medications, etc. Antihistamines should not be used if a person has glaucoma, except under the care of an experienced clinician [297].

- **Steroids**
  Long term use of steroids can cause cataracts and glaucoma.

- **Alcohol (Ethanol)**
  Acute intoxication leads to pupillary dilation, temporary affected vision, double vision, eye redness, and difficulty in focusing.
Drugs for treating eye disorders

Though every eye disorder is treated differently in terms of medicines, the most generally prescribed medications for treating various drug disorders are listed below [298].

Glaucoma:
  - Prostaglandin analogs
    - Bimatoprost ophthalmic solution (Lumigan)
    - Travoprost (Travatan Z)
    - Xalatan
  - Beta blockers
    - Levobetaxolol (Betaxon)
    - Timolol
  - Alpha agonists
    - Brimonidine (Alphagan)
    - Iopidine
  - Combined alpha/beta blockers (Brimonidine+Timolog (Combigan))
  - Carbonic anhydrase inhibitors (CAIs)
    - Acetazolamide (Diamox)
    - Azopt
    - Methazolamide (Neptazane)
    - Trusopt
  - Other
    - Unoprostone isopropyl ophthalmic solution (Rescula)

Infections
  - Conjunctivitis
    - Besifloxacin ophthalmic suspension (Besivance)
    - Erythromycin (Ilotycin)
    - Gatifloxacin (Zymaxid)
    - Gentamycin (Garamycin)
    - Levofloxacin (Quixin)
- Neosporin (neomycin, bacitracin, polymyxin)
- Polytrim (trimethoprim/ polymyxin B sulfate)
- Sulfacetamide (Bleph-10, Sulamyd)
- TobraDex (Tobra + dexamethasone)
- TobraDex (Tobra + dexamethasone)
- Corneal Ulcers
  - Ciprofloxacin (Ciloxan)
  - Ofloxacin (Ocuflox)
- Viral keratitis
  - Acyclovir
  - Cidofovir (Wistide)
  - Famciclovir
  - Ganciclovir (Zirgan)
  - Trifluridine (Viroptic)
  - Valacyclovir (Valcyte)
- Blepharitis (topical)
  - Bacitracin
  - Erythromycin
- Ocular decongestants (anti-allergy medications)
  - Alrex
  - Azelastine hydrochloride nasal spray (Astepro)
  - Bepotastine besilate ophthalmic solution (Bepreve)
  - Cromolyn sodium (Croloam)
  - Ketotifen Fumarate (Zaditen)
  - Levocabastine (Livostin)
  - Lodoxamide tromethamine (Alomide)
  - Naphazoline (Naphcon, Vasocon)
- Anti-inflammatory agents
  - Difluprednate (Durezol)
  - Ketorolac tromethamine ophthalmic solution (Acular, Acuvail)
  - Lotemax
Diabetic Macular Edema and (wet) Age Related Macular Degeneration (ARMD)

- Dexamethasone (Ozurdex)
- Pegaptanib (Macugen)
- Ranibizumab (Lucentis)
- Verteportfin (Visudyne)

Low tear production
- Cyclosporine (Restasis)

*Ear disorders and conditions*

The ear has exterior, middle, and internal portions. The external ear is called the pinna and consists of cartilage enclosed by skin. Sound passes through the pinna into the exterior auditory canal, a small tube that ends at the tympanic membrane [295]. Sound causes the eardrum and its minute attached bones in the center portion of the ear to vibrate, and the sensations are conducted to the nearby cochlea. The spiral-shaped cochlea is division of the internal ear; it converts sound into nerve impulses that go to the brain. Following are some of the most common ear disorders [299].

- **Earache:**
  Pain in the ear may be due to many causes. Some of these are severe; some are not as severe.

- **Otitis media (middle ear inflammation):**
  Inflammation or disease of the middle ear (behind the eardrum). Generally, this is due to an infection.

- **Swimmer’s ear (Otitis externa):**
  Inflammation or disease of the outer ear (pinna and ear canal). Acute cases are generally infections; chronic otitis is usually a skin condition (dermatitis).
Meniere’s disease:
A state in which the internal ear on one side malfunctions. Vertigo, hearing loss, tinnitus, and pain are general symptoms.

Tinnitus:
Ringing in one or both ears. Generally this is due to injury from noise exposure, or from aging.

Cerumen (ear wax) impaction:
Ear wax might block the ear canal and stick to the eardrum. The eardrum’s reduced sensations impair hearing.

Ruptured eardrum:
Extremely loud noises, rapid changes in air pressure, or foreign objects can scratch or puncture the eardrum. The hole generally heals within a few weeks.

Acoustic neuroma:
A noncancerous cancer that rises on the nerve traveling from the ear to the brain. Hearing loss, tinnitus and vertigo, can be major symptoms.

Mastoiditis:
Disease of the mastoid bone, just at the back of the ear. Mastoiditis was once a general difficulty of unprocessed ear infections.

Benign paroxysmal positional vertigo (BPPV):
A disturbance of function in the inner ear, causing episodes of vertigo. Although it is not medically severe, its symptoms can be upsetting.

Cholesteatoma:
Is the buildup of fibrous tissue inside the middle ear and nearby bones. Cholesteatomas may be congenital or as a result of chronic ear infections. The cyst can become infection and can affect hearing and balance.

Drugs causing ear disorders
Ototoxicity is an ear poisoning which results from contact to chemicals or drugs that damages the inner ear or the vestibulo-cochlear nerve (the nerve transmitting balance and hearing information from the internal ear to the brain) [300].
Many chemicals and drugs have ototoxic potential, like over-the-counter drugs, recommended medications, and environmental chemicals. The substances mentioned below are thought to be a cause of ototoxicity.

Aspirin and Quinine derivatives:
Aspirin and quinine Aspirin (acetylsalicylic acid, ASA) and quinine are most general cause of the temporary ototoxicity eventually resulting in tinnitus. They might also decrease hearing, mainly when given at elevated doses. Quinine products can also for the moment reduce balance capability. Once aspirin or quinine analog are stopped, the ototoxicity normally disappears. Some quinine products are listed below: [301]

- Chloroquine
- Quinidine
- Quinine (including Q-vel)

Loop diuretics:
Loop diuretics are a particular family of “water pills” that are thought to cause temporary ototoxicity. These drugs may result ringing in the ears or reduced hearing that reverses when the medicine is stopped [301].

An increased possibility of ototoxicity is thought to happen with loop diuretics when they are controlled during the similar time period that an aminoglycoside antibiotic is given. The loop diuretics are listed below:

- Bumetanide (Bumex)
- Ethacrynic acid (Edecrin)
- Furosemide (Lasix)
- Torsemide (Demadex)

Aminoglycoside antibiotics:
All members of the aminoglycoside antibiotic class are well known for their capability to cause long term ototoxicity. Some of these medicines are more likely to lead to hearing
loss; others are more likely to result in vestibular loss. Others can cause either problem [302].

A danger greater risk for aminoglycoside-antibiotic induced ototoxicity happens when a patient receives simultaneous ototoxic drugs (like a loop diuretic or some other antibiotic, i.e. vancomycin), has inadequate kidney function, is taking a drug that causes inadequate kidney function, or has a hereditary vulnerability.

The danger of ototoxicity becomes increased with an increasing dose, longer half-life, and is related to the period of time that the medication is taken.

Members of the aminoglycoside class include:

- Amikacin
- Dihydrostreptomycin
- Gentamicin
- Kanamycin
- Neomycin
- Netilmicin
- Ribostamycin
- Streptomycin
- Tobramycin

Anti-neoplastics (anti-cancer drugs):
Anti-cancer drugs function by killing cancer cells. These agents can also damage cells elsewhere in the body, including the ears. Cisplatin is thought to result in significant and enduring hearing loss. Carboplatin is also considered ototoxic [298].

*Drugs for treating ear disorders*

The most common drugs used to treat the ear are listed below [302].

- Acetaminophen (Tylenol) and nonsteroidal anti-inflammatory drugs (Motrin, Advil, and Aleve), for fever and pain. Do not offer aspirin to anyone younger than 20 since it has a link to Reye syndrome, a severe illness.
• Pain medicines like codeine and some eardrops, which relieve severe earache. But do not make use of eardrops if the eardrum is cracked.

• Sometimes corticosteroids are given with antibiotics to eliminate fluid at the back of the eardrum (otitis media with effusion). Steroids are not an ideal choice for curing ear infections. Do not apply steroids for a child that has been around somebody with chickenpox within the last three weeks.

**DRUG INTERACTIONS**

A drug interaction is a state in which a drug affects the action of another drug when both are being administered together. This act can be additive, synergistic (when the net effect is greater than the sum of any individual drug) or antagonistic (when one drug’s effect is decreased). In addition, a novel effect can be produced [303].

Interactions might also be present between drugs and different kinds of foods (drug-food interactions), as well as drugs and herbs or plants (drug-herb interactions). People consuming antidepressant drugs such as monoamine oxidase inhibitors must avoid food containing tyramine as hypertensive crisis might occur (an instance of a drug-food interaction). These interactions might happen out of unintentional abuse or due to lack of information about the ingredients involved in the pertinent substances.

It is thus easy to see the significance of these pharmacological drugs interactions in the practice of medicine. If a patient is taking two drugs and one of them boosts the effect of the other it is probable that an overdose might occur. The contact of the two drugs might also amplify the risk that side effects will take place.

On the other hand, if the stroke of a drug is decreased it might stop to have any healing use due to under dosage. Over time these interactions might be sought in order to get a better therapeutic result [303].

Examples of this include the utilization of codeine with paracetamol to boost its analgesic effect or the blend of clavulanic acid with amoxicillin to conquer bacterial
resistance to the antibiotic. It should also be kept in mind that there are drug interactions that, from a theoretical point of view, might occur but which in medical practice have no significant clinical repercussions.

**Types of Drug Interactions**

There are fundamentally two kinds of drug interactions: *pharmacodynamic* and *pharmacokinetic*

*Pharmacodynamic interactions*

In pharmacodynamic interactions, the effect of one medicine is distorted by the existence of another drug acting at the similar biochemical or molecular site (e.g., drug receptor or second messenger system), on the similar target organ, or on a diverse target but one that is linked with a general physiological procedure; fundamentally, this is when one medicine adjusts the pharmacologic result of another by producing additive, synergistic or antagonistic effects [304].

For instance, as noted earlier, blending two or more CNS depressants — like opioid analgesics, benzodiazepines, first-generation antihistamines or alcohol — can be synergistic, and can lead to marked CNS depression, including loss of consciousness, respiratory depression, coma or death.

Similarly, using two or more drugs that create vasodilation can boost the risk of deep syncope, hypotension, or even myocardial infarction. Pharmacodynamic interactions that are antagonistic usually diminish the advantage of one or more drugs in the mix. A good example would be the utilization of an anticholinergic medicine, such as oxybutynin, for treating urge incontinence in a patient taking a cholinesterase inhibitor (e.g., donepezil) for dementia.

Some pharmacodynamic interactions might not be as simple to predict since the mechanisms of action and molecular targets of the drugs being used are distinct. Often these are interactions that involve the effects of drugs in diverse physiological processes that create additive, synergistic or antagonistic actions at a more general level.
A prototypical instance is the combined use of digoxin and furosemide. Both have diverse targets (e.g., myocardium versus renal tubule) and diverse mechanisms (e.g., Na+/K+ ATPase versus Na+ Cl- co-transport), however the diuretic-induced secondary loss of potassium allows for increased digoxin binding and toxicity to the heart.

Another interaction is the utilization of co-trimoxazole in patients consuming angiotensin-converting-enzyme, or ACE, inhibitors or angiotensin II receptor blockers, or ARBs. Trimethoprim is pharmacologically and structurally similar to potassium-sparing diuretics and might further boost potassium preservation and the danger of hyperkalemia in those patients [304].

**Pharmacokinetic interactions**

In pharmacokinetic interactions, one drug causes modification (increase or decrease) of the concentration of another medicine in the system. Diverse parameters can be influenced by pharmacokinetic interactions, like a drug’s bioavailability, peak level, and volume of distribution, clearance and half-life. Such modifications can lead to variations in drug plasma concentrations and eventually boost the risk of side effects or reduce the effectiveness of one or more drugs. Pharmacokinetic interactions are more complex and hard to predict since the interacting drugs frequently have unconnected actions [305].

**The process of drug interaction**

There are numerous mechanisms by which drugs interact with food, other drugs and other substances. A contact occurs when there is an increase or decrease in:

- The absorption of a medicine into the body;
- Distribution of the medicine within the body;
- Changes made to the medicine by the body (metabolism), particularly by the detoxification pathways of the liver; and
- Elimination of the medicine from the body.

Most of the significant drug interactions arise from a modification in the absorption, metabolism, or removal of a drug. Drug interactions also might take place when two
drugs that hold similar (additive or synergistic) impacts or antagonistic effects on the body are administered together. For instance, there might be significant sedation when two medicines that have sedation as primary side effects are given. An example of this would be the use of narcotics and antihistamines in a patient [304].

*Change in absorption*

Most of the drugs are dispersed into the blood and then go to their site of action. Most of the drug interactions that are due to changes in absorption happen in the intestine. There are a variety of potential mechanisms through which the drugs’ absorption can be reduced. These mechanisms are listed below: [305]

- A modification in blood flow to the intestine;
- alteration in drug metabolism (breakdown) by the intestine;
- increased or decreased intestinal motility (movement);
- changes in stomach acidity, and
- A change in the bacteria that exist in the intestine.

*Change in drug metabolism and elimination*

Most of the drugs are eliminated by means of kidney in either an unprocessed form or as a by-product that arises from the metabolism of the drug by the liver. Thus, the liver and the kidney are very significant sites of possible drug interactions. Some drugs are able to decrease or boost the metabolism of other drugs by the liver by inducing or inhibiting one or more of the CYP450 family of enzymes [303]. Factors affecting drug interaction are identified as: [305]

- genes
- physiology
- age
- lifestyle (diet, workout)
- underlying diseases
- drug doses
- the period of combined therapy
- The relative point of administration of the two drugs

**How to avoid drug interactions?**

- The medical provider should be provided a complete list of all of the medicines that the patient has been prescribed. This should include OTC supplements, vitamins, and herbal remedies.

- The medical provider should be informed whenever drugs are added or discontinued.

- The medical provider should be informed regarding changes in lifestyle (for instance, exercise, alcohol intake, diet).

Since the incidence of drug interactions amplifies with the number of medications, it’s necessary that both the medical provider and patient clearly communicate together on the medical plan of care to improve outcomes related to the use of pharmacopeia.

**SUMMARY**

Drug administration falls squarely at the intersection of two main responsibilities. Not only do nurses need to have an understanding of the basic scientific elements of pharmacology—the science of how drugs are administered and processed by the body—but also the social component; nurses need to build relationships in order to glean important information from their patients and serve as educators for both the patient and the patient’s family. The information that nurses obtain from their patients is critical for avoiding drug-drug interactions, drug-food interactions, allergic reactions, and other adverse effects.

This study is comprehensive in nature to make the nurses, clinicians and other health care professionals learn the significance of drug and their monitoring in the life of a patient. Further, it has also taken a systems approach and discussed their functions,
along with the associated disorders and drugs that can be harmful or beneficial for these disorders.

Further, in order to make professionals aware of their legal and social responsibilities, this study also discusses regulatory compliances and processes of drug approval and checking so that drug administration can be made more secure and effective on the part of professionals. This will help nurses and drug administrators and prescribers learn the complexities that can arise because of various drug interactions and how they can make the most of the benefits while minimizing the possible errors and harm to the patient.

Finally, it is imperative that nurses continue to develop their knowledge of pharmacology behind the common drugs that they administer. Advanced practice registered nurses, registered nurses and licensed vocational nurses constitute the group that works in the closest proximity to patients receiving medications. Therefore, it is important that they understand the potential and can recognize drug interactions and side effects, which this study addresses. More studies are needed in the future to determine nursing knowledge gaps in the ever evolving area of pharmacology and best practice outcomes.
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