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**MLS512**

**ASSIGNMENT**

**QUESTIONS**

1. With relevant examples, describe the classification of poisonous substance

2a. A hydrophobic substance Q was orally administered on an individual. Discuss from the point of entry, the fate of the said substance.

 b. what would have been different if the substance had been hydrophilic in nature

3a. In a tubular form list 20 poisonous substance and their respective antidotes.

b. Explain ways by which the clinical effects of poisons can be studied.

**ANSWER**

1. **Poisons** are substances that cause death, injury or harm to organs, usually by chemical reactions or other activity on the molecular scales, when an organism absorbs a sufficient quantity. The fields of medicine (particularly veterinary) and zoology often distinguish a poison from a toxin, and from a venom. Toxins are poisons produced by organisms in nature, and venoms are toxins injected by a bite or sting (this is exclusive to animals). The difference between venom and other poisons is the delivery method.

**Classification of poisonous substances**

In regard to poisoning, it can be divided into three broad groups: agricultural and industrial chemicals, drugs and health care products, and biological poisons—i.e., plant and animal sources, along with these three groups there is a fourth, radiation.

**Agricultural and industrial chemicals**

**Agricultural chemicals**

The majority of agricultural chemicals are pesticides, which include insecticides, herbicides, fungicides, fumigants, and rodenticides.

**Insecticides**: The four main classes of insecticides are organophosphates, [carbamates](https://www.britannica.com/science/carbamate), chlorinated hydrocarbons, and insecticides derived from plants (botanical). Organophosphate and carbamate insecticides act by [inhibiting](https://www.merriam-webster.com/dictionary/inhibiting) acetylcholinesterase, the enzyme that degrades acetylcholine (the messenger of the parasympathetic nervous system). As a result, acetylcholine levels remain high, exaggerating the normal functions of the parasympathetic system. Effects such as salivation, lacrimation, urination, defecation, twitching of the skeletal muscles, and in severe poisoning, death from respiratory depression occur. Chlorinated hydrocarbons used as insecticides, such as chlorophenothane (DDT), are larger molecules than the chlorinated hydrocarbons used as organic solvents, such as chloroform. It stimulates the central nervous system then later depresses it.

**Herbicides**: Herbicides are chemicals used to kill plants. Their potential to produce toxicity in humans is rather low. During the Vietnam War, Agent Orange, a mixture of 2,4-D and 2,4,5-T, was used as a defoliant. The 2,4,5-T used in the Agent Orange was contaminated with tetrachlorodibenzodioxin (TCDD), or dioxin. The major toxicity of TCDD in humans is in the production of chloracne, a condition characterized by acne that appears between the eyes and the ears. In more severe form, acne may be found on the face, trunk, and buttocks.

**Rodenticides**: These are chemicals used to kill rodents like rats, mice etc. An example of rodenticide is warfarin. Warfarin was originally developed as a drug to treat thromboembolism, a disease caused by blood clots, since it inhibits the synthesis of a factor essential for the clotting of blood. The inhibition of blood clotting by warfarin can lead to internal bleeding. It has the ability to induce internal bleeding, warfarin is also used as a rodenticide.

## Industrial chemicals

## The term industrial chemicals used to refer to chemicals used in industry, as well as chemicals found in or near households. Poisoning with industrial chemicals occurs most often by either percutaneous or inhalation routes.it can divided into organic and inorganic compounds.

**Organic compounds**: Depression of the central nervous system is a common effect of most hydrocarbon. Examples of common hydrocarbons include gasoline, toluene, and heptanes (hexane and benzene). The hydrocarbons are lipid-soluble and dissolve in the membrane of nerve cells in the brain, disrupting their functions. Depression, such as drowsiness, occurs as a result. The hydrocarbon n-hexane also causes damage to peripheral nerves. Benzene is toxic to organs like the bone marrow that form blood cells and can lead to the production of leukemia.

**Inorganic compounds**: Examples of metal compounds toxic to humans include manganese, lead, cadmium, nickel, and arsenic compounds, beryllium oxide, and the elemental vapours, inorganic salts, and organic compounds of mercury. Chronic manganese exposure can damage the brain, resulting in a condition with symptoms similar to Parkinson’s disease, such as slurred speech, masklike face, and rigidity. Mercury can also damage the brain, leading to behavioral changes. It can also be toxic to the peripheral nervous system, causing sensory and motor symptoms. Mercury can be toxic to the kidney.

## Drugs and health care products

## Poisoning with drugs predominantly involves oral exposures. With drugs, irritation of the respiratory tract is rare, but anorexia, nausea, and vomiting resulting from gastrointestinal irritation are common. Painkillers, Tranquilizers and sleeping pills, Cold medications, Hard drugs common drugs that are poisonous to the body when taken in excess.

## Poisons of biological origin

Bio-toxins can be conveniently grouped into three major categories:

* Microbial toxins, poisons produced by bacteria, blue-green algae, dinoflagellates, golden-brown algae, etc.,
* Phytotoxins, poisons produced by plants, E.g. angiosperms, or flowering plants.
* Zootoxins, poisons produced by animals. Example shore crab, Greenland shark, gila monster, stonefish, etc.

 The geographic distribution of poisonous organisms varies greatly; poison-producing microorganisms tend to be ubiquitous in their distribution. Poisonous plants and animals are found in greatest abundance and varieties in warm-temperate and tropical regions. Relatively few toxic organisms of any kind are found in polar latitudes.

# **Radiation**

# Radiation is a flow of energy through space or matter. It takes the form of particles (e.g., alpha and beta particles) or electromagnetic waves (e.g., X rays, gamma rays, and visible and ultraviolet [UV] light). [Radiation](https://www.britannica.com/science/radiation) can be classified as either ionizing or nonionizing depending on its ability to produce ions in the matter it interacts with. Ionizing radiation is more toxic than nonionizing radiation. Radiation quickly kills rapidly dividing cells. Immature blood cells in bone marrow, cells lining the mucosa of the gastrointestinal tract, and cells in the lower layers of the epidermis and in hair follicles are the most rapidly dividing cells in the body. Which can lead to the decreased production of blood cells, nausea, vomiting, diarrhea, malabsorption by the intestine, skin burns, and hair loss. Some cells in the embryo and fetus also divide rapidly, and thus radiation can cause malformations, DNA alteration and even fetal death.

1. The hydrophobic substance Q is a water insoluble substance and the route of administration is oral. The fate of the substance Q starts with absorption and assimilation into the bloodstream, distribution into the cell, metabolism and excretion.

Absorption is defined as the passage of a drug from its site of administration into the plasma.

## Oral route of drug administration

## Oral administration is a route of administration where a substance is taken through the mouth. Many medications are taken orally because they are intended to have a systemic effect, reaching different parts of the body through the bloodstream. For drugs administered orally, absorption may begin in the mouth and stomach. However, most drugs are usually absorbed from the small intestine. The drug passes through the intestinal wall and travels to the liver before being transported via the bloodstream to its target site. The intestinal wall and liver chemically alter (metabolize) many drugs, decreasing the amount of drug reaching the bloodstream. During these processes the drug undergo a process known as first-pass effect.

**Drug absorption**

The mechanism of absorption is the same as that of other epithelial barriers, which are passive transfer at a rate determined by the ionization and lipid solubility of the drug molecules for most drugs. Intestinal drug absorption depends on carrier-mediated transport rather than simple lipid diffusion. The main factors that affect gastrointestinal absorption are:
•  gut content (e.g. fed versus fasted)
•  gastrointestinal motility
•  splanchnic blood ﬂow
•  particle size and formulation
•  physicochemical factors including some drug interaction

**First-pass effect**

## The first pass effect is a phenomenon in which a drug gets metabolized at a specific location in the body that results in a reduced concentration of the active drug upon reaching its site of action or the systemic circulation. The first pass effect is often associated with the liver, as this is a major site of drug metabolism. However, the first pass effect can also occur in the lungs, vasculature, gastrointestinal tract, and other metabolically active tissues in the body. This effect can become augmented by various factors such as plasma protein concentrations, enzymatic activity, and gastrointestinal motility. The extent to which a patient may experience the first pass effect varies from patient to patient, and this must also be taken into consideration when determining appropriate dosing. If the first-pass effect is exceptionally prominent in a patient, the drug may require administration through a different route to bypass the first-pass effect.

**Drug metabolism**

Drug metabolism is the chemical alteration of a drug by the body. Some drugs are chemically altered by the body (metabolized). The substances that result from metabolism (metabolites) may be inactive, or they may be similar to or different from the original drug in therapeutic activity or toxicity. Some drugs, called prodrugs, are administered in an inactive form, which is metabolized into an active form. The resulting active metabolites produce the desired therapeutic effects. Metabolites may be metabolized further instead of being excreted from the body. The subsequent metabolites are then excreted. Excretion involves elimination of the drug from the body, for example, in the urine or bile. Most drugs must pass through the liver, which is the primary site for drug metabolism. Once in the liver, enzymes convert prodrugs to active metabolites or convert active drugs to inactive forms. The liver’s primary mechanism for metabolizing drugs is via a specific group of cytochrome P-450 enzymes. The level of these cytochrome P-450 enzymes controls the rate at which many drugs are metabolized. The capacity of the enzymes to metabolize is limited, so they can become overloaded when blood levels of a drug are high. Many substances (such as drugs and foods) affect the cytochrome P-450 enzymes. If these substances *decrease* the ability of the enzymes to break down a drug, then that drug's effects (including side effects) are increased. If the substances *increase* the ability of the enzymes to break down a drug, then that drug's effects are decreased.

**Drug excretion**

Drug excretion is the process of eliminating a drug from the body. A drug, which is either biologically active itself or a prodrug, may be excreted in its original chemical state. Alternatively, all or a portion of a drug may undergo chemical modification and be eliminated as biologically active, or inactive, metabolites. There are several routes for drug elimination from the body. The majority of drugs are eliminated by pathways that involve the kidneys or the liver. Renal excretion plays an important role in eliminating unchanged drugs or their metabolites into urine. A major characteristic of compounds excreted in urine is that they are polarized (i.e., charged) and water-soluble. Drugs that are lipid soluble are not readily removed by the kidneys and require hepatic metabolism (e.g., phase I and phase II biotransformation reactions) to increase their water solubility for possible urinary excretion. Drugs entering the hepatic circulation may also enter the bile and be excreted into the duodenum and small intestines. Depending on the chemical properties of the drug, it may then be re-absorbed from the small intestine and recirculate throughout the body (enterohepatic recycling). Those drugs that are not re-absorbed will pass through the large intestines and be excreted in the feces. In some cases, drugs may also be excreted from the body through the lungs, milk, sweat, tears, skin, hair, or saliva. These are considered secondary processes for drug excretion.

**b)** Hydrophilic substance differ from hydrophobic in their excretion pattern. Hydrophobic substance passes through the blood into the liver where it is metabolized and conjugated before excretion can be possible while hydrophilic substance passes through the blood into the kidney.

**Renal excretion**

**This** is quantitatively the **most important route** of excretion for most drugs and drug metabolites. Renal excretion involves three processes: glomerular filtration, tubular secretion, and/or **tubular reabsorption**. The sum of these processes determines the extent of net renal drug excretion.

 **Glomerular filtration**: The kidney filters approximately 180 L of fluid per day. There is a large capacity of drug excretion through this route. The glomerular barrier restricts passage of plasma proteins, red blood cells, and other large blood constituents. Free drug in the plasma will be carried by bulk flow through the glomerulus into the renal tubules. Factors influencing the amount of drug excreted by filtration include the following:

* **Renal blood flow** influences the rate of delivery of drug to the kidney.
* **Glomerular filtration rate** can be affected by disease or age. Glomerular filtration rate decreases by approximately 1% per year and may be significantly compromised in elderly patients. The decline in glomerular filtration rate is accelerated by disease states such as diabetes. For drugs that are eliminated by glomerular filtration, dosages are often adjusted based on the patient's glomerular filtration rate.
* **Tubular secretion**: Secretory mechanisms in the renal tubules **actively transport** endogenous substances and drug molecules from the plasma in peritubular capillaries to the **tubular lumen.** Although quite diverse in some characteristics, the tubular transporters can be classified into two major groups: the **organic anion transporter** (OAT) and the **organic cation transporter** (OCT) families. Drugs that are **highly plasma protein bound** are not excreted effectively by glomerular filtration.

**Tubular reabsorption**

Once in the renal tubule, the **non-ionized** form of the drug is able to diffuse across the tubular membrane and **re-enter the plasma.** As water is reabsorbed along the renal tubule the tubular drug concentration increases, providing a concentration gradient favoring drug reabsorption. Manipulation of the **pH of the tubular fluid** can be used to enhance or inhibit tubular reabsorption according to the Henderson-Hasselbalch relationship. Acidification of urine can be used to decrease reabsorption of weak bases by increasing the proportion of drug in the ionized form. Conversely, alkalinization of urine can be used to increase the renal excretion of acidic drugs because a greater proportion of the drug is in the ionized form.

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| POISON | ANTIDOTES |
| Absinthe | Give an active emetic; then flaxseed tea freely; stimulate. |
| AMMONIA | Lemon juice, diluted vinegar or acetic acid. |
| CARBOLIC ACID | Give flour and water, or other glutinous drinks. |
| BED-BUG POISON | Give milk or white of eggs in large quantities. |
| BITTER ALMONDS | Spirits of hartshorn, strong coffee; cold applications. |
| TARTARIC ACID | Soap water, lime water, magnesia or chalk. |
| SUMACH | Apply to parts a paste of equal parts of starch and glycerine |
| TOBACCO | Encourage vomiting with salt and mustard water, then stimulate with spirits of ammonia, or whiskey and water. |
| TIN | White of eggs and milk, or sugar water |
| VERMILION | Milk or white of eggs in large quantities. |
| SNAKE BITES, POISON | Tie band around limb above bite; suck out venom with mouth; cauterize wound; give strong stimulants. |
| STINGS | Apply salt water, or sweet oil, or fresh mould. Always take out the sting of a bee |
| OXALIC ACID | Magnesia or soap dissolved in water, every two minutes |
| PEACH KERNELS | Spirits of hartshorn, strong coffee; cold applications |
| PHOSPHORUS | Excite vomiting, then give milk and magnesia, followed by tea of flaxseed or slippery elm. |
| MEATS, PUTREFIED | Emetic, followed with vinegar or lemon juice |
| LUNAR CAUSTIC | A strong brine of salt; then milk and sweet or castor oil |
| LYE | Give vinegar or oil |
| CORROSIVE SUBLIMATE | Milk or white of eggs, freely |
| GAS | Remove patient to air, use artificial respiration, apply heat to extremities; send for doctor |

**b)** The first step of diagnosis of poisoning is to assess the overall status of the patient. Severe poisoning may require rapid intervention to treat airway compromise or cardiopulmonary collapse.

Poisoning may be known at presentation. It should be suspected if patients have unexplained symptoms, especially altered consciousness. If purposeful self-poisoning occurs in adults, multiple substances should be suspected.

History is often the most valuable tool. Because many patients (eg, preverbal children, suicidal or psychotic adults, patients with altered consciousness) cannot provide reliable information, friends, relatives, and rescue personnel should be questioned. Even seemingly reliable patients may incorrectly report the amount or time of ingestion. When possible, the patient’s living quarters should be inspected for clues (eg, partially empty pill containers, a suicide note, evidence of recreational drug use). Pharmacy and medical records may provide useful information. In potential workplace poisonings, coworkers and supervisors should be questioned. All industrial chemicals must have a material safety data sheet (MSDS) readily available at the workplace; the MSDS provides detailed information about toxicity and any specific treatment.

In many parts of the world, information about household and industrial chemicals can be obtained from poison control centers. Consultation with the centers is encouraged because ingredients, first-aid measures, and antidotes printed on product containers are occasionally inaccurate or outdated. Also, the container may have been replaced, or the package may have been tampered with. Poison control centers may be able to help identify unknown pills based on their appearance. The centers have ready access to toxicologists.

Physical examination sometimes detects signs showing particular types of substances (eg, toxidromes, presence of topical drugs, needle marks or tracks suggesting injected drug use, stigmata of chronic alcohol use). Even if a patient is known to be poisoned, altered consciousness may be due to other causes (eg, central nervous system infection, head trauma, hypoglycemia, stroke, hepatic encephalopathy, Wernicke encephalopathy), which should also be considered.

In most cases, laboratory testing provides limited help. Standard, readily available tests to identify common drugs of abuse (often called toxic screens) are qualitative, not quantitative. These tests may provide false-positive or false-negative results, and they check for only a limited number of substances. Also, the presence of a drug of abuse does not necessarily indicate that the drug caused the patient’s symptoms or signs (ie, a patient who had recently taken an opioid may in fact be obtunded because of encephalitis rather than the drug). Urine drug screening is used most often but has limited value and usually detects classes of drugs or metabolites rather than specific drugs. For example, an opioid urine immunoassay test does not detect fentanyl or methadone but does react with very small amounts of morphine or codeine analogues. The test used to identify cocaine detects a metabolite rather than cocaine itself.

For most substances, blood levels cannot be easily determined or do not help guide treatment. A few substances like acetaminophen, aspirin, carbon monoxide, digoxin, ethylene glycol, iron, lithium and methanol blood levels may help guide treatment. Many authorities recommend measuring acetaminophen levels in all patients with mixed ingestions because acetaminophen ingestion is common, is often asymptomatic during the early stages, and can cause serious delayed toxicity that can be prevented by an antidote. For some substances, other blood tests (eg, PT [prothrombin time] for warfarin overdose, methemoglobin levels for certain substances) help guide treatment. For patients who have altered consciousness or abnormal vital signs or who have ingested certain substances, tests should include serum electrolytes, blood urea nitrogen (BUN), creatinine, serum osmolality, glucose, coagulation studies, and arterial blood gases (ABGs). Other tests (eg, methemoglobin level, carbon monoxide level, brain CT) may be indicated for certain suspected poisons or in certain clinical situations.

For certain poisonings (eg, due to iron, lead, arsenic, other metals, or to packets of cocaine or other illicit drugs ingested by so-called body packers), plain abdominal x-rays may show the presence and location of ingested substances. Poisonings with drugs that have cardiovascular effects or with an unknown substance, electroencephalography (ECG) and cardiac monitoring are indicated. If blood levels of a substance or symptoms of toxicity increase after initially decreasing or persist for an unusually long time, a bezoar, a sustained-release preparation, or re-exposure (ie, repeated covert exposure to a recreationally used drug) should be suspected.