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Answers

1. A Poison is a substance, natural or synthetic, that causes damage to living tissues and has an injurious or fatal effect on the body, when it is ingested, inhaled, or absorbed or injected through the skin.

Classification of poisonous substances

1. Domestic chemicals

These are non-food chemicals that are commonly found and used in and around the average household. They are a type of consumer goods, designed particularly to assist cleaning, house and yard maintenance, cooking, pest control and general hygiene purposes. Chemicals such as Bleach is especially toxic and should not be mixed with anything other than water. Some of the most deadly combinations are ammonia and bleach, vinegar and bleach, and rubbing alcohol and bleach. Many medications such as analgesics (pain relievers), diabetes medicines, iron tablets, sedatives, heart and blood pressure tablets can be dangerous if taken incorrectly. Examples of these chemicals include Bleach, Vinegar, Detergent, Latex paint.

1. Animal poisons /Toxins

Animal toxins are a complex mixture of polypeptides, enzymes and chemicals which can cause cellular injury. Toxins may be classified as exotoxins (those excreted by an organism, for example, bufotoxin) or endotoxins (toxins that are structurally part of bacteria, for example, botulinum). They are usually transferred through the bites and stings of venomous terrestrial (poisonous snakes, scorpions, spiders, and ants) or marine animals (sea snakes, stingrays, and jellyfish).

1. Drugs

Many medications such as analgesics (pain relievers), diabetes medicines, iron tablets, sedatives, blood pressure tablets can be dangerous if taken incorrectly. Drug toxicity can occur as a result of the over-ingestion of a medication, having too much of a drug in a person's system at once. This can happen if the dose taken exceeds the prescribed dose, either intentionally or accidentally. Drugs with a longer half-life can build up in a person's bloodstream and increase over time. Factors such as age, kidney function, and hydration can affect how quickly the body is able to clear a medication from the system. Examples of this drugs include herbal medicines, over the counter drugs, Yew Plant. With certain medications, drug toxicity can also occur as an adverse drug reaction (ADR).

1. Agricultural chemicals

The majority of agricultural chemicals are pesticides, which include insecticides, herbicides, fungicides, fumigants, and rodenticides. Insecticides derived from plants are low in toxicity. Example, Insecticides such as organophosphates ( malathion, parathion) can cause parasympathetic excess. Warfarin rodenticide causes internal bleeding.

1. Industrial chemicals

The term industrial chemicals is used to refer to chemicals used neither in agriculture or as drugs. Therefore, it includes 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. Industrial chemicals include chlorine, ammonia, phosgene, hydrogen cyanide, acids, solvents, pesticides, herbicides, fertilizers, fuels, petrochemicals.

1. Food additives

Food additives are chemicals added to foods to keep them fresh or to enhance their colour, flavour or texture. They may include food colourings (such as tartrazine or cochineal), flavour enhancers (such as MSG). Other examples of food additives include Anti-caking agents, Antioxidants which prevents foods from oxidising, or going rancid, Artificial sweeteners to increase the sweetness, Emulsifiers which stops fats from clotting together.

2) Hydrophobic molecules are non-polar molecules that do not have any charge-to-charge interactions that will allow them to interact with water. Hydrophobes are also nonpolar molecules and usually have a long chain of carbons that do not interact with water molecules. Examples of Hydrophobic Substances include Oils, fats, alkanes. Drugs that are lipid soluble are not readily removed by the kidneys and thus requires hepatic metabolism.

Point of entry: The Hydrophobic substance Q was administered orally in the body where it is taken by the mouth, swallowed, and then absorbed via the digestive tract. The fate of the substance is determined by Absorption/ Assimilation into the blood stream, Distribution, Drug Metabolism, Drug excretion.

Absorption/ Assimilation into the blood stream: Oral drug absorption is the movement of a drug from its site of application into the bloodstream. The drug will then move to the liver and then back into the bloodstream to be transported to its destination. Drugs that are repelled by water (hydrophobic) are difficult to absorb in the body due to poor water solubility and complexity of administration. For drug absorption to occur, a drug must cross biologic barriers (e.g. epithelial/endothelial cells, etc.) Only a few drugs move across cellular barriers in an “active” way; that is, a way that requires energy (ATP) and moves the drug from an area of low concentration to an area of higher concentration. Most drugs cross cellular barriers via passive diffusion; that is, drugs simply move from an area of higher concentration to an area of lower concentration by diffusing through cell membranes. This type of drug movement does not require any energy expenditure, but will be influenced by the size of the drug and the solubility of the drug. Passive diffusion is comprised of two pathways: the paracellular pathway, in which drug diffuses through the aqueous pores at the tight junctions between the intestinal enterocytes; and the transcellular (lipophilic) pathway, which requires drug diffusion across the lipid cell membrane of the enterocyte.

Factors that impact drug absorption include the following:

1. Physiologically, a drug’s absorption is enhanced if there is a large surface area available for absorption (e.g. villi/microvilli of intestinal tract) and if there is a large blood supply for the drug to move down its concentration gradient.
2. The presence of food/other medications in the stomach may impact drug absorption – sometimes enhancing absorption and other times forming insoluble complexes that are not absorbed (it depends on the specific drug).
3. Some drugs are inactivated before they can be absorbed by enzymes, acidity, bacteria, etc.

First Pass Metabolism

A first-pass effect is the rapid uptake and metabolism of an agent into inactive compounds by the liver, immediately after enteric absorption and before it reaches the systemic circulation. First pass metabolism can occur in the gut and the liver. Drug absorbed from the gastrointestinal tract travels immediately to the liver through the hepatic portal vein. Hepatic first pass occurs when drug absorbed from the gastrointestinal tract is metabolized by enzymes within the liver to such an extent that most of the active agent does not exit the liver and, therefore, does not reach the systemic circulation

Distribution

Once absorbed, most drugs do not spread evenly throughout the body. Once a drug enters into systemic circulation by absorption or direct administration, it must be distributed into interstitial and intracellular fluids. The distribution of a drug between tissues is dependent on vascular permeability, regional blood flow, cardiac output and perfusion rate of the tissue and the ability of the drug to bind tissue and plasma proteins and its lipid solubility. Drugs that dissolve in water (water-soluble drugs), tend to stay within the blood and the fluid that surrounds cells (interstitial space). Drugs that dissolve in fat (fat-soluble drugs), tend to concentrate in fatty tissues. Other drugs concentrate mainly in only one small part of the the tissues because there have a special attraction for (affinity) and ability to retain that drug.

Drug Metabolism

Biotransformation or drug metabolism is the process by which the drug is chemically converted in the body to a metabolite. Biotransformation is usually an enzymatic process. A few drugs may also be changed chemically by a nonenzymatic process (eg, ester hydrolysis). The enzymes involved in the biotransformation of drugs are located mainly in the liver. Other tissues such as kidney, lung, small intestine, and skin also contain biotransformation enzymes. 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.

Metabolism is often divided into two phases:

Phase 1 metabolism

This involves chemical reactions such as oxidation (most common), reduction and hydrolysis. There are three possible results of phase 1 metabolism.

1. The drug becomes completely inactive. (The metabolites are pharmacologically inactive).
2. One or more of the metabolites are pharmacologically active, but less so than the original drug.
3. The original substance is not pharmacologically active, but one of its metabolites is. The original substance is called a prodrug.

Phase 2 metabolism

This involves reactions that chemically change the drug or phase 1 metabolites into compounds that are soluble enough to be excreted in urine. In these reactions, the molecule (drug or metabolite) is attached to an ionisable grouping. This is called conjugation and the product is called a conjugate. Metabolites formed in phase 2 are unlikely to be pharmacologically active.

Drug excretion

The main organs responsible for drug excretion are the kidneys (renal excretion) and the liver (biliary excretion).

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. The renal excretion of drugs is mainly controlled by three factors: glomerular filtration, tubular secretion and tubular reabsorption. Only relatively polar drugs are excreted in appreciable amounts by the kidneys. Factors affecting renal excretion of drugs include: kidney function, protein binding, urine pH and urine flow. Impaired renal function may lead to a clinically significant accumulation of drugs eliminated by the kidneys, if more than 50% of the dose is normally excreted unchanged in the urine and the renal function is less than 50% of the normal value. Successful removal of a drug by dialysis requires that it possesses a polar character, low protein binding and a small to moderate volume of distribution.

Filtration

Filtration takes place in the glomerulus, which is the vascular beginning of the nephron. Approximately one-fourth of the blood flow from cardiac output circulates through the kidney, the greatest rate of blood flow for any organ. A considerable amount of the blood plasma filters through the glomerulus into the nephron tubule. This results from the large amount of blood flow through the glomerulus, the large pores (40 Angstrom [Å]) in the glomerular capillaries, and the hydrostatic pressure of the blood. Small molecules, including water, readily pass through the sieve-like filter into the nephron tubule. Both lipid soluble and polar substances will pass through the glomerulus into the tubule filtrate. The amount of filtrate is very large, about 45 gallons per day in an adult human. About 99% of the water-like filtrate, small molecules, and lipid-soluble substances, are reabsorbed downstream in the nephron tubule.

Secretion

Secretion, which occurs in the proximal tubule section of the nephron, is responsible for the transport of certain molecules out of the blood and into the urine. Secreted substances include potassium ions, hydrogen ions, and some xenobiotics. Secretion occurs by active transport mechanisms that are capable of differentiating among compounds based on polarity. Two systems exist, one that transports weak acids (such as many conjugated drugs and penicillins) and the other that transports basic substances (such as histamine and choline).

Reabsorption

Reabsorption takes place mainly in the proximal convoluted tubule of the nephron. Nearly all of the water, glucose, potassium, and amino acids lost during glomerular filtration reenter the blood from the renal tubules. Reabsorption occurs primarily by passive transfer based on a concentration gradient, moving from a high concentration in the proximal tubule to the lower concentration in the capillaries surrounding the tubule. A factor that greatly affects reabsorption and urinary excretion is the pH of the urine. This is especially the case with weak electrolytes. If the urine is alkaline, weak acids are more ionized and excretion is increased. Weak acids (such as glucuronide and sulfate conjugates) are less ionized if the urine is acidic and undergo reabsorption and renal excretion is reduced. Since the urinary pH varies in humans, the urinary excretion rates of weak electrolytes also vary.

Biliary Excretion

Biliary excretion involves active secretion of drug molecules or their metabolites from hepatocytes into the bile. The bile then transports the drugs to the gut, where the drugs are excreted. The transport process is similar to those described for renal tubular secretion. The efficiency of biliary excretion is quite variable. Although many drugs may reach the gut through this route, deconjugating enzymes in the gut and the gut pH cause many drugs to assume nonpolar lipophilic forms that then are promptly reabsorbed by diffusion into the plasma. This process is referred to as enterohepatic cycling.

2b) Hydrophobic drugs are different from Hydrophilic drugs because of their excretion pattern.

A hydrophilic molecule or substance is attracted to water. Hydrophilic drugs are typically directly excreted by the kidneys, while the hydrophobic drugs undergo biotransformation before excretion. Also for Hydrophobic drugs to be excreted, it must undergo metabolic modification making them more polar. Hydrophilic drugs on the other hand can undergo excretion directly, without the need for metabolic changes to their molecular structures.

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| S/N | Poisonous substances | Antidotes |
| 1 | Heparin | Protamine sulfate |
| 2 | Coumadin (warfarin) | Vitamin K |
| 3 | Opioids | Naloxone |
| 4 | Beta Blockers | Glucagon |
| 5 | Anticholinergics | Physostigmine |
| 6 | Methotrexate | Leucovorin |
| 7 | Benzodiazepines | Romazicon (flumazenil) |
| 8 | Digoxin | Digoxin Immune Fab (Digibind) |
| 9 | Methemoglobinemia | Methylene blue |
| 10 | Organophosphates and carbamates | Atropine |
| 11 | Inorganic mercury poisoning, Gold. | Dimercaprol |
| 12 | Acetaminophen poisoning | Acetylcysteine |
| 13 | Most poisons | Activated charcoal |
| 14 | Benzodiazepine overdose | Flumazenil |
| 15 | Snake bite | Polyvalent immune fab |
| 16 | Toxic alcohols (methanol) | Fomepizole |
| 17 | Sodium channel blocking agents | Sodium bicarbonate |
| 18 | Cyanide | Cyanocbalamin/ Sodium thiosulphate |
| 19 | Lead | Dimercaprol |
| 20 | Tricyclic antidepressants | Sodium bicarbonate |

3a)

3b) Clinical effects of poison can be studied by :

History / Physical findings

Histories taken will consist of a list of all medicines (prescribed and purchased) that a patient was taking prior to their admission to hospital, details of allergies or sensitivities to medicines, recently stopped medicines (e.g. in the past month).Breath odors, findings of vomitus, skin color, body temperature, autonomic nervous system findings, and seizures are important physical findings.

Toxidromes

Toxidromes are toxic syndromes or the constellation of signs and symptoms associated with a class of poisons. Rapid recognition of a toxidrome, if present, can help determine whether a specific poison or class of toxin is involved.

Diagnostic Testing

1. Immunoassay drug test: The most commonly used immunoassay (IA) drug test panel includes

Urinalysis

A urinalysis will show the presence of a drug in the system after the drug effects have worn off. Urine screening may detect amphetamines or methamphetamines, barbiturates, benzodiazepines, cocaine, marijuana, MDA-analogues (MDA or MDMA), opiates (codeine, morphine, 6-acetylmorphine [indicative of heroin use], hydromorphone, hydrocodone, oxymorphone, oxycodone), nicotine, or alcohol.

Blood testing

This may be performed in the emergency room for toxicology testing, as well. However, blood analysis often has a short period of detection, as many illicit drugs are metabolized quickly and eliminated from the body. A variety of drugs can be tested for in blood: examples include alcohol, amphetamines, cocaine, fentanyl, marijuana, methamphetamines, opiates, phencyclidine, nicotine, and tramadol.

Saliva drug testing

It may be referred to as a mouth swab test, it is used if a tester is interested in knowing about recent drug use. It is not ideal to survey long-term use of drugs. Most saliva drug tests can detect usage within a few hours up to 2 days. Saliva is an easy lab test to gather samples, is less susceptible to adulteration or substitution, and can be tested for alcohol, barbiturates, benzodiazepines, cocaine, ecstasy, marijuana (THC), opiates, amphetamines, phencyclidine (PCP), and methamphetamines.

1. Basic serum electrolytes, blood urea nitrogen (BUN), and creatinine

Nephrotoxicity is one of the most common kidney problems and occurs when the body is exposed to a drug or toxin that causes that causes damage to the kidneys. When kidney damage occurs, you are unable to rid the body of excess urine, and wastes. The blood electrolytes (such as potassium, and magnesium) will all become elevated.

Blood Urea Nitrogen (BUN)

The BUN reflects the amount of nitrogen that is present in the body in the form of a waste product called urea. BUN is used to determine if there is extra nitrogenous wastes in the blood stream, which should have been filtered out of the kidneys.One of the symptoms of kidney problems is the failure to filter as much urea as is necessary. An excess of nitrogen compounds in the blood may lead to uremia.

Creatinine:

The serum Creatinine is present after the chemical Creatine is broken down by the body in order to make energy for the muscles. The kidneys are normally able to filter out large amounts of creatinine on a daily basis. However, when kidney problems are present, the creatinine levels will increase, reflecting less creatinine being filtered out through the kidneys.

1. Serum lactate:

Serum lactate level measures the amount of lactic acid in the blood and is a fairly sensitive and reliable indicator of tissue hypoperfusion and hypoxia. Elevation in the blood lactate level is a sensitive marker for cyanide toxicity.

1. Liver Function Tests:

Alcohol, drugs, some herbal supplements, and toxins can also pose a threat to the Liver. Liver function tests helps to determine the health of the liver by measuring the levels of proteins, liver enzymes, and bilirubin in the blood.

Alanine transaminase (ALT) test

Alanine transaminase (ALT) is used by the body to metabolize protein. If the liver is damaged or not functioning properly, ALT can be released into the blood. This causes ALT levels to increase. A higher than normal result on this test can be a sign of liver damage.

Aspartate aminotransferase (AST) test

Aspartate aminotransferase (AST) is an enzyme found in several parts of the body, including the heart, liver, and muscles. Since AST levels aren’t as specific for liver damage as ALT, it’s usually measured together with ALT to check for liver problems. When the liver is damaged, AST can be released into the bloodstream. A high result on an AST test might indicate a problem with the liver or muscles.

Alkaline phosphatase (ALP) test

Alkaline phosphatase (ALP) is an enzyme found in the bones, bile ducts, and liver. An ALP test is typically ordered in combination with several other tests. High levels of ALP may indicate liver inflammation, blockage of the bile ducts, or a bone disease.

Albumin test

Albumin is the main protein made by the liver. It performs many important bodily functions. An albumin test measures how well the liver is making this particular protein. A low result on this test can indicate that the liver isn’t functioning properly.

Bilirubin test

Bilirubin is a waste product from the breakdown of red blood cells. It’s ordinarily processed by the liver. It passes through the liver before being excreted through the stool. A damaged liver can’t properly process bilirubin. This leads to an abnormally high level of bilirubin in the blood. A high result on the bilirubin test may indicate that the liver isn’t functioning properly.

Gamma-glutamyltransferase (GGT). GGT is an enzyme in the blood. Higher-than-normal levels may indicate liver or bile duct damage.

L-lactate dehydrogenase (LD). LD is an enzyme found in the liver. Elevated levels may indicate liver damage but can be elevated in many other disorders.

Prothrombin time (PT). PT is the time it takes for blood to clot. Increased PT may indicate liver damage but can also be elevated if one takes certain blood-thinning drugs, such as warfarin.

1. Electrocardiogram (ECG):

The ECG is used to assess human cardiovascular health. In toxicology, the ECG provides a collection of end points that may be used to assess both the quality and magnitude of cardiac toxicity. Classic ECG changes may hint at blockade of ion channels, alterations of adrenergic tone, or dysfunctional metabolic activity of the myocardium.