Uttar Pradesh Rajarshi Tandon Open University

PGBCH-117N

Environmental Toxicology and Occupational Health Hazards

COURSE INTRODUCTION

In this course, you will study about **environmental toxicology & occupational health hazards**. The occupational toxicity evaluates detrimental effects of toxicants on living things and is essential for preserving public health. Comprehending systemic toxicity, which impacts numerous organs or systems, which is essential for evaluating and managing risks. In toxicology, carcinogenesis the process by which substances causes cancer is a major problem. Today, toxicologists must use strict testing procedures to identify substances that may be carcinogenic. To assess toxicity levels, forecast unfavorable health outcomes and the testing methods include epidemiological research, computational models, and both in vitro and in vivo assays. By using these techniques, toxicology supports public health policy by facilitating the detection, control, and reduction of toxicants to protect human health and the integrity of the environment. The course is organized in the following blocks:

Block-1 covers the toxicityandtoxicants

Block-2 deals the toxicityand publichealth

Block-3 describes the systematictoxicity

Block-4 this block covers the carcinogenesis and testing methods

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BLOCK

1

TOXICITY AND TOXICANTS

UNIT-1

Introduction to Toxicology

UNIT-2

Toxicants

UNIT-3

Duration and Euposure of Toxicant

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BLOCK INTRODUCTION

The following three units are included in the first block of environmental toxicology & occupational health hazards are as:

Unit-1: The introduction to toxicology is to covered in this unit, which looks at how chemicals affect living things. It examines toxicity, dose effects, and dose-response correlations to distinguish between target and non-organic toxicity. This unit also discusses dose effects and the dose response relationship, as well as toxicity and toxic agents, factor impacts toxicants, target and non-organ toxicity.

Unit-2: The classification of toxicant is covered in this unit. The various kinds of poisons found in nature, including those found in animals and plants are discussed here. This article also discusses chemical toxins, genetic poisons, and food poisons.

Unit-3: The topics covered in this unit are acute and chronic exposure. Here, the many forms of human exposure internal, occupational, and environmental as well as the consequences of unintentional and internal poisoning on human health are discussed.

UNIT-1 : INTRODUCTION TO ENVIRONMENTAL TOXICOLOGY

Structure

1.1 INTRODUCTION

The term "environmental toxicology" refers to the toxicity of environmental pollutants that affect the health of biological organisms. The toxicity occurs due to the result of both natural and manmade action and reactions. Variety of toxicants present in environment has adverse impact on Human health and activities. Environmental toxicology is a multidisciplinary science that examines the adverse effects of physical, chemical, and biological chemicals on ecosystems and living beings in the environment. Contaminants originating from industrial processes, natural sources, agriculture, and urbanization is the main sources of environmental toxicity that have direct or indirect impact on ecological integrity and public health. Environmental toxicology also includes the regulation of environmental contaminants and toxicity, as well as the development of environmental and human safety precautions. It includes the different chemicals like metals, herbicides that contribute to environmental toxicity. Natural activity that is influenced by human activity, whether directly or indirectly, also contributes to environmental contamination. Before we can delve more into environmental toxicology, we must first comprehend toxicants. Environmental toxicology is a multidisciplinary scientific field that studies the harmful effects of various chemical, biological, and physical agents on living organisms. Rachel Carson is considered as the creator of environmental toxicology after publishing her book Silent Spring in 1962, which outlined the implications of unregulated pesticide use. The term "toxicant" refers to any physical or chemical agent that, when in touch with the biological system. The produce response may long period or a short time and have negative impact on natural system. This response could continue a long time or be permanent. The reaction to toxicant exposure is used to assess acute and chronic consequences.

Environmental toxicologists study the fate, transport, transformation, and bioaccumulation of toxic substances in air, water, soil, sediments, and biota to identify their dangers, understand their toxicity processes, and formulate plans for environmental management

Objectives

- To discuss environmental toxicity and its impacts.
- Learn about bioaccumulation, biotransformation, biomagnifications, and bioremediation.
- Identify the xenobiotics substances and their toxicity.

1.2 ENVIRONMENTAL TOXICOLOGY OVERVIEW

Toxicology is the study of toxicants or substances. Environmental toxicology is the study of the many effects of both man-made and natural toxins on the environment. It is primarily concerned with the examination of environmental chemicals of human origin. It covers the effects of toxicants on living creatures and how they generate toxicity, as well as methods to prevent or limit unwanted consequences, such as defining acceptable handling or exposure recommendations. Toxicants can have immediate (acute) or long-term (chronic) effects after exposure. Acute toxicity, which varies from dizziness and nausea to death, happens immediately or within a few days of a single encounter. Chronic toxicity, on the other hand, typically causes harm to important organs such as the kidneys or liver after a lengthy period of low-level chemical exposure.

Ecotoxicology and environmental health toxicology are two subfields of environmental toxicology. Ecotoxicology is the study of how toxic chemicals harm living organisms. It primarily affects the biosphere, environment, and community. Environmental health toxicology is primarily concerned with the harmful impact of environmental pollutants on human health. Environmental toxicology gathers and combines knowledge from several domains. Mathematicians, chemists,

molecular biologists, geneticists, land and water ecologists work together to assess the effects of chemicals on biological systems (Figure 1.1). Ecology refers to relationships between biological and chemical environment and their impacts of species in ecosystems. When tissues are studied in analytical chemistry can be utilized to determine a concentration of a substance in the surrounding environment. Organic chemistry provides the underlying lexicon and structural basis for both abiotic and biotic interactions in an ecosystem. Biostatistics is the use of statistics to biological problems, as well as the development of tools for data analysis and hypothesis testing. Mathematical and computer modelling can help researchers forecast repercussions and enhance hypotheses.

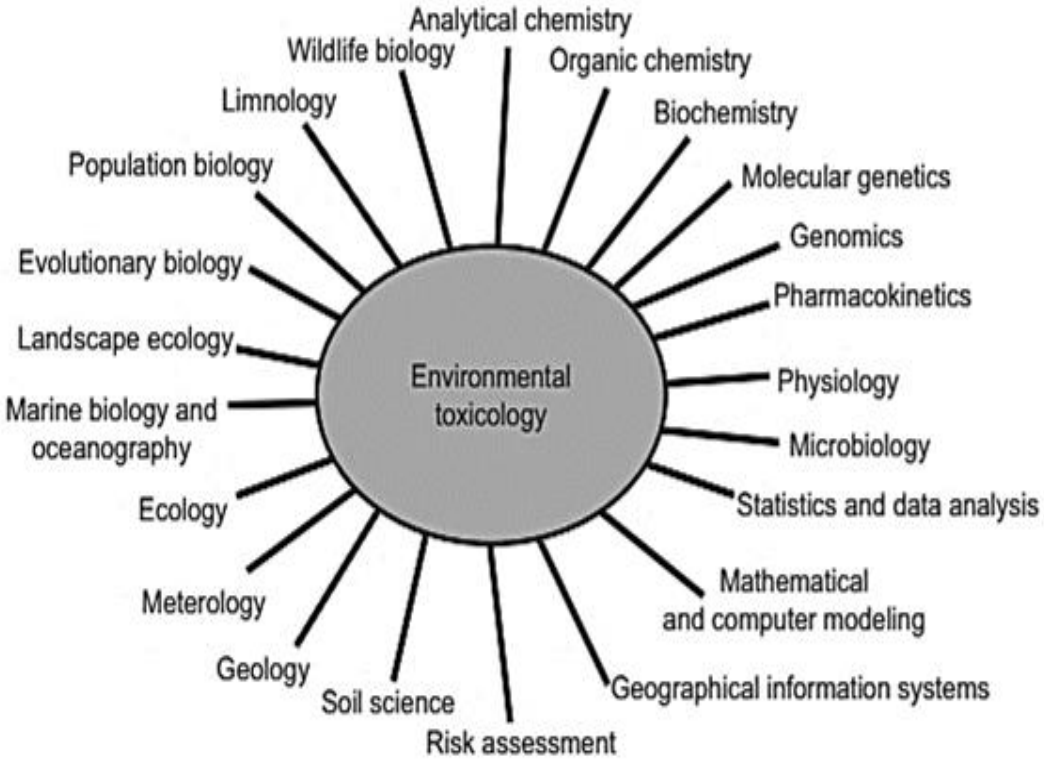


Fig. 1.1 : The components of environmental toxicology

Environmental toxicology investigates how compounds migrate through the environment and the possible harm they may do to wildlife, vegetation, and the overall ecosystem. Ecotoxicology systems require both chemical and species-specific knowledge. The effects of man-made chemicals, including industrial organics, agricultural chemicals, pharmaceuticals, and its by-products such as chlorinated compounds from waste incineration are harmful. Toxins, on the other hand, are any physical or chemical agents that interact with the biological system and create adverse effects. Responses might be either long-term or short-term. The response of body to toxicant exposure is used to identify both acute and long-term effects. When exposed to a high concentration of a pollutant, an acute impact occurs quickly. Chronic effects can take years to show, which makes quantification difficult. It is thought that moderate alcohol use, low-level radiation exposure, and persistent cigarette smoking can all have long-term consequences. Toxins can enter our bodies via a variety of routes, including food, drink, breath, medication, and inadvertent or occupational exposure.

Some chemicals change when they enter the body after being exposed to toxins, as the body's physiological systems attempt to eliminate them via the excretory system. Aside from its impact on human health, the toxin poses a significant threat to the existence of many biotas. To be hazardous to our health, chemicals must enter our bodies.

1.2.1 Definition

Toxicology studies poisons, their causes, effects, and treatment. Environmental toxicology investigates how toxins affect human health and the environment, whether intentionally manufactured or industrially produced. Environmental toxicologists use biological, chemical, and epidemiological concepts to understand the impact of chemicals on humans and the environment. They predict chemical exposure and monitor exposure limits to protect human health and the ecosystem. Environmental toxicology is a part of the environmental sciences that studies how hazardous contaminants are to the environment. Despite having a toxicological base, environmental toxicology heavily draws on concepts and methodologies from other disciplines such as genetics, biochemistry, cell biology, and developmental biology. Rachel Carson has been considered as the pioneer of environmental toxicology since the publication of her book Silent Spring in 1962, which studied the repercussions of unregulated pesticide use. Lucille Farrier Stickel's articles on the ecological repercussions of the insecticide DDT was a key source of inspiration for Carson's book.

We measure toxicity by the dose at which unfavourable consequences occur. A toxicant dosage is the quantity that an exposed organism absorbs. The reaction refers to the type and extent of harm caused by exposure to a specific dose. A dose may induce death (lethal dose) or injury without death (sublethal dose). Lethal dosages, commonly expressed in milligrams of toxicant per kilogram of body weight, differ based on the organism's age, gender, health, metabolism, genetic makeup, and how the amount was administered (all at once or over time). Many toxicants have lethal levels in humans, as evidenced by homicides and accidental poisoning.

One method for determining acute toxicity is to deliver different doses to groups of laboratory animals, assess their responses, and use this information to anticipate the chemical effects on people. The lethal dose (L.D.) for 50% of a population of test animals is the lethal dose-50%, or LD_{50}. It is commonly expressed as milligrams of chemical toxicant per kilogram of body weight. A chemical's acute toxicity is inversely proportional to its L.Ds. The lower the LDs, the more dangerous the chemical, conversely, the higher the LDs, the less toxic the chemical. The LDs are calculated for all new synthetic compounds, thousands of which are generated each year, in order to estimate their hazardous potential. It is commonly assumed that a chemical with a low LD_{50} for numerous kinds of test animals is harmful to humans.

1.2.2 History

Environmental toxicology is a relatively new science, dating back to the mid-1900s. In contrast, the field of toxicology as we know it today was established in the early 1800s, and by the late 1800s, some scientists had begun to consider the repercussions of dangerous compounds mistakenly discharged into the environment. However, until the 1962 publication of American biologist Rachel Carson's book Silent Spring; public awareness of environmental poisons did not considerably increase. Scientists studying environmental toxins in the 1970s focused primarily on the impacts of biological warfare agents (such as Agent Orange), industrial pollution, and mine drainage. The Bhopal tragedy and the Chernobyl disaster highlighted the significance of environmental toxicology in modern society. It expanded rapidly in the late 20th and early 21st centuries, focusing on oil spills, radioactive waste dumping, air and water pollution, and the consequences of drugs like synthetic hormones dumped into environmental reserves. These events highlighted the need for a comprehensive understanding of environmental toxicology.

1.2.3 Scope of Environmental Toxicology

Regulatory bodies, decision makers, and others can rely on toxicology's critical information and understanding to minimize human exposure to the substances and avoid or lessen the likelihood of

developing a disease or other unfavourable health results. Environment toxicologists are employed by businesses, governments, universities, and other institutions. An environmental toxicologist has training in subjects such as pharmacology, environmental chemistry, or public health. The chemical effects on species are:

1. Examines effects of chemical concentrations on different species
2. Investigates bioaccumulation in animals and other organisms, crucial for human exposures.
3. Advocates for government laws and policies to protect environment and public health.
4. Provides consumer information for health and illness prevention decisions.

1.3 CONCEPTS IN ENVIRONMENTAL AND OCCUPATIONAL TOXICOLOGY

Environmental toxicology is the study of the interactions between environmental contaminants and their sources, routes, and consequences on a variety of scales on living beings. It brings together principles from toxicology, ecology, chemistry, epidemiology, risk assessment, and environmental science to better understand pollutant fate and consequences on ecosystems, biodiversity, and human populations. Toxins can be found in food, drink, air, and clothes. It comes from both natural and human causes. These chemicals have a variety of effects on plants and animals. People frequently have little control over their exposure, whether through dirty air from nearby power plants or direct contact with harmful fumes from cleaning goods.

Pollutants and Contaminants: Environmental toxicology encompasses various pollutants and contaminants, including air pollutants, industrial wastes, heavy metals, organic compounds, pesticides, nanoparticles, and new contaminants, which pose a threat to human health and environmental quality due to their entry from point sources or diffuse sources.

Routes of Exposure: Humans are exposed to dangerous substances through various routes, including ingestion, inhalation, skin contact, and maternal transfer. These pollutants can change in dispersion, bioavailability, and toxicity due to physical, chemical, and biological changes. Toxicants cause a wide range of effects, some causing and mediating them. Some immediate symptoms are minimal, like a mild cough or headache, while others, like violent convulsions, can be severe. These effects usually diminish after exposure ceases, as they are typically caused by high concentrations from short-term exposures.

Bioaccumulation and Biomagnifications: Bioaccumulation and biological magnifications are significant factors influencing toxicity. Bioaccumulation involves the accumulation of chemicals within the body's tissues and organs due to selective absorption, chemical resistance, and prolonged storage. Environmental toxicology studies how contaminants accumulate and escalate through ecological pathways and food chains. Bioaccumulation is the process by which organisms absorb contaminants from their food or surroundings. Heavy metals accumulate due to their resistance to chemical breakdown, while chlorinated hydrocarbons like DDT accumulate in body fat due to their fat solubility. Both factors contribute to the accumulation of contaminants in the environment.

Toxicokinetics and Toxicodynamics: Environmental toxicologists study the toxicity processes, target organ effects, and toxicokinetics (absorption, distribution, metabolism, and excretion) of contaminants in living organisms to better understand, how they interact with biological systems and cause harm. Environmental risk assessment necessitates the prediction of pollutant fate and effects, which necessitates knowledge of toxicokinetic and toxicodynamic mechanisms.

- **Ecological Risk Assessment:** Environmental toxicology use ecological risk assessment frameworks to assess the potential dangers posed by contaminants to populations, ecosystems, and ecological services. The purpose of risk assessment is to predict the likelihood and severity of negative consequences and to offer data for risk management decisions. It includes hazard identification, exposure assessment, dose-response analysis, and risk characterization.
- **Human Health Impacts**: Environmental toxicology assesses environmental contaminants' long- and short-term impacts on human health, including carcinogenicity, neurotoxicity, reproductive toxicity, developmental toxicity, and immunotoxicity. Exposure to environmental toxins can have serious health repercussions and a high disease burden through a variety of means, including food consumption, water contamination, air pollution, occupational exposures, and living near contaminated areas. The hazardous substances have delayed impacts, such as cancer or birth defects. Emphysema caused by tobacco smoking and air pollution, for example, can develop months or years after exposure and often lasts for years. Delayed effects are frequently caused by prolonged low-level exposure (chronic exposures). However, short-term exposures may have delayed effects. A single exposure to certain cancer-causing substances, for example, may actually cause the disease to manifest many years later.

Environmental toxicology plays a crucial role in environmental management, public health protection, and policy development by providing scientific data and methodologies for pollution control, remediation, and regulatory decisions. To safeguard both ecological integrity and human health, it has an impact on environmental justice, risk communication, environmental monitoring, and sustainable development strategies. Environmental toxicology faces several challenges and uncertainties, including the complexity of environmental systems, the cumulative and interactive effects of multiple stressors, the emergence of novel contaminants, a lack of comprehensive toxicity data for many chemicals, the need for interdisciplinary collaboration, and stakeholder engagement. Addressing these concerns requires research, innovation, and adaptive management solutions to reduce environmental risks and enhance environmental sustainability.

1.4 ENVIRONMENTAL TOXICANTS

Toxicants are substances that impair the environment. Toxicants have been shown to be harmful to all living creatures, even at very low quantities. The majority of toxicants contain a variety of chemical or physical components. When toxicants are discharged into the environment, they can contaminate ecosystems' abiotic constituents, such as the air, land, and water. The biotic communities of ecosystems, which include bacteria, plants, and animals, are harmed by the toxicants' impacts on the environment and their health. Toxicants can be either natural or manufactured.

1.4.1 Types of Environmental Toxicant

An environmental toxicant is any harmful agent or substance formed or released into the environment as a result of human activities. Toxicants can come from both natural and man-made sources, and they can assume a range of shapes and sizes. As a result, a wide range of compounds, including organic components such as pharmaceutical medications and inorganic substances such as metals, are classified as toxicants. Because environmental contamination plays an important role in the pathophysiology of several human diseases, it has been a major worldwide health concern in various forms.

Toxicants can come in a variety of shapes and sizes, both manmade and natural. Plant tissues are the principal storage sites for naturally occurring toxicants. Animals primarily come into touch with toxicants via vegetation. Unsuitable human conduct for the environment is responsible for the creation

of manufactured toxicants through human activities. Although natural volumes of crude oil can be discovered many meters beneath the surface, only a few man-made biological toxicants are composed of biological poisons. Furthermore, biological toxins almost seldom become pollutants. Biological pollutants include germs present in soil, such as bacteria and algae. Other pollutants for examples petroleum products, metals, and both manmade and natural organic molecules that is hazardous to the environment. Inaddtion, Environmental toxicants include tobacco smoke, mercury compounds, polychlorinated biphenyls (PCBs), exhaust particles, particulate matter, and phthalates. They are classified into five types: neurotoxins, endocrine disruptors, allergens, mutagens, and carcinogens. These environmental poisons can enter the body via the skin, food and beverage consumption, inhalation, and a variety of other means. There are numerous forms of environmental toxins, including neurotoxins, allergens, carcinogens, mutagens, and endocrine disrupters. These are dangerous materials that people create or discharge into the environment as a byproduct of their daily actions. The health of organisms is negatively impacted by their exposure. a toxic material capable of killing a biological system or seriously harming its composition and operations. One way to define the negative response would be as a measurement that is beyond the usual range for well-functioning organizations. Intentional or unintended introduction of hazardous or alien chemicals can increase the amount of space available for inter-ecosystem organization within the ecosystem.

1. Non-point sources include agricultural, land runoff, contaminated groundwater, sediments, urban runoff, bottom segment dumping, and atmospheric fallout.
2. Point sources of hazardous waste include emissions from manufacturing facilities and municipal waste treatment plants.

Anthropogenic elements such as industrial waste discharge from lipid factories, metal salt, petroleum, hydrocarbons, synthetic organic pesticides, and other industrial compounds used in chemical manufacturing are responsible for pollution. The concept that no chemical is ever completely safe or dangerous is central to toxicology. The relationship between the amount of chemicals to which an organization is exposed and the duration of exposure determines whether a chemical agent is potentially hazardous or safe. The concentration-response relationship measures the severity of the exposure. If the chemical concentration is less than a specific minimal effective threshold, the chemical interaction with a biological memorial system may not be harmful. Toxicology has grown into a quantitative study of biological or chemical system effects. For example, how much of the required chemical can be injected into the living beings without causing damage.

1.4.2 Mode of Action of Toxicants

Toxicants' chemical properties have an impact on organisms. These consequences occur, when a harmful chemical enters plants via their leaves or roots. Animals can contract these via their respiratory, digestive, or cutaneous systems. The circulatory fluids in a plant or animal's body deliver these toxicants to the location of action. A part of the initial chemical, or its bio transformed active metabolites, may reach the site of action; the remainder may be retained in fatty tissues or removed and converted, typically into non-toxic molecules. Toxicants' mechanisms of action include oxidation and dehydrogenation, as well as carcinogens. Plasticizers, fire retardants, biofumes, and insecticides are among the many sources of these toxins.

1.5 TOXICITY AND TOXIC AGENTS

Toxicity refers to the ability of a compound to harm living beings at trace levels. Low toxicity drugs have no effect unless present in large concentrations. Toxicity is difficult to define without considering the amount of the chemical, its administration, dispersion over time, type of injury, and the

duration of injury creation.

Toxicity is the ability of a chemical to injure a living being, which is determined by exposure time and concentration. It is a relative feature that is widely utilized in chemical comparisons. Toxins can be synthetic, produced, or naturally occurring and come from minerals, plants, or animals. Animal poisons and venom are prevalent in this group. Many plants contain toxic compounds, some of which have medicinal properties, such as quinine, curare, opium, atropine, reserpine, and picrotoxin.

1. Toxic agents are substances that can have a negative biological effect and can be biological, physical, or chemical. They can be classified based on the classifier's interests and needs, and the best rating system may be a combination of categorization systems based on diverse features. Exposure characteristics are also useful in toxicology, as they can be classified in various ways, including biological, physical, or chemical. Therefore, no single classification system can cover the entire range of dangerous compounds.

1) Classification based on sources of toxicants

- Plant toxins
- Animal toxicants
- Mineral toxicants
- Synthetic toxicants
- Physical or mechanical agents

2) Classification based on physical state of toxicants

- Gaseous toxicants
- Liquid toxicants
- Solid toxicants
- Dust toxicants

3) Classification based on target organ or system

- Neurotoxicants
- Hepatotoxicants
- Nephrotoxicants
- Pulmotoxicants
- Hematotoxicants
- Dermatotoxicants
- Development and reproductive toxicants

4) Classification based on chemical nature/structure of toxicants

- Metals
- Nonmetals
- Acids and alkalis
- Organic toxicants (carbon compounds other than oxides of carbon, the carbonates, and metallic carbides and cyanides)

5) Classification based on analytical behavior of toxicants

- Volatile toxicants
- Extractive toxicants
- Metals and metalloids

6) Classification based on type of toxicity

- Acute
- Subacute
- Chronic.

7) Classification based on toxic effects

- Carcinogens
- Mutagens
- Teratogens
- Clastogens.

8) Classification based on their uses

- Insecticides
- Fungicides
- Herbicides
- Rodenticides
- Food additives

9) Classification based on symptoms produced

- Corrosive poisons
- Irritant poison
- Systemic poisons
- Miscellaneous poisons.

1.5.1 Factors Affects Toxicants

Toxic substances are determined by three things: its chemical makeup, how much of it the body absorbs, and how well the body is able to detoxify the toxin into less harmful forms and get rid of it. In the environment the concentration, transport, transformation and disposition of chemical are primary controlled by the following factors such as

1. The physical and chemical properties of compounds

2. The physical, chemical, and biological properties of ecosystem

3. The source and rate of input of chemical into the environment

Vapour pressure and a solubility of compounds in water are two important physical-chemical properties. The rate constants for partition coefficients, as well as the organism's hydrolysis, photolysis, biodegradation, sorption, evaporation, and depression processes, provide valuable information. Temperature, salinity, pH, and velocity are some aquatic environment variables, as are depth, amount of suspended matter, segment particle size, and carbon content. All of which can affect a chemical's fat

content or surface area to volume ratio. Predicting environmental conditions necessitates knowledge of usual input rates as well as the frequency of single significant chemical sludge introductions into the ecosystem. The aforementioned statistics are not only valuable in estimating environmental concentrations, but also determining such as:

i. The chemical mobility and the regions of the environment where they are most likely to be found.

ii. The kinds of substances and biological processes that occur both during and following deposition.

iii. The eventual chemical forms

iv. The persistence of chemical.

A chemical may be different types that effect on ecosystem. For example, a chemical in water can exist in three different forms, which affects its bioavailability, its ability to dissolve, absorb, and assimilate into biotic or abiotic components, as well as be suspended in the water column within an organism. Chemicals that dissolve readily can be arranged in a water column. They can also be gathered, organized in various tissues, bio transformed, and released into the gaming environment. Chemicals that are soluble in water can preserve their physical and chemical properties while being transported and spread throughout the environment. Persistent chemicals can even reach toxic levels. Chemical persistence can be characterized in terms of half life, which is the time required to lower a chemical's original concentration by half. The factors related to the substances are:

(i) the physical-chemical characteristics, such as the functional groups,

(ii) water and organic solvent solubility,

(iii) dose/concentration,

(iv) ionic characteristics

(v) translocation and biotransformation,

(vi) their mode of action, and interaction with other chemicals.

Almost all these characteristics are dependent on the structure of compound. The factors related to the exposures are:

(i) routes of exposure,

(ii) exposure systems,

(iii) exposure duration, etc.

More research has been conducted on the aquatic medium to identify how the surrounding medium influences xenobiotics toxicity. As a result, we now have a better knowledge of how the physicochemical features of water affect chemical toxicity. The details about how these factors influence a chemical’s toxicity are as:

(i) water temperature

(ii) dissolved oxygen

(iii) pH

(iv) salinity

(v) water hardness

(vi) suspended and dissolved substances

Abiotic modifying factors refer to the combination of chemical toxicity, exposure, and

surrounding medium toxicity modifying factors. The factors related to the organisms may also be termed as biotic modifying factors. The elements related to the living things are

(i) type of species

(ii) sex

(iii) age

(iv) stage of the life cycle

(v) weight and size of individual

(vi) health and nutritional status

(vii) seasonal physiological state

(viii) acclimation of individuals

Here we are separated into the following four sections for ease of reading:

- Factors pertaining to chemical
- Factors pertaining to exposure
- Factors pertaining to surrounding medium
- Factors pertaining to organisms

Factors pertaining to chemical

Chemical composition: A chemical composition of compound is essentially dictates the physicochemical properties, which include solubility, vapour pressure, ionization, functional groups, and so on. Each of these qualities has a substantial impact on the material's toxicology. The functional groups of a chemical determine the type of chemical reaction, and toxicity is an organism's response to a chemical that reacts with a specific section of the organism.

Dose or concentration of chemical: When a drug interacts with the appropriate receptors, it can have negative consequences. The effect of the chemical is determined by its concentration at the target place, which is frequently proportional to the dose or concentration of the chemical exposed. Chemicals have fewer effects at lower doses that depend on concentrations.

Translocation of toxicant: Toxicants are classified into two types: (a) those that cause local effects and (b) those that have systemic repercussions. The latter group places a high value on effective translocation. Toxicants cannot cause adverse effects unless they can easily be transferred to the designated locations. Certain toxicants interact with certain macromolecules in the body of organism during translocation, resulting in their storage in relatively inactive tissues known as storage depots.

Biotransformation of toxicants: Certain substances are often inert. These compounds are biocatalytically converted into active forms during their translocation in body of animals using specialized enzymes. When xenobiotics undergo biotransformation and are activated, their toxicity increases. However, during translocation, active xenobiotics can transform into inactive equivalents, which are typically retained in nontarget or relatively inactive tissues.

Chemical interactions: Nature contains numerous chemicals, and organisms are exposed to multiple drugs, which can have significant toxicological implications. In contrast, lab organisms can be exposed to two chemicals concurrently or sequentially, affecting each other's toxicity and potentially causing three different negative outcomes.

The total of the effects of each chemical when administered alone may be equal to the combined

effect of two substances. This type of interaction is considered as additive

i. Synergistic interactions occur when two substances have combined effects on the exposed organisms that are higher than their sum.

ii. The combined effect of two chemicals to the organisms exposed may be less than the sum and this type of interaction is termed as antagonistic.

Factors pertaining to exposure: Many aspects of an exposure of chemical to an organism can have a significant impact on its toxicity. Among the crucial element pertaining to exposures are:

Exposure routes: Toxins enter the body of organisms through the skin, mouth, and inhalation, as well as intraperitoneal, intramuscular, subcutaneous, and intravenous injections. Chemical toxicity is heavily determined by the routes of exposure. A substance's intravascular administration produces a more immediate and potent effect since the chemical is transported directly to the target area in an active form and optimizing its effects.

Exposure duration: Exposure time rises, lowering toxicant LC50 or LD50 levels. Long-term exposure numbers are much lower than short-term exposures, demonstrating that the same toxicant's effects change over time.

Exposure systems: Toxicants can be exposed via a variety of exposure strategies. For example, in aquatic media, different exposure mechanisms are employed to expose organisms to toxicants, such as:

- **Static system:** In this system, organisms are exposed to a mixed toxicant in still water.
- **Recirculatory system:** This system uses specific pumps to recirculate the toxicant solution.
- **Renewal system:** In this system, the toxicant solution is replaced every specific amount of time.
- **Flow through system:** The point at which the toxicant solution periodically or continuously enters and exits the test chamber.

Factors pertaining to the surrounding medium: For the aquatic medium, the environmental parameters influencing chemical toxicity have been thoroughly studied. The physico-chemical properties of the water, which influence the toxicity of substances, are medium-related factors. Therefore, those factors are taken into account in this section.

Water: It is anticipated that water temperature will have a significant impact on xenobiotics toxicity. A rise in water temperature influences the chemical form of certain chemicals, makes a lot of substances more soluble, and controls the concentration of dissolved oxygen in the water. Depending on the chemical, species, reaction, and specific process, a shift in temperature in a certain direction may enhance, reduce, or have no effect at all on a chemical's toxicity.

Dissolved Oxygen: At 0 degrees Celsius, freshwater can dissolve 14.6 mg/1 of oxygen; this amount progressively drops to 9.1 mg/1 as the temperature rises to 20 degrees Celsius, and it reaches 7.5 mg/1 at 30 degrees Celsius. Thus, it is evident that a rise in temperature reduces the dissolved.

pH: The toxicity of substances that ionize when pH changes may be more impacted by pH. Because undissociated versions of chemicals can more readily pass through cell membranes, they are typically more harmful to organisms. The toxicity of ammonia is known to be greatly affected by pH of the water.

Salinity: It is reasonable to assume that the biggest variations between the chemical properties of freshwater and seawater will have a significant impact on chemical toxicity. However, the toxicity of substances is not considerably changed by these changes. When evaluated in their respective habitats, the close relatives of marine and freshwater creatures have nearly similar tolerance.

Suspended and dissolved matter: Organic ligands and chelators are among the suspended and dissolved materials that are frequently found in natural water. Because they bind or sorb some of the xenobiotics substances, they may partially detoxify them.

Factors pertaining to organisms: Chemical toxicity is assessed in relation to a specific organism or set of species. Consequently, the study of xenobiotic toxicity places a great deal of importance on characteristics pertaining to organisms.

Test species: Much as the tolerance to chemicals varies throughout groups of animals, so too does the toxicity of xenobiotics with diversity in test organisms. Within the same group of animals, a chemical's toxicity varies according to the organisms' species. In addition, Chemical toxicity varies even among individuals of the same species due to differences in sensitivity caused by certain genetic variables.

Sex: Because of hormonal and metabolic variations, the responses of males and females to toxins vary, resulting in disparities in chemical toxicity. Certain species have men that biotransform chemicals more quickly than females, however not all species exhibit this trait.

Age: Generally, young animals are typically more vulnerable to xenobiotics. The children are 1.5–10 times more vulnerable than the adults to most toxins. Younger children may be more susceptible due to a lack of biotransformation enzyme systems and a decreased capacity for resistance. It has previously been documented that newborns lack the enzyme systems necessary to catalyze biotransformation events.

Life-stage: Chemicals' levels of toxicity change as they progress through their life cycles. Early life phases, often known as immature stages, are typically more vulnerable to toxicant exposures than are later life stages, or mature humans. Fish fingerlings and fry are the most delicate stages.

Size: The size of the organisms has an impact on chemical toxicity as well. It has been observed that larger individuals are frequently more resistant to toxins; this is also the case with some fish species.
Health and nutrition: The state of an organism's health and nutrition has an impact on how hazardous substances are to it. In general, healthy people can tolerate toxins better than sick people. It has been noted that people with diseases and parasites are more susceptible than healthy people to a variety of toxicants.

1.6 TARGET ORGAN TOXICITY

The term "target organ toxicity" refers to how dangerous compounds damage specific human organs or tissues. Toxicants can induce injury in a variety of ways, including inflammation, structural damage, functional impairment, and, ultimately, organ malfunctions. The term "toxicity" refers to the extent to which a drug may harm an organism. Understanding target organ toxicity is critical for identifying sensitive groups, calculating the risks of toxic chemical exposure, and taking preventive measures to preserve human health. In addition, the target organ toxicity also refers to toxicants' that have negative effects on specific organs or tissues, such as organ dysfunction, structural damage, or functional impairment. Toxicity affects an substructure of organism, which includes the cells that comprise an animal, bacteria, or plant.

Toxicants can injure cells through a variety of methods, including oxidative stress, genotoxicity, inflammation, immunological dysregulation, and interference with signaling networks. Dose, duration, exposure route, metabolic activity, individual vulnerability, and underlying medical problems. All have negative impact of target organ damage. Understanding the causes and symptoms of target organ poisoning is critical for assessing the risks of toxic substance exposure, identifying sensitive populations, and taking preventative measures to preserve human health.

The liver, kidney, heart, lungs, cardiovascular system, hematological system, visual apparatus, skin, reproductive system, and endocrine system are among the major organs that might be affected by xenobiotics exposure. Toxic responses can be influenced by a number of events, causes, or previous or concurrent exposure to many foreign chemicals. In liver, the damage could lead to cirrhosis or even liver enlargement. Hepatotoxicity can result from any toxicant or toxin, including prescription drugs, herbal treatments, and natural substances. The liver contains the majority of the enzymes found in other tissues that are involved in xenobiotic biotransformation. The liver removes bile from the circulation to aid in the breakdown, storage, and/or elimination of ingested minerals, vitamins, metals, medicines, environmental pollutants, and bacterial waste. Inaddtion, the kidney is the most critical organ for regulating extracellular volume and balancing electrolytes and acid-base levels. The functions of kidney include the elimination of metabolic waste, the generation and release of renin and erythropoietin, and the regulation of the extracellular fluid volume, electrolyte composition, and acid-base balance. Following a single or recurrent high dosage exposure to cardiotoxic substances, cardiac toxicity may manifest as heart enlargement and, eventually, heart failure.

1.6.1 Mechanisms of Target Organ Toxicity

1. **Direct Cytotoxicity**: Certain toxicants induce direct damage to cellular organelles and structures, interfering with cellular activities and eventually resulting in death. Oxidative stress, mitochondrial dysfunction, membrane rupture, DNA damage, protein denaturation, and organelle toxicity can all cause direct cytotoxicity. Direct cytotoxicity commonly targets hepatocytes, nephrons, cardiomyocytes, neurons, and epithelial cells in the gastrointestinal and respiratory systems.
2. **Oxidative Stress:** Reactive oxygen species (ROS) and free radicals created during metabolism, as well as exposure to environmental contaminants, can all cause oxidative stress. This can cause lipid peroxidation, protein oxidation, DNA strand breakage, and cellular damage. Oxidative stress is primarily responsible for a wide range of ailments and organ toxicity, including liver damage, renal failure, dementia, cardiovascular disease, and pulmonary disorders. Antioxidant defenses help to minimize oxidative damage and protect against target organ toxicity. These defenses include both enzymatic antioxidants (such as superoxide dismutase, catalase, and glutathione peroxidase) and non-enzymatic antioxidants (such as glutathione, vitamins C, and E).
3. **Inflammation:** Toxicants induce inflammatory responses, which are primarily responsible for the pathophysiology of target organ poisoning. Fibrosis, leukocyte recruitment, endothelial cells, and other resident cells all create pro-inflammatory cytokines, chemokines, and inflammatory mediators that damage tissue and increase vascular permeability. Immune cells, including neutrophils, macrophages, and endothelial cells, release these mediators. Chronic inflammation has been linked to the development of organ-specific conditions such as lung fibrosis, inflammatory bowel disease, atherosclerosis, diabetic nephropathy, and alcoholic liver disease.
4. **Genotoxicity:** Genotoxicity is the adverse effect of toxicants on DNA, which can result in mutations, chromosomal abnormalities, and DNA damage, potentially leading to cancer, cell cycle arrest, apoptosis, or senescence. These compounds, which include industrial chemicals, medicines, and environmental toxins, can interact directly with DNA or inhibit DNA repair, harming a variety of organs.
5. **Immune Dysregulation:** Toxicants that disrupt the immune system can cause immunotoxicity, autoimmune diseases, hypersensitivity reactions, and impaired host defenses against pathogens. Immunotoxicants disrupt immune cell function, create cytokines, promote lymphocyte proliferation, and modify antibody responses. As a result, they impair immune surveillance, making patients more susceptible to infections, allergies, and autoimmune illnesses.

Immunological dysregulation affects many organs, including the thymus, spleen, lymph nodes, bone marrow, skin, and mucosal tissues.

6. **Disruption of Cellular Signaling Pathways:** Toxicants can disrupt physiological processes and cause toxicity in specific organs by interfering with cellular signaling pathways involved in growth, differentiation, apoptosis, metabolism, and homeostasis. Signaling cascades such as Wnt/β-catenin, JAK/STAT, NF-κB, PI3K/Akt, and MAPK/ERK can alter gene expression, cell survival, proliferation, and differentiation,. It leading to aberrant tissue remodeling, fibrosis, or carcinogenesis.

1.6.2 Toxicants Targeting Specific Organs

1. **LiverToxicity:** Liver toxicity also refers to Hepatotoxicity. Hepatotoxicity" refers to a substance's harmful effects on the liver. Hepatotoxins include pharmaceuticals, chemicals, alcohol, herbal supplements, and viruses. Hepatotoxicity can appear in a variety of forms, ranging from small increases in liver enzymes to severe liver damage, liver failure, and even death. The liver is responsible for the metabolism, detoxification, and the production of essential components. Hepatotoxicity can injure or alter the function of liver in a variety of ways. Additional Hepatotoxins can damage or disturb cells by interfering with physiological processes such oxidative Phosphorylation, protein synthesis, or bile flow.

The type of Hepatotoxins, the amount, the time of exposure, and the susceptibility of each individual all have an impact on the severity of Hepatotoxicity. A single high dosage of a hepatotoxin can cause acute Hepatotoxicity, with symptoms such as jaundice, abdominal pain, nausea, vomiting, or hepatic encephalopathy appearing quickly. Repeated exposure to low doses of Hepatotoxins can cause chronic Hepatotoxicity, which can progress to cirrhosis, fibrosis, or liver damage over time. Several chemical families, each with its unique mode of action and accompanying health hazards, have been discovered as possible Hepatotoxins.

One of the leading causes of drug-induced liver injury (DILI) is medication, which includes prescription, over-the-counter, and herbal supplements. Certain medications have the potential to cause direct damage to liver cells, while others may cause immune-mediated or unique reactions in susceptible individuals. Alcohol is another well-known Hepatotoxins that contributes to alcoholic liver damage. ALD can present as fatty liver, cirrhosis, or alcoholic hepatitis. Long-term alcohol intake can cause inflammation, oxidative stress, and liver cell death, all of which can exacerbate liver damage and dysfunction. Hepatotoxicity has also been linked to industrial toxins, herbal therapies, and certain nutritional supplements. Industrial chemicals such as vinyl chloride, carbon tetrachloride, and chloroform can induce acute or chronic liver injury via direct toxicity or metabolic activation. Hepatotoxicity can cause a number of liver disorders and complications, posing substantial risks to liver health. To protect people from the harmful effects of Hepatotoxins and improve liver health, it is critical to understand the causes of Hepatotoxicity, identify vulnerable populations, and implement preventative measures. Early detection and treatment are critical for controlling Hepatotoxicity and preventing it from progressing to severe liver damage.

Renal Toxicity: Renal toxicity also refers to Nephrotoxicity. Nephrotoxicants, which include environmental toxins, heavy metals, medications, and contrast agents, can injure the kidneys by producing acute kidney injury, chronic kidney disease, tubular necrosis, glomerulonephritis, and renal fibrosis. These deleterious consequences are induced by decreased blood flow, oxidative stress, inflammation, tubular cell death, and mitochondrial failure. People who have already suffered renal failure are more vulnerable to the severe Nephrotoxic effects of most medicines. Therefore, it is critical to be aware of these potential risks.

2. **Cardiovascular Toxicity:** Cardiovascular toxicity refers to the harmful effects of substances on the heart and blood vessels, which may include drugs, toxins, environmental pollutants, or medical therapies. These compounds can cause a variety of symptoms, ranging from minor to severe, depending on the type of toxin, quantity, duration, and individual susceptibility. Long-term exposure to low levels of these compounds can cause heart failure, coronary artery disease, and hypertension.

Cardiotoxicants are divided into various categories, each with its own mode of action and associated health hazards. They are a side effect of many medications, notably those used in cancer chemotherapy, and they can raise the risk of cardiovascular events such as heart attacks and strokes. Environmental contaminants such as heavy metals, industrial chemicals, and air pollution all contribute to cardiovascular toxicity. Fine particulate matter (PM2.5) emissions from industry or automobiles have been related to an increased risk of cardiovascular disease and mortality. To avoid cardiotoxicant toxicity and promote cardiovascular health, risk groups must be identified, preventative actions implemented, and the underlying mechanisms understood.

3. **Neurotoxicity:** The term "neurotoxicity" refers to a substance's adverse effects on the nervous system's composition or function. These substances are known as neurotoxins and can include pesticides, medications, chemicals, heavy metals, and even naturally occurring compounds. Neurotoxicity can cause a range of consequences, including moderate cognitive impairment, major neurological problems, and even death. One of the most essential characteristics of neurotoxicity is its ability to impede normal neuronal function. Neurotoxins can disrupt the electrical signals and neurotransmitters that neurons use to communicate with one another. Certain neurotoxins, for example, can block neurotransmitter receptors, making it difficult for neurons to interact. Others may induce structural damage to neurons, so impeding signal transmission. The effects of neurotoxicity are influenced by a variety of parameters, including toxin type, dose, duration of exposure, and individual vulnerability. High doses of neurotoxins can cause acute exposure, resulting in severe symptoms such as convulsions, unconsciousness, or respiratory arrest. These symptoms can develop swiftly. Long-term repercussions of frequent exposure to lower quantities of neurotoxins may include mood difficulties, movement disorders such as Parkinson's disease, memory loss, and cognitive decline. Neurotoxins, including pesticides and insecticides, are prevalent in agriculture and have been linked to neurodevelopmental and neurodegenerative disorders in children and adults. Industrial pollutants like dioxins and PCBs can accumulate in the food chain, posing significant health risks. Neurotoxicity alters the structure and performance of the nervous system, posing substantial health risks. To mitigate these effects, it is crucial to understand the mechanisms of neurotoxicity, identify vulnerable populations, and implement preventive measures for human health.

4. **Pulmonary toxicity:** The word "pulmonary toxicity" refers to a substance's adverse effects on the respiratory system, namely the lungs. Pulmonary toxicity is the term used to describe extensive respiratory injury. It encompasses a wide spectrum of conditions, ranging from minor irritations to chronic disorders. It is critical to understand pulmonary toxicity in a range of settings, including clinical medicine, drug research, environmental protection, and occupational health. Pneumonitis, or inflammation, is a typical symptom of lung injury. Coughing, chest tightness, dyspnea, and other symptoms may be caused by lung issues. For example, mucus obstructs airways in cystic fibrosis patients, limiting lung function. Mucus also traps bacteria inside the lungs, preventing them from escaping, resulting in recurring lung infections. Occupational exposure to airborne pollutants such as gases, vapors, dust, and fumes increases the

risk of pulmonary toxicity significantly. Workers in areas such as manufacturing, construction, mining, and agriculture are more susceptible to the effects of medications. Exposure to these compounds can result in acute symptoms such as coughing, wheezing, shortness of breath, and chest tightness, as well as chronic conditions such as pneumoconiosis, occupational asthma, and chronic obstructive pulmonary disease (COPD). Environmental contaminants such as nitrogen dioxide, particulate matter, ozone, and volatile chemical compounds can cause pulmonary toxicity, resulting in lung cancer, asthma exacerbation, and respiratory infections. To ensure medication safety and efficacy, it is critical to understand non-targeted organ toxicity, which can occur via direct cytotoxicity, oxidative stress, immunological dysregulation, inflammation, genotoxicity, disruption of cellular signaling pathways, and interference with physiological functions.

Dermatotoxicity: The pharmaceutical and healthcare businesses face a challenging challenge due to the detrimental effects of chemicals on the skin, often known as dermatotoxicity. Because the skin is the body's first line of protection against external threats, everything that may harm this vital organ must be carefully evaluated. Dermatotoxicity can be caused by a wide range of substances, including pharmaceuticals, industrial chemicals, cosmetics, and environmental toxins. Direct irritation, allergic responses, photochemical reactions, and systemic effects that cause cutaneous symptoms are a few of these. Dermatotoxicity testing is critical in the development of medications to ensure their safety and efficacy. Preclinical research involves appraising.

1.7 NON-TARGETED ORGAN TOXICITY

Systemic toxicity, also known as non-targeted organ toxicity, refers to toxicants' adverse effects on organs or tissues other than the primary target organ. Some toxicants might be harmful to specific organ systems due to selective absorption, metabolism, or binding to specific cellular receptors, whilst others can diffuse throughout the body via circulation. Non-targeted organ toxicity can be caused by exposure to environmental toxins or the systemic distribution of drugs, affecting organs such as the liver, kidneys, heart, lungs, and nervous system. Non-targeted organ toxicity causes inflammation, oxidative stress, immune-mediated responses, and direct cellular damage. Drugs intended to treat one organ may mistakenly affect another due to same metabolic pathways or off-target interactions with cellular receptors. Preclinical research and clinical trials are frequently utilized to evaluate pharmaceutical candidates and environmental toxins for potential non-targeted organ damage. Understanding and managing non-targeted organ toxicity is critical to the safety and efficacy of drugs. Multiple mechanisms can cause systemic toxicity, including disruption of physiological processes, interactions with cellular receptors, circulation-based distribution, and metabolic activation. Understanding the processes and manifestations of non-targeted organ toxicity is critical for assessing the overall health risks associated with toxic substance exposure and putting preventative measures into place.

Mechanisms of Non-Targeted Organ Toxicity

1. **Metabolic Activation:** To form reactive intermediates that can covalently bond to cellular macromolecules and induce toxicity. The several toxicants must be metabolically metabolized by phase I enzymes such as cytochrome P450. Toxins that have been metabolically activated can bioactivity in the liver or other tissues, resulting in systemic exposure and unintended organ damage. Procarcinogens include heterocyclic chemicals, aromatic amines, and polycyclic aromatic hydrocarbons (PAHs), which are metabolically transformed to electrophonic

metabolites capable of generating DNA adducts and initiating the carcinogenesis process in a variety of organs.

2. **Distribution via Circulation:** Toxins that are taken systemically can circulate throughout the body. It can cause damage in distant organs and tissues. Lipophilic or protein-bound toxins can pass through cell membranes, cross biological barriers (such as the placental or blood-brain barrier), and accumulate in a range of organs with high blood flow or lipophilic environments. Examples include drugs like statins and antiretroviral, which can spread throughout the body and cause multi-organ toxicity, heavy metals like lead, mercury, and cadmium, and environmental pollutants like dioxins and PCBs.

3. **Inflammation:** The path physiology of non-targeted organ toxicity is mostly based on inflammatory responses triggered by toxicants. Pro-inflammatory cytokines, chemokines, and inflammatory mediators produced by immune and resident cells have an impact on tissue damage, leukocyte recruitment, vascular permeability, and fibrosis. Atherosclerosis, metabolic syndrome, autoimmune diseases, and neurodegenerative illnesses are some of the systemic diseases associated with chronic inflammation. Inflammatory mediators include interleukins (IL-1, IL-6, and IL-8), prostaglandins, reactive oxygen species (ROS), and TNF-α.

4. **Immune Dysregulation:** Toxicants that disrupt the immune system can cause immunotoxicity, autoimmune diseases, hypersensitivity reactions, and impaired host defenses against pathogens. Immunotoxicants disrupt immune cell function, create cytokines, promote lymphocyte proliferation, and modify antibody responses. As a result, they impair immune surveillance, making patients more susceptible to infections, allergies, and autoimmune illnesses. Pesticides (such as carbamates, organophosphates, and mercury), industrial chemicals (such as dioxins and PCBs), heavy metals (such as lead and mercury), and some medications (such as antibiotics and immunosuppressants) are all examples of substances that might impair immune function and raise the risk of systemic toxicity.

1.8 DOSE-RESPONSE

A basic idea in toxicology and pharmacology, the dose-response connection denotes the quantitative link between an organism's biological response and the dose of a drug that is supplied or encountered. Our comprehension of how the length and degree of exposure to different drugs affect their effects on biological systems is supported by this relationship. Knowing the dose-response connection is crucial for evaluating risks, establishing exposure limits, and directing regulatory choices, regardless of whether one is examining the toxicity of environmental contaminants or the therapeutic efficacy of pharmaceuticals.

Characteristics of the Dose-Response Relationship

1. **Threshold:** The dose-response relationship may exhibit a threshold below which no observable effect occurs. The response is regarded as minimal or nonexistent below this threshold dosage. The presence of a threshold indicates that there is an exposure level below which the material has no discernible effects. It is imperative to acknowledge that certain toxicants, including teratogens or carcinogens, may not have a safe threshold.

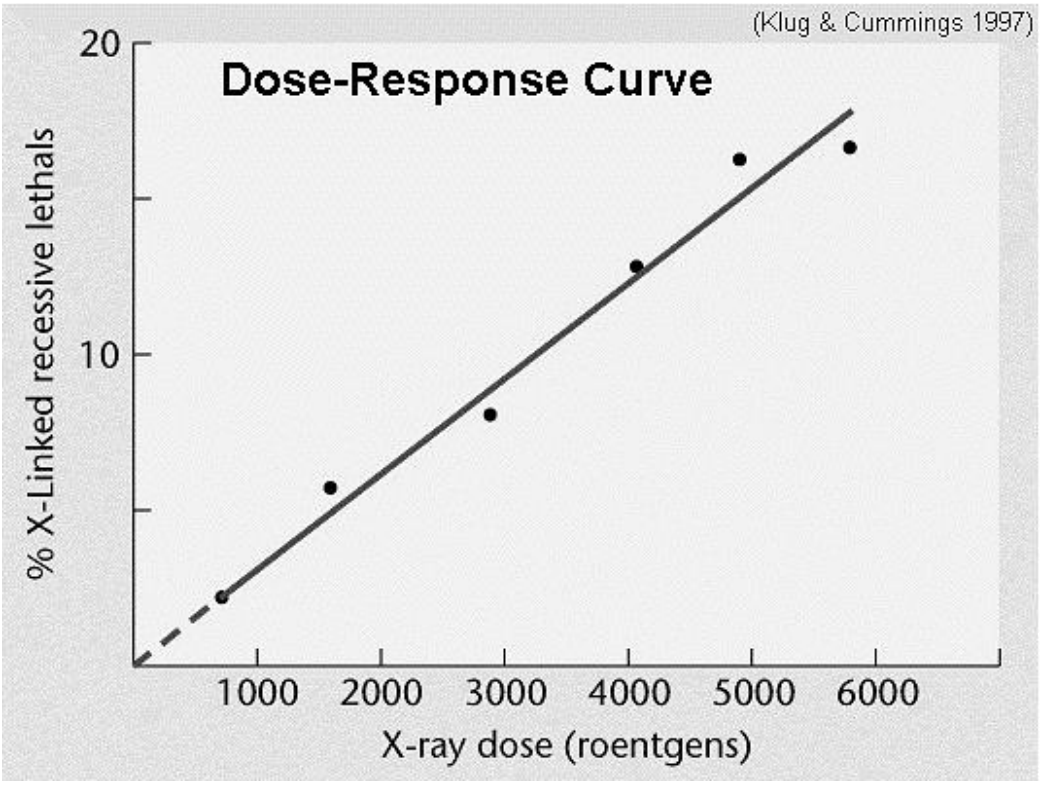
2. **Linearity vs. Non-Linearity**: The dose-response relationship can be linear or non-linear. In a linear relationship, the response increases proportionally with increasing dose, maintaining a constant slope. In contrast, a non-linear relationship may exhibit a curved or sigmoid dose-response curve, where the rate of response changes at different dose levels. Non-linear

relationships may involve saturation kinetics, receptor binding, or complex biological interactions.

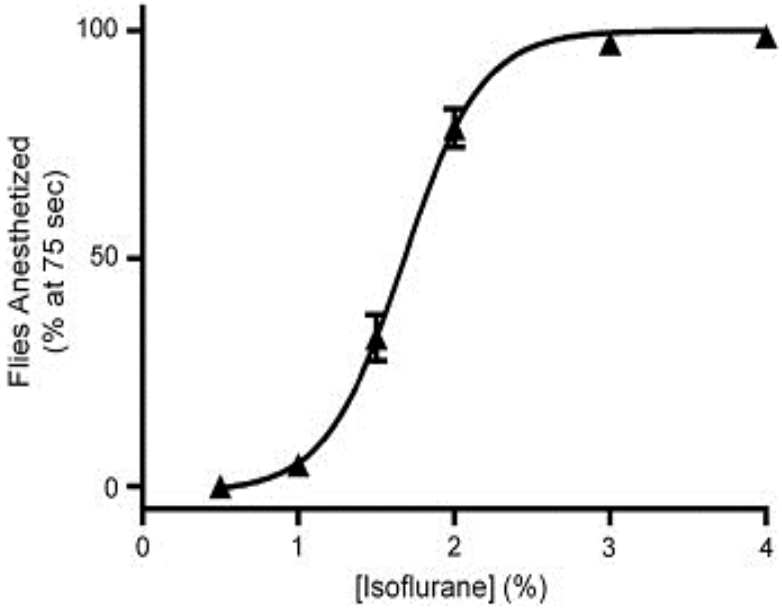
3. **Maximum Response (Efficacy):** The maximum response represents the highest level of response achievable at sufficiently high doses. It reflects the intrinsic activity or potency of the substance and is often expressed as a percentage of the maximum response attainable. Understanding the maximum response is crucial for assessing the therapeutic efficacy of drugs or the toxicity of chemicals and determining the dose required to achieve a desired effect.
4. **Sensitivity and Variability:** The form and strength of the dose-response relationship can be modified by the sensitivity of an organism or population to a given chemical. Age, gender, heredity, nutritional condition, health status, and environmental influences can all have an impact on individual sensitivity and response variation. Understanding inter-individual and inter-species variability is critical for assessing risks, establishing safety margins, and forecasting population-level outcomes.
5. **Duration of Exposure:** The dose-response relationship can be affected by the length of exposure to a substance; distinct reactions may be elicited by acute, sub-acute, sub-chronic, and chronic exposures. While extended or repeated exposures may cause cumulative toxicity, adaptive responses, or delayed effects, short-term exposures may have reversible consequences. It is essential to take the duration of exposure into account when assessing hazards and establishing acceptable exposure thresholds.

Mathematical Models of Dose-Response: Several mathematical models are used to describe and characterize dose-response relationships, each with its assumptions, parameters, and applications:

1. **Linear Model:** The linear dose-response model posits that the dose and response are linearly related, with the response increasing proportionally with the dose. The linear model is straightforward and commonly used to quantify responses at low to moderate doses. However, it may not adequately represent the dose-response relationship at large dosages or account for nonlinear dynamics.

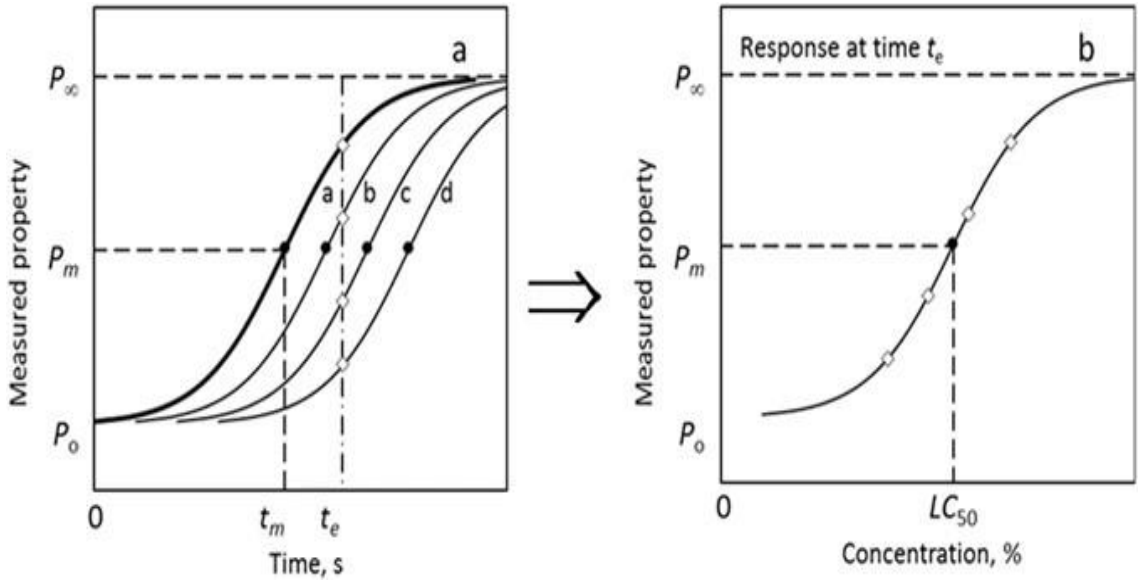


2. **Hill Model (Sigmoid Curve):** The Hill equation defines a sigmoid dose-response curve in which the response approaches its maximum asymptotic value (Emax) as exposure increases. The Hill equation includes parameters such as the slope factor (Hill coefficient) and the concentration that generates 50% of the maximum reaction (EC50 or ED50). The Hill model is frequently used to study receptor-ligand interactions, enzyme kinetics, and pharmacological dose-response relationships.

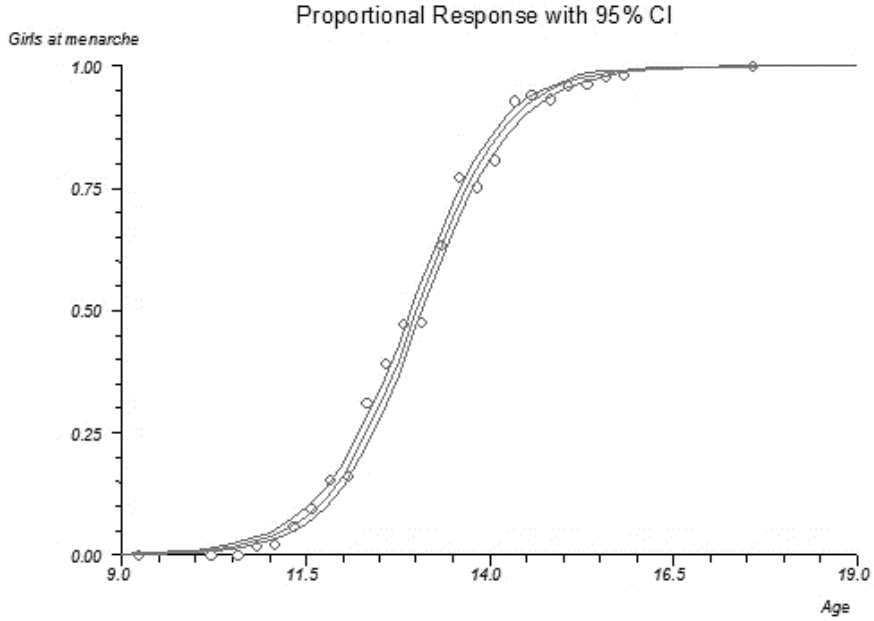


3. **Threshold Model:** The threshold model assumes that there is a threshold dose below which no observable effect occurs, and that responses rise linearly or nonlinearly above the threshold. The threshold model is often used to analyze the risks associated with carcinogens, mutagens, and teratogens, with the goal of determining a safe exposure level.

4. **Logistic Model:** The logistic dose-response model depicts a sigmoid curve with a low initial response phase, followed by a sharp increase and plateau phase at larger dosages. The logistic model is used to fit dose-response data and estimate parameters like the median lethal dosage (LD50) and median toxic dose (TD50). It offers information on the dose required to produce a specific level of response or toxicity.



5. **Probit Model:** The probit dose-response model transforms response data into probit units (standard deviations from the mean) and fits a linear regression model to estimate parameters such as the median effective dose (ED50) or median lethal dose (LD50). The probit model is commonly used for analyzing dose-response data in toxicology and calculating potency estimates, confidence intervals, and dose-response curves.



Factors Influencing Dose-Response- Several factors influence the shape, magnitude, and variability of the dose-response relationship:

1. **Chemical Properties of the Substance**: The absorption, distribution, metabolism, and elimination kinetics of a substance can be influenced by its physicochemical qualities, such as molecular size, polarity, solubility, stability, and bioavailability. These characteristics may also have an effect on the dose-response relationship.
2. **Route of Exposure:** The exposure route determines where a chemical enters the body, where it is absorbed, distributed, and metabolized. Different exposure routes, such as parenteral administration, cutaneous contact, inhalation, or oral ingestion, may result in varying dose-response profiles and systemic effects.
3. **Duration and Frequency of Exposure**: The cumulative dose, the temporal pattern of exposure, and the possibility of adaptive or compensatory responses are all determined by exposure duration and frequency. Intermittent or short-term exposures may have an impact on the dose-response relationship because they elicit different reactions than continuous or long-term exposures.
4. **Metabolic Activation and Biotransformation:** Phase I and II enzymes can change a drug's toxicity and bioavailability via metabolic activation or detoxification. The dose-response relationship may change if metabolites have differing pharmacokinetic and pharmacodynamic properties from the parent substance.
5. **Individual Susceptibility and Variability:** Individual sensitivity to the chemical can varies depending on heredity, age, gender, nutritional state, health status, and environmental factors. Certain people may be more sensitive or resistant to the substance's effects due to previous exposures, pre-existing conditions, or genetic polymorphisms.

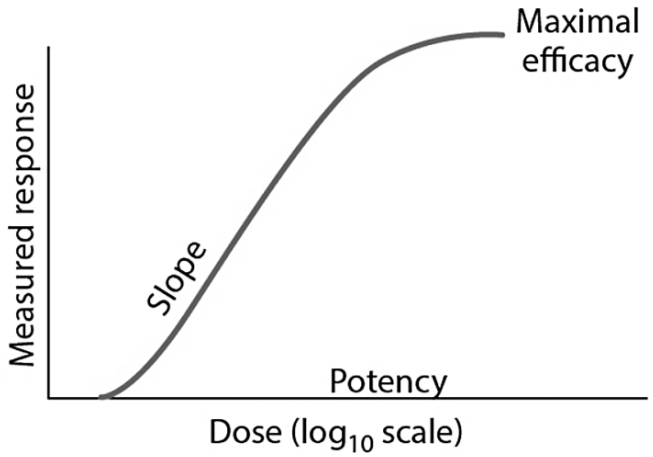
6. **Biological Factors and Homeostatic Mechanisms**: Biological characteristics can influence a person's vulnerability to toxicity as well as their ability to tolerate or adjust to bad outcomes. These variables include organ function, tissue healing ability, immune responses, and homeostatic processes.

1.9 DOSE RESPONSE RELATIONSHIP

A graph of dose-response data typically displays the measured impact (response) on the y-axis and the dose or dose function (such as log10 dose) on the x-axis. Because a pharmacological impact is a function of both dose and time, this graph depicts the dose-response connection that is independent of time. When an effect peaks or when conditions are stable, the effect is typically measured as maximal (for example, during continuous IV infusion). Drug effects can be assessed at the molecular, cellular, tissue, organ, organ system, and organism levels. A hypothetical dose-response curve has characteristics that vary.

- Potency (curve placement along the dose axis)
- Maximal efficacy or ceiling effect refers to the highest possible response level.
- Slope (response per unit dosage)

Biologic variance (differences in response magnitude across test volunteers in the same population given the same drug dose) also occurs. Graphing dose-response curves of medications examined under same settings can aid in the comparison of their pharmacologic characteristics.



A dose-toxicity connection must always exist, and how it appears depends on the processes at work as well as the adverse effects sensitivity to drug concentration and time. This relationship is complex in reality and can appear nonexistent at times. Chemicals and medicines can cause harm in a variety of methods and circumstances, including routine therapeutic use, drug addiction, acute overdose, unintentional poisoning, and workplace exposure. When pharmaceuticals are provided under ideal controlled settings, dose-toxicity correlations for a restricted range of side effects can usually be easily established; in fact, these investigations are an important part of the early clinical evaluation of novel treatments and clinical trials. A comprehensive examination of clinical experience can offer crucial new guidelines, even for extremely old patients.

(1) However, due to the variety of the patient population and a number of confounding and predisposing factors, things are not always so simple in the competitive world of everyday clinical practice. It might be difficult to definitively trace an adverse event to a specific

prescription, and clinicians are not always good at recognizing drug toxicity.

(2) The broader spectrum of acute toxic effects can only be examined in cases of overdosage or poisoning, as drug dosage has a very narrow therapeutic range.

1.10 DOSE RESPONSE CURVES

The manner a medicine induces side effects plays an important role in determining the dose-toxicity relationship. Regardless of the underlying metabolic processes, toxicity is frequently directly proportional to the quantity of the active substance at specific receptor sites.

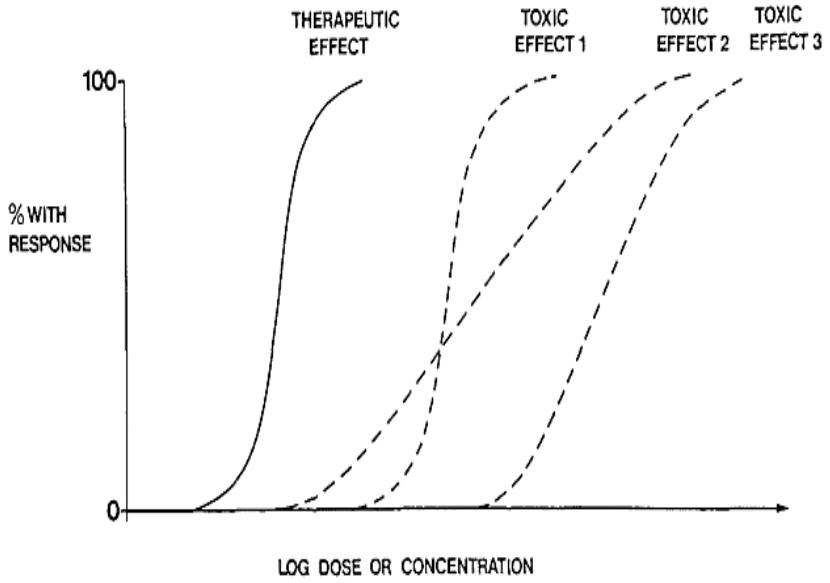


Fig. 1.2 : Hypothetical dose-response curves for therapeutic and different toxic effects. The relative positions of these curves in an individual determine susceptibility to toxicity in relation to the dose required for therapeutic effects.

(Sources: https://www.esteve.org/wp-content/uploads/2018/01/138174.pdf)

The response pattern to a drug's toxicity is similar to the guantalpharmacodynamic dose-effect curve, with distinct toxic effects increasing with dose. Individual sensitivity to toxicity can influence the relative positions and slopes of the curves for therapeutic and toxic effects. The major impact curve shifts to the left, causing "Type A" side effects such an exaggerated therapeutic response. Predisposed or extremely vulnerable individuals also suffer harmful outcomes within the average dose range. As the toxicity curves approach the therapeutic effect curve, the therapeutic index declines. This reaction is shown by the dose-effect relationship between teniposide systemic exposure, therapeutic activity, and severe gastrointestinal toxicity.

1.11 SUMMARY

Toxicology is the study of how chemicals, physical agents, and biological materials cause harm to living organisms. It studies how they interact with biological processes, including as absorption, distribution, metabolism, and excretion. Toxicologists evaluate medication toxicity levels and identify factors that influence vulnerability, such as age, heredity, and medical conditions. Toxicology has sub disciplines include environmental, clinical, forensic, and regulatory. Environmental toxicologists

investigate the effects of poisons on ecosystems and public health, clinical toxicologists manage poisoning patients, and forensic toxicologists evaluate biological material for legal purposes. Toxicologists are critical in determining the safety of chemicals and establishing guidelines for their usage in food, medicine, and consumer goods. They forecast toxicity using modern testing techniques such as in vitro assays and computational modeling.Toxicologists also make evidence-based recommendations to protect the environment and public health from dangerous compounds, which help guide decisions in halthcare, industry, government regulation, and environmental protection.

1.12 TERMINAL QUESTIONS

Q. 1. What is the toxicity? Define the environmental toxicology.

Answer:----------

Q. 2. Writ the history and scope of toxicology.

Answer:----------

Q. 3. What is the environmental toxicants and write it effects on human being.

Answer:----------

Q. 4. Write the types of environmental toxicant.

Answer:----------

Q. 5. Define toxicity and toxic agents with examples.

Answer:----------

Q. 6. What the target and non organ toxicity.

Answer:----------

1.13 FURTHER SUGGESTED READINGS

1. Environmental Toxicology, Kees van Gestel, Vrije University, Amsterdam, Environmental Toxicology
2. Environmental Toxicology, Third Edition, Sigmund F. Zakrzewski, oxford university press
3. A Textbook of Modern Toxicology: Ernest Hodgson A John Wiley & Sons, Inc., Publication
4. Principles of Environmental Toxicology, I. Shaw, J. Chadwick, CRC Press
5. Occupational Toxicology, Chris Winder, Neill H. Stacey, CRC Press.

UNIT-2 : TOXICANTS

Structure

2.1 INTRODUCTION

Toxicants, or toxins, are compounds that can harm living organisms when they come into contact with or swallow them. Several factors, including the type of toxicant, the amount, the duration of exposure, and the individual's vulnerability, can cause harm ranging from mild discomfort to severe sickness or death. Toxins must be understood in order to assess the risks to the environment and human health; it is also necessary to implement preventive measures to avoid exposure and limit the impact of toxicant-related occurrences and consequences on living creatures. Toxicants are both natural and man-made substances produced by fungi, bacteria, animals, and plants as a means of protection, predation, or competition. Plant alkaloids, fungal mycotoxins, mammal poisons, or microbial toxins.Toxicants can originate from man-made or artificial sources such as air pollution, industrial chemicals, pesticides, food additives, pharmaceuticals, and household products. These synthetic toxicants are used for a number of purposes, including production, agriculture, transportation, and consumer consumption. Advances in detection technologies, such as mass spectrometry, immunoassays, and chromatography, allow for reliable toxicant identification and quantification in a variety of matrices. These advancements make it easier to analyze risks, make decisions, and respond to hazards.

Objectives :

After reading this unit, the learner will be able to know about:

- Toxicant and toxicity and classification of toxic agents
- Types of toxins and its sources and its effects on human beings
- Chemical, Animal, plant and foods toxins
- Genetic poisons and its effects

2.2 CLASSIFICATION OF TOXIC AGENTS

Toxic agents are chemicals that, when consumed, can cause harm to living creatures. They can be artificially made or have natural origins and they appeared in a variety of forms. Understanding their classification is essential to identifying possible threats and reducing risks to the environment and public health. Natural sources like fungi, bacteria, plants, and animals are the source of these harmful substances. Toxins generated by certain bacteria, toxic substances in plants, snake venom, and mycotoxins in molds are a few examples. Industrial, agricultural, and pharmaceutical applications are only a few of the uses for which synthetic hazardous compounds are produced by humans.

2.2.1 Natural Toxins

Natural poisons, which are chemical compounds that serve ecological functions like competing with other species, catching prey, and repelling predators, can be toxic when swallowed by humans and cattle. The toxicity and biological function of these poisons vary based on their structures and origin. Understanding their origins, modes of action, effects on organisms, and mitigation and management measures is crucial for preventing their harm. Natural selection and contemporary breeding practices that improve these defense mechanisms may cause food plants to inherently contain toxins. Plants frequently cause medical concerns due to their phytochemicals. The numerous types of flowering plants differ not only in appearance but also in their limitless biochemical properties. Phytochemicals substances were developed to protect flowering plants from potentially hazardous animals and to reward animal pollinators and seed distributors.

2.2.1.1 Plant Toxins

As a defense against infections and herbivores, plants generate a vast variety of poisons. Among these are lectins, glycosides, alkaloids, and cyanogenic glycosides. Alkaloids are nitrogen-containing substances that are present in tobacco, opium poppy, nightshades, and other plants. They can be poisonous or psychedelic. Sugar-bound substances called glycosides, which are present in foxglove and oleander plants, have the potential to harm the heart and other organs. Beans and some grains include proteins called lectins, which can upset the stomach and prevent the absorption of nutrients. The cyanogenic glycosides, which are present in plants like bitter almonds and cassava, emit cyanide, which can be poisonous if ingested in excessive amounts. Plant-based toxins can enter the body by eating, inhalation, or touch. Alkaloids, glycosides, proteins, tannins, volatile oils, terrenes, and steroids are examples of phyto-constituents found in plants that function in the bodies of animals and humans through certain mechanisms involving receptors, transporters, enzymes, and genetic material. Because several plants include harmful elements throughout, the most crucial aspect of these treatments is their dosage.

Classification of Plant Toxins

Alkaloids: Alkaloids are fundamental chemical compounds derived from amino acids that include

nitrogen in a heterocyclic ring. The majority of alkaloids exert significant physiological effect. The harmine a plant toxin that have effect on central nervous system is inhibits monoamine Oxidase A (MAO-A), an enzyme that degrades monoamines, making it a reversible inhibitor of monoamine Oxidase A (RIMA). Harmine does not inhibit MAO-B. Harmine is also known as banisterin, telopathin, telepathine, leucoharmine, and yagin/yageine.

Pyrrolizidine: Pyrrolizidine causes liver veno-occlusive disease. Tropanes act on the autonomic nervous system; atropine, scopolamine, and hyoscyamine. The main worry with glycoalkaloid poisoning is its acute toxicity.

Glycosides: Cyanogenic glycosides, which are connected to sugar chains, release prassic acid and block electron transport by binding to mitochondrial cytochrome oxidase. Acute cyanide intoxication symptoms include cyanosis, twitching, convulsions, coma, fast breathing, low blood pressure, dizziness, headache, stomach aches, vomiting, diarrhea, mental disorientation, and stupor.

Tannins: These chemicals possess the ability to precipitate proteins. They toughen the skin by deceiving its proteins.

Proteins: Many protein poisons that are produced by plants infiltrate eukaryotic cells and use enzymes to restrict the synthesis of new proteins. White acacia, abrin (rosary pea), and ricin (castor plant) are a few examples of harmful proteins.

Oxalates: Crystallized fluids or saps are known as oxalates. These needle-shaped crystals have the potential to irritate the throat, tongue, lips, and skin. Burning feelings, respiratory problems, sore throats, and upset stomachs may result from this. These components may be present as trichomes, or needle-like structures, called raphides. They might mechanically annoy you. There will be absorption of the oxalate that is ingested. In blood, oxalate and calcium combine to generate insoluble calcium oxalate. Severe hypocalcemia and tetany could occur.

Anti-vitamins: Certain compounds, such as Coumadin, which is anti-vitamin K, and thiaminases found in horsetails and bracken, which degrade thiamine, work against the vitamins.

Volatile oils: Volatile oils are liquid compounds produced by oil cells, glands, hairs, and channels. All of them dissolve in alcohol. Some are emetic and irritant (producing blisters) at certain concentrations. Nephrotoxic oils are among the volatile oils.

Furocoumarins: These poisons can be found in a variety of plants, including celery roots, parsnips (which are related to carrots and parsley), citrus plants (lemon, lime, grapefruit, and bergamot), and several medicinal plants. Stress-causing elements include physical injury to the plant and the secretion of furocoumarins, which are stress poisons. Some of these poisons can cause gastrointestinal problems in sensitive people. Furocoumarins are phototoxic and can cause severe skin reactions when exposed to UVA light.

Lectins: Kidney beans, especially red kidney beans, have the highest concentration of lectins. Raw beans may cause vomiting, diarrhea, and a terrible stomachache. To remove lectins, dried beans must be soaked for at least 12 hours before being properly cooked in water for at least ten minutes.

Solanines and chaconine: All solanace plants, including potatoes, tomatoes, and eggplants, contain natural toxins known as solanines and chaconine, both glycoalkaloids. Green tomatoes, potato sprouts, and the bitter-tasting peel and green parts all contain more of this chemical, though the levels are often minimal. Plants produce poisons in response to a variety of stresses, including damage, ultraviolet radiation, infections, and insect pest and herbivore attacks.

Poisonous mushrooms: A number of toxins, including muscimol and muscarine, which are found in wild mushrooms, can induce hallucinations, vomiting, diarrhea, disorientation, and salivation. The onset

of symptoms happens at least six to twenty-four hours after eating mushrooms.

Mechanism of Action of Plant Toxins: Plant poisons have a wide range of medical applications and are found in foods used in ethno medicine and cosmetics, thus understanding their toxicity mechanism is very important.

Neurotoxins: Neuroactive alkaloids can operate as antagonists or agonists, inhibiting or stimulating certain neuroreceptors. They target neuronal cells and inhibit the enzymes that degrade neurotransmitters. Neurotoxins have an effect on key ion channels such Na+, K+, and Ca2+, which can be permanently activated or deactivated.

Cytotoxins: Many phytochemicals are classed as cytotoxins because they disrupt essential cellular functions. However, these chemicals, which play a role in the import and export of metabolites and ions in cells, primarily target bio-membranes. Saponins, including steroidal and triterpenoids, have the ability to dramatically degrade membrane fluidity and integrity.

2.2.1.2 Animal Toxins

Although environmental toxins that occurs from food, water, and animals has global issue, because they most commonly in tropical and underdeveloped areas cause higher risk. Animal poisons are a complicated concoction of chemicals, enzymes, and polypeptides that can harmful to cells. Venom poisoning path physiology involves multiple pathways. Enzymes, polypeptides and chemicals can all cause direct harm. Polypeptides work by interfering with ion channels and cell membrane receptors. Toxins are even produced by many animals as a kind of protection or to seize prey.

Venom from snakes, spiders, scorpions, and marine life such as jellyfish and cone snails are a few examples. Nonetheless, a variety of chemicals are available to venomous animals for both defense and predation. The precise number of venomous species and the quantity of toxins they produce are difficult to understand. The biological activity and therapeutic potential of several venomous animals and their poisons have been studied. A complex blend of proteins and peptides found in snake venoms can impact tissue damage, neuromuscular transmission, and blood coagulation. Enzymes, polypeptides, and proteins are examples of protein components. Numerous pharmacological actions, including myotoxic, neurotoxic, hypotensine, hemolytic, platelet-aggregation inhibition, anticoagulant, inflammatory, analgesic, and bactericidal, have been documented for these toxins.

Numerous neurotoxic, cardiotoxic, cytotoxic, nerve growth factor, lectins, disintegrins, and other substances are found in snake venom. The deadly neurotoxic protein found in Indian king cobra venom. Envenomation by cobras or sea snakes frequently results in respiratory arrest prior to the manifestation of any localized or systemic cardiovascular damage. Acetylcholine (Ach), a neurotransmitter, is competitively antagonistic by the toxin at the neuromuscular junction of skeletal muscle.

Protein hemorrhagic toxins assault the capillary endothelium, causing it to bleed plasma proteins and blood cells, which cause localized tissue swelling (edema). Muscle necrosis may result from the abnormal release of intracellular calcium reserves in skeletal muscle brought on by protein myotoxins. A strong neurotoxin is present in the venom of the Brazilian rattlesnake, Crotaludurissusterrificus. While vipers are found only in Africa and Europe, pit vipers are found throughout North and South America. Pit vipers and their venoms have more concentrated effects on the circulatory system and the tissues where they bite. Poisonous snakes are classified into four families: The pit vipers (family Crotalidae)

- The vipers (Viperidae)
- The cobra (Elapidae) and
- The sea snake (Hydrophiidae)

Scorpions' toxins: Scorpions produce action potentials that quickly immobilize the majority of their prey, primarily insects, by acting on voltage-gated sodium and potassium channels via a complex mix of peptides. Mesobuthustamulus, an Indian red scorpion, has been associated to several cardiac diseases, including acute myocarditis, bradyarrhythmias, and various degrees of heart block.

Spider venoms: Alpha latrotoxin, a potent protein toxin, is the main cause of their venom's neurotoxin effects. Spider venom often contains neurotoxins, which damage nerve function. Peptide poisoning is present at one of the highest amounts. Humans who are poisoned by shellfish may have paralysis, amnesia, or diarrhea as a result of the buildup of marine toxins created by din flagellates and other organisms. Spider venom (Loxoceles sp.) operates entirely differently since its primary constituent is the tissue-damaging enzyme sphingomyelinase.

Snail toxins: Cone snails are one of the several aquatic species whose potential for medicine has been thoroughly investigated. Conotoxins are the poisons that are primarily used by cone snails to kill, immobilize, and shock their prey, while they can also be used defensively. Exendin-4 is the name of the hormone in the human digestive tract that is referred to as glucagon-like peptide-1 (GLP-1), which is analogous to the glucagons found in lizard venom. The hormone called GLP-1, which promotes the manufacture of insulin, is released in response to elevated blood sugar.

Frog toxins: Frog skin has yielded a multitude of strong bioactive chemicals with intriguing structures. By attaching to the open channel of the nicotinic receptor in skeletal muscle, the alkaloidal toxin histrionicotoxin induces neuromuscular paralysis. The epidermis and parotid glands behind the eyes of Bufo toads are particularly powerful venomous. Epinephrine and bufotenin, a methylated version of serotonin, are examples of biogenic amines. The principal poisonous components are cardiac glycosides known as bufotoxins. Dendrobates and Phyllobates frogs secrete more than a hundred different toxins, according to skin secretions analysis. In several species of South American poison-dart frogs belonging to the genus Phyllobates, there are strong steroidal alkaloids called batrachotoxins that have neurotoxic and cardiotoxic effects. By permanently obstructing the transmission of nerve signals, batrochotoxin causes death. It is employed in the research of the Na^+ channel as a biochemical instrument. Hombobatrachotoxinin, bathachotoxinin A, and bathachotoxin R are the remaining members of the family. The skin of the poisonous Dentrobateshistrionicus arrow frog was used to extract a piperidine alkaloid known as histrionicotoxin. Nicotine receptors are blocked non-competitively as a result. It performs the role of a biochemical probe for the neuromuscular signal transmission process.

Fish and mollusk toxins: The majority of fish species do not possess venom, and those that do are always utilizing it as a defensive mechanism to deter potential predators. Catfish and Stingrays are the two most frequently seen venomous fish species. After being identified, the stonefish toxin is a big protein that increases the release of neurotransmitters from nerve terminals. In order to examine the Na^+ channel, electro physiologists and biochemists most frequently use two toxins like saxitoxin and tetrodotoxin. Many fish species in the Tetradoxtidae family, particularly the globe fish Spheroidesrubripes, release tetrodotoxin from their ovaries and liver. As per the Ishikawa Health According to the Service Association of Japan, tetrodotoxin is over 100 times more poisonous than cyanide. Gonyaulaxcatenella and G. tamarensis are two species of marine dinoflagellates that produce saxitoxin, a neurotoxin.

2.2.1.3 Microbial Toxins

Toxins that are produced by bacteria, fungus, and other microorganisms are called microbial toxins. The toxins produced by fungus and bacteria can sicken both people and animals. Examples are the bacterial toxins that cause botulism, a potentially fatal condition that affects the neurological system are produced by Clostridium botulinum. Mycotoxins, or fungus-induced toxins, can cause poison food crops including grains, nuts, and spices, causing either short-term or long-term harm. Mycotoxins

include the powerful carcinogens aflatoxins produced by Aspergillus species and the convulsive and hallucinogenic ergot alkaloids produced by Claviceps species. Microbiological toxins are substances that, when in contact with or absorbed by bodily tissues, can cause disease. They do this by directly harming host tissues and by impairing the immune system. The earliest bacterial virulence factors to be discovered were thought to be toxins. A common way that bacterial infections cause disease is by a process called toxicity, or the capacity to create toxins.

Toxins are of two types:

Endotoxins: Endotoxins are compounds linked to cells that are part of the bacterial structure. The cell envelope is where most endotoxins are found. The term "endotoxin" particularly describes the lipopolysaccharide (LPS) or lipooligosaccharide (LOS) found in Gram-negative bacteria's outer membrane. Soluble endotoxins, although being structural components of cells, can be produced by developing bacteria, lysed cells brought on by strong host defenses, or bacteria exposed to specific drugs.

Exotoxins: Exotoxins often function at a location apart from bacterial growth and are released by bacteria. But sometimes, the bacterial cell's lysis is the only way for exotoxins to be produced. Exotoxins are mostly proteins, seldom polypeptides that interact directly or through enzymes with host cells to trigger a range of host reactions. The majority of exotoxins function at tissue locations that are far from the original site of bacterial invasion or growth. Nonetheless, several bacterial exotoxins function at the site of pathogen colonization and might contribute to invasion. Some characters of bacterial toxins:

1. Some bacterial toxins that clearly cause an animal's death are referred to as fatal toxins. The exact process by which death transpires is unclear, despite the fact that the tissues impacted and the target site or substrate may be understood.
2. Certain bacterial toxins are used as invasive agents because they stimulate bacterial invasion at the local level. Extracellular enzymes are one example; they break down fibrin or tissue matrices, facilitating the bacteria's spread. This comprises the enzymes streptokinase, hyaluronidase, and collagenase.
3. The pore-forming toxins that cause a pore to open up in eucaryotic membranes are also regarded as invasins.
4. Certain protein poisons attack particular cell types due to their very selective cytotoxic effect. For instance, only neurons are harmed by botulinum toxin and tetanus.
5. Some toxins produced by staphylococci, streptococci, clostridium, and other microorganisms have a somewhat wide cytotoxic action, leading to non-specific cell death or tissue damage that ultimately culminates in necrosis.
6. Phospholipase-containing toxins function in this manner. Leukocidins and hemolysins that produce pores also exhibit this property.
7. The poisons produced by bacteria are highly antigenic. Specific antibodies operate as an in vivo counteractant to the toxicity of these bacterial exotoxins.
8. A particular antitoxin might not completely stop their activity in vitro. This implies that the toxin's antigenic determinant and the protein molecule's active component can be different.
9. The toxin is completely neutralized in vivo, it is likely that other host components are involved in the natural process of toxin neutralization.

10. Exotoxins made of proteins are by nature unstable. Over time, their poisonous qualities disappear while their antigenic qualities persist. Ehrlich made the initial discovery of this and gave this product the moniker "toxoid".

Toxoids: Toxoids are poisons that have been cleansed but still have the ability to immunize and be antigenic. By treating toxins with a range of reagents, such as formalin, iodine, pepsin, ascorbic acid, ketones, etc., the synthesis of toxoids can be expedited. The combination is kept for a few weeks at 37 degrees with a pH between 6 and 9.

Biological Accumulation:Natural poisons have the capacity to accumulate in the food chain and increase in abundance in predators at higher trophic levels. Phenomena called as biological magnification, or biomagnifications, may occur when people or animals eat poisoned prey, putting both groups in danger. For example, marine contaminants produced by algae can accumulate in fish and shellfish, thereby posing a threat to marine mammals and humans that consume them.

2.2.2 Artifical Toxins

Artificial poisons are toxic compounds created by humans, such as pesticides, industrial chemicals, and pollution. PCBs, for example, are commonly used in hydraulic systems and electrical equipment but are banned due to their negative impact on the environment and human health. These poisons can have long-term health consequences, including cancer, brain damage, and developmental abnormalities. They have the potential to devastate ecosystems and wipe out species. To offset these negative effects, effective management and regulation are required. To lessen our reliance on hazardous synthetic toxins, we must work to create safer alternatives as well as environmentally friendly industrial and agricultural methods. Pesticides, including carbamates and organophosphates, are a prominent type of man-made poisons. However, they can be harmful to non-target animals such as wildlife, humans, and beneficial insects like bees. Heavy metals such as lead, mercury, and arsenic can be released into the environment by industrial operations, accumulating in soil, water, and living creatures and causing serious health hazards.

2.3 FOOD TOXINS

The term "food toxins" refers to substances contained in the food which human consumed; it can be hazardous to human health. These poisons may be naturally present in some foods or added during food preparation, processing, or storage. To ensure food safety and prevent food borne illnesses, it is critical to understand food toxins. In other words the food toxins refer of hazardous substances that pose substantial health risks to people when consumed in contaminated food. To prevent food borne illnesses caused by toxins, a variety of tactics are required, including strict food safety legislation, proper handling and storage practices, agricultural practice monitoring, and public education on safe food preparation methods. We can protect public health and the integrity of our food supply by knowing the sources and consequences of food toxins, as well as implementing effective preventive actions.

Bacterial Toxins: Pathogenic bacteria can create toxins that kill cells and impair their ability to operate normally. Hemolysins, lysins, and phospholipases are examples of how they act on the cell membrane, but they also have an impact on other intracellular targets. They are sometimes the single cause of illness, but most of the time they work in tandem with other virulence factors to help bacteria establish themselves in the host while avoiding or opposing defenses. Many bacterial toxins are proteins encoded by phages, plasmids, or bacterial chromosomal genes. Although lysis is routinely used to remove toxins from organisms, some are released in outer membrane vesicles with proteins. Gram-negative bacteria's lipopolysaccharide, often known as endotoxin, is a primary non-protein toxin found in their cell wall. Toxins can harm or affect the function of eukaryotic cell membranes when they interact with particular

structural properties. Bacteria including Staphylococcus aureus, Salmonella, and E. coli can produce toxins when cultivated in food. These substances can induce digestive problems and food poisoning. To prevent bacterial contamination and toxin generation, use proper food handling, storage, and cooking practices.

Mycotoxins: Molds on food crops such as grains, nuts, and dried fruits produce toxic chemicals known as mycotoxins. Aspergillus molds create one of the most well-known mycotoxins, aflatoxin, which has been associated to liver damage and an increased risk of liver cancer. Mycotoxin contamination can be reduced through thorough monitoring of farming processes, optimal storage conditions, and timely harvesting.

Heavy Metals: Heavy metals such as lead, mercury, and cadmium can accumulate in the body over time and cause a number of health problems, including neurological disorders, kidney damage, and developmental issues in children. These metals can be found in some foods. Heavy metal contamination in food is typically induced by contaminated soil, water, and air. Controlling heavy metal levels in food necessitates both regulatory efforts and careful monitoring. Mycotoxin contamination of crops such as maize, wheat, peanuts, and other grains is common during cultivation and postharvest storage. Mycotoxins are mostly produced by fungus belonging to the genera Aspergillus, Penicillium, and Fusarium. Their growth and multiplication can be exacerbated by factors such as humidity, temperature, and inadequate storage conditions. Consuming food contaminated with mycotoxin might result in both short- and long-term health problems. Acute effects may appear immediately after consumption, including nausea, vomiting, and abdominal discomfort. Severe cases might lead to organ failure or death. Long-term exposure to low levels of mycotoxin has been linked to immunological suppression, developmental abnormalities, neurological disorders, and an increased risk of cancer. Mycotoxins pose a substantial risk to human health and food safety, thus governments, industries, and researchers must work together to limit their impact. Ensuring the safety and quality of the world's food supply can be accomplished by reducing the hazards associated with mycotoxin contamination and implementing enhanced detection techniques, regulatory measures, and preventive strategies. nic into the environment, which can build up in soil, water, and living beings, creating serious health concerns.

Chemical Contaminants: Throughout food manufacturing, processing, or packaging, chemicals including pesticides, herbicides, and food additives can contaminate food. These substances can cause long-term harm to human health, such as imbalanced hormones, cancer, and problems with reproduction. To reduce chemical contamination in food processing, strict laws, appropriate use of agricultural chemicals, and compliance with safety standards should be followed. Chemical pollution in food can come from a variety of sources, including synthetic fertilizers and pesticides used in agriculture, veterinary medication residues in animal products, industrial pollution of the environment, toxins leaking from food packaging materials, and accidental or intentional contamination during food processing and handling. There are distinct dangers to food safety associated with each of these sources, necessitating specific risk management techniques. Chemical toxins found in food can cause a variety of harmful health consequences, from acute poisoning to chronic illnesses and long-term health problems. For instance, pesticide residues may raise the risk of cancer, reproductive issues, and developmental anomalies when exposed over an extended period of time. They can also induce acute toxicity, allergic reactions, and neurological diseases. A similar accumulation of pollutants in the body over time can result in systemic toxicity and long-term health issues. Examples of these contaminants include industrial chemicals, heavy metals, and persistent organic pollutants (POPs).

Natural Toxins: Toxins included in food naturally assist food items to protect themselves against pests and predators. For example, lectins and phytohaemagglutinin contained in certain bean varieties can cause poisoning and stomach issues if cooked incorrectly. Furthermore, certain seafood can accumulate toxins such as saxitoxin and ciguatoxin, which can cause neurological symptoms and food poisoning.

Natural poisons can be decreased by cooking safely and removing potentially toxic components from some meals.

2.4 GENETIC POISONS

The term "genetic poisons" refers the substances or processes that can damage genetic material, such as DNA or RNA, and its negative impact on human health. however, there is no specific class of toxins designated as "genetic poisons," a range of chemicals and conditions can induce genetic damage, mutations, or disturbances in normal cellular activities, all of which can result in diseases or disorders. This essay will discuss the numerous types of genetic toxins, their sources, mechanisms of action, health consequences, and mitigation and prevention measures. Many agents and situations can damage DNA, RNA, or other genetic material, causing negative health effects. These chemicals and conditions are known as genetic poisons. Many genotoxicity assays, both in vitro and in vivo, have been developed to detect DNA damage or its biological effects in prokaryotic (such as bacteria) or eukaryotic (such as mammalian, avian, or yeast) cells utilized. These tests are used to determine the mode of action of known or suspected carcinogens, as well as to evaluate the safety of consumer items and environmental pollutants. Examples include ionizing radiation, chemical mutagens, genotoxic medications, environmental and occupational exposure, and lifestyle choices. Developing solutions to stop and reduce genetic damage and the associated health dangers involves an understanding of the causes, mechanisms of action, and impacts of genetic poisions.

Radiation-induced Genetic Damage: Ionizing radiation can produce mutations in gonads or germ cells, altering the genetic code and causing genetic illnesses (hereditary abnormalities). Ionizing radiation, such as gamma and X-rays, as well as some other particles, can break or cross-link DNA strands, causing direct damage to DNA molecules. This damage may cause cell death, chromosomal abnormalities, and mutations. Ionizing radiation can be emitted by a variety of sources, including nuclear accidents, medical imaging procedures (e.g., CT scans and X-rays), and occupational exposures. Long-term ionizing radiation exposure has been associated to an increased risk of genetic abnormalities, cancer, and other adverse health outcomes.Even now, no link has been established in people between radiation exposure and the development of genetic harm. The International Commission on Radiological Protection (ICRP) estimates that for every 500 newborns, radiation-induced mutations cause one new major disease for each parent who received a single (acute) gonadal dose of one gray (Gy).

Chemical Mutagens: Chemical mutagens are compounds that cause mutations and can be synthesized chemically or naturally. Chemical agents that increase the risk of cancer might be characterized as biological, physical, or chemical. Interactions between specific substances and DNA molecules can result in mutations, structural alterations, or chemical changes. These agents, known as mutagens, can include tobacco smoke, industrial toxins, environmental pollutants, and some prescription drugs. The chemical mutagens include the following:

- PAHs can be found in car exhaust, cooked food, and tobacco smoke.
- Aflatoxin-producing molds in food crops such as peanuts, corn, and tree nuts.
- Cyclophosphamide and cisplatin are examples of alkylating medicines used in cancer chemotherapy.
- Benzene, a solvent found in gasoline and cigarette smoke, is also present in industrial processes.
- Chemical mutagen exposure increases the risk of genetic disorders, cancer, birth defects, and reproductive difficulties.

Genotoxic Pharmaceuticals: Certain pharmaceuticals can disrupt DNA or obstruct regular biological

functions, which are known as their genotoxic effects. These medications can be used for antibiotic therapy, chemotherapy, and other medical conditions, but if not taken correctly, they can be dangerous for patients. Pharmaceuticals that are genotoxic include:

- Drugs based on platinum, like cisplatin, alkylating agents like cyclophosphamide, and topoisomerase inhibitors, like etoposide, are examples of chemotherapeutic medicines.
- Some antibiotics that can harm bacterial cells' DNA include nitroimidazoles (like metronidazole) and fluoroquinolones (like ciprofloxacin).
- Antiretroviral medications, such zidovudine (AZT), which are used to treat HIV/AIDS and have the ability to block DNA replication and repair processes.
- Patients may have adverse medication reactions, treatment-related problems, and long-term health hazards as a result of the genotoxic effects of pharmacological pharmaceuticals.

Environmental and Occupational Exposures: Genetically harmful substances can be acquired by people from occupational or environmental sources, including chemicals used in the workplace, hazardous waste sites, industrial emissions, and pollution of the air and water. As an illustration:

- Environmental exposures to pollutants such as heavy metals (e.g., lead, mercury), persistent organic pollutants (e.g., dioxins, PCBs), and pesticides (e.g., organophosphates, glyphosate).
- Occupational exposures to carcinogens such as benzene, asbestos, and formaldehyde in industries such as manufacturing, construction, and mining.
- Lifestyle choices including drinking alcohol, smoking cigarettes, and eating a poor diet can potentially exacerbate genetic harm and raise the chance of developing chronic illnesses.

2.5 CHEMICAL TOXINS

Chemical toxins are compounds that can harm humans or other living organisms whether found in food, drink, air, or the environment. Bacteria, fungi, and plants naturally create these poisons. Pollution, industrial operations, and agricultural practices are all instances of human activity that might generate these toxins. To preserve human and environmental health, it is vital to understand the dangers posed by chemical toxins, be able to identify their origins, and employ effective mitigation techniques.

Chemical toxins can enter the environment and food chain through a variety of mechanisms. Industrial processes such as mining, manufacturing, and waste disposal emit pollutants into the atmosphere, water, and land. This poisoning of the environment occurs. Chemical residues can get up in crops and livestock products as a result of agricultural activities including fertilizer and pesticide use. Natural occurrences such as algal blooms and volcanic eruptions, as well as food processing, packaging, and storage, can all cause chemical contamination.

Chemical toxins include heavy metals (such as lead, mercury, and cadmium), pesticides, herbicides, industrial chemicals (such as dioxins and polychlorinated biphenyls, or PCBs), food additives, persistent organic pollutants (POPs), and microorganism-produced toxins (such as mycotoxins and bacterial toxins). Exposure to different types of toxins may have varied health consequences due to their distinct features and toxicity pathways. Chemical toxin exposure can have a variety of unfavorable health effects, depending on the toxin type, dose, duration of exposure, and individual sensitivity.

Acute poisoning can induce immediate symptoms such as vomiting, nausea, respiratory difficulty, and neurological damage. Long-term exposure to low levels of pollutants can cause cancer, reproductive illnesses, neuro-developmental problems, immunological dysfunction, and organ damage.

Chemical toxins endanger public health, environmental integrity, and food safety all across the world. Governments, corporations, academics, and consumers must collaborate to successfully manage chemical toxins by detecting sources of contamination, analyzing risks, implementing mitigation measures, and supporting sustainable practices. It is feasible to lessen the negative effects of chemical toxins on public health and build a safer and healthier environment for present and future generations by placing a high priority on prevention, regulation, education, and innovation. Addressing emerging threats and ensuring the health of global ecosystems and populations necessitates continuous research, observation, and attention. Chemical toxicity reduction and prevention must be approached from several perspectives, taking into account both non-regulatory and regulatory approaches. Governments and international organizations develop regulatory frameworks that establish standards and upper limits for the levels of toxins in food, water, air, and the environment. Surveillance systems, enforcement actions, and monitoring programs all work together to ensure that these requirements are followed and the public's health is protected. Non-regulatory measures reduce or eliminate harmful exposure by implementing best practices and technologies, with a focus on prevention. These could consist of as follows:

- The use of fewer pesticides in agriculture through integrated pest management (IPM).
- Industry use of pollution control and cleaner production methods.
- Putting appropriate waste management procedures into place to stop environmental contamination.
- Campaigns for agro-ecology, organic farming, and sustainable agricultural methods;
- Education and training programs to inform stakeholders about the dangers of chemical poisons and the value of taking preventative action.

2.6 SUMMARY

The number of substances is toxicants, posing substantial dangers to both human health and the environment. These hazardous compounds can contaminate food, water, air, and consumer products, among other areas of daily life, and can come from either human or natural causes. Heavy metals, herbicides, industrial chemicals, pollutants, and naturally occurring toxins are only a few of the numerous toxicants. Toxicant exposure can cause both short-term symptoms like nausea and respiratory discomfort, as well as long-term consequences such as cancer, reproductive issues, and neurological impairments. The elderly, children, and pregnant women are especially vulnerable since even low amounts of exposure can have a major deleterious impact on their development and health. Toxic risks must be avoided and reduced through a multidimensional approach that includes public awareness campaigns, technical developments, and regulatory initiatives. Governments and international organizations can establish rules and regulations to control toxicant levels in food, water, air, and consumer goods. Monitoring programs and enforcement activities protect public health while ensuring standard compliance. Finally, collaboration and coordination among governments, corporations, academic institutions, and local communities are required to address the complex concerns created by toxicants. It is possible to lessen toxicants' negative impacts on the environment and human health by prioritizing prevention, regulation, education, and innovation. Continuous inquiry, observation, and vigilance are required to identify new threats and change strategies to protect public health and ensure a sustainable future.

2.7 TERMINAL QUESTIONS

Q. 1. How does one define a toxicant? Write about the origins and impacts of toxicants on people.

Answer: ----------

Q. 2. How do you define bacterial toxins? Which processes do bacterial toxins act through?

Answer: ----------

Q. 3. What do you mean by the endo and exobacterial toxins?

Answer: ----------

Q. 4. What do the immune system's bacterial toxins represent?

Answer: ----------

Q. 5. How do chemical and physical mutagens differ from one another?

Answer: ----------

Q. 6. What is toxicity determined by genetics? What does genetic toxicity look like?

Answer: ----------

2.8 FURTHER SUGGESTED READINGS

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3. A Textbook of Modern Toxicology: Ernest Hodgson A John Wiley & Sons, Inc., Publication

4. Principles of Environmental Toxicology, I. Shaw, J. Chadwick, CRC Press

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UNIT-3 DURATION AND EXPOSURE OF TOXICANT

Structure

3.1 INTRODUCTION

The duration and intensity of exposure of toxicant have a significant impact on how the body reacts to it and cause discomfort. Long-term exposure i.e. called chronic exposure may produce cumulative damage over time, whereas short-term exposure i.e. called acute exposure may trigger symptoms immediately. Acute exposure is usually brief and might cause symptoms such as nausea, vomiting, and difficulty breathing. Chronic exposure, on the other hand, occurs over a longer period of time and may not result in immediate symptoms, but it can have long-term harmful effects on health, including also a risk of cancer and organ damage. Toxicity is affected by the level of exposure of toxicant, which is determined by factors such as its concentration, route of exposure, and ambient conditions. The long term exposure levels are often associated with higher risks; whereas short term exposure includes oral consumption, cutaneous contact, and inhalation are often associated with lower risk. To reduce the negative effects of toxicant exposure on human health and the environment, here is necessary to drive preventative measures which should be risks assessed, public education, legislation, and monitoring.

Objectives :

After reading this unit the learn will be able to know

- the acute exposure and chronic exposure and its effects
- the types of human exposure like internal and external exposure and its control
- the occupational and environmental exposure
- the accidental and internal poisoning and is effects, prevention and control

3.2 ACUTE EXPOSURE

The term "acute exposure" refers to the level of exposure to a hazardous material or chemical. It usually occurs after a single event of exposure, and workers may suffer long-term health problems if they are uninformed of the dangers. Acute exposure is defined as short-term, high-level exposure to a material or environmental element that has the potential to cause harm or has an immediate detrimental impact on health. This type of exposure typically occurs quickly, between seconds to hours, and can be caused by spills, accidents, or unanticipated releases of hazardous compounds into the environment. In most situations, the consequences of acute exposure show fast, typically within minutes or hours after contact. The chemical's toxicity, the mode of exposure (e.g., ingestion, skin contact), the length and intensity of exposure, and individual factors like age, health, and susceptibility all affect how severe the effects are. Acute exposure can cause major health problems when combined with environmental risks such as radiation or excessively high or cold temperatures. Exposure to ionizing radiation can cause acute radiation sickness, which appears as fever, diarrhea, vomiting, and, in extreme cases, organ failure and bone marrow suppression.

Acute exposure refers to prolonged interaction with a certain item. Any drug do not matter whether it’s how hazardous, can only depend on cause harm if is exposed. Exposure typically refers to contact. The dose of chemical or drugs to which a person is exposed is known as acute exposure. For example, an adult may not suffer the same amount of harm from the same chemical dosage as a child. The likelihood of serious health consequences increases with increasing exposure to a specific substance. Exposure to varied amounts can be dangerous depending on an individual's weight and medical conditions. The lethal dose/concentration of a compound that kills 50% of the test population after a brief exposure (LD/LC50) is determined via acute toxicity testing.

These are the only standardized toxicity tests with the purpose of causing death. It is vital to understand the safe exposure threshold, which varies according to the chemical. It's also important to understand the various exposure approaches and how their impacts can differ. Acute exposure to a drug might manifest in three ways. It describes how the chemical enters the body.

Acute exposure occurs through ingestion, when a dangerous chemical is eaten or consumed. This might result in nausea, vomiting, diarrhea, stomach discomfort, and, in severe cases, organ failure or damage. The systemic effects of eating specific chemicals or pollutants may have an impact on a variety of organs and physiological processes.

Toxic gases can enter the bloodstream through the lungs after being inhaled. Inhalation is one of the most common routes of exposure, especially in the absence of PPE or adequate respiratory protection.

Skin contact with potentially dangerous substances can cause dermatitis, burns, irritation, or the absorption of poisons into the bloodstream. This is referred to as dermal exposure. Insecticides, solvents, acids, and alkalis can all cause serious skin damage if they come into direct contact.

The Acute Exposure Guideline Levels ($AEGL_S$) are exposure guidelines developed to help emergency responders deal with scenarios involving chemical spills or other catastrophic catastrophes that expose the public to harmful substances in the air.AEGLs estimate the concentrations (periods) at which most people, particularly those who are vulnerable, such as the old, sick, or very young, begin to feel the effects of a hazardous chemical exposure. A chemical can have up to three AEGL values for a given exposure time, each representing a different level of health impacts. The three AEGL tiers are defined as follows.

AEGL-3: The airborne concentration of a chemical, known as AEGL-3, is measured in parts per million (ppm) or milligrams per cubic meter (mg/m^3). It shows the likelihood that the general public, including the vulnerable, would experience potentially deadly health repercussions or lose their lives.

AEGL-2: The airborne concentration of a material, known as AEGL-2 (ppm or mg/m^3), is the amount at which it is expected that the general public, including those who are vulnerable, will suffer serious, long-term health consequences that are irreversible or will impede their ability to evacuate.

AEGL-1: The amount of a material in the air that is estimated (ppm or mg/m^3) to induce obvious pain, irritation, or other asymptomatic non-sensory effects in the general public, including those who are sensitive. The side effects, however, are quite transient and do not incapacitate.

The five exposure intervals used to determine the AEGL-1, AEGL-2, and AEGL-3 levels are: 10 minutes, 30 minutes, 60 minutes, 4 hours, and 8 hours. The table below shows how chlorine AEGL values vary with exposure period.

	10 minutes	30 minutes	60 minutes	4 hours	8 hours
AEGL-1	0.50	0.50	0.50	0.50	0.50
AEGL-2	2.8	2.8	2.0	1.0	0.71
AEGL-3	50	28	20	10	7.1

Identification of hazards thorough risk assessment, and application of suitable control measures, including administrative, engineering, and personal protective equipment (PPE) and emergency response protocols are necessary to prevent acute exposure accidents. Hazardous materials must be handled, stored, and disposed of correctly to reduce the risk of unintended exposure in workplaces, industrial facilities, and communities. To mitigate the impacts of acute exposure incidents, public awareness, education, and training programs strongly promote safety precautions and emergency preparedness. Stakeholders can work together to reduce the impacts of acute exposure to hazardous substances and environmental hazards, prevent accidents, and protect public health by establishing a safety culture and proactive risk management.

3.3 CHRONIC EXPOSURE

The word "chronic exposure" refers to extended or repeated contact with a drug. Prolonged exposure can cause neurological disorders, cancer, reproductive problems, and organ damage. It is a concern in a variety of industries and settings where people may be exposed to toxins through their food, drink, air, or occupations. Common tactics for managing chronic exposure include understanding risk factors, putting preventative measures in place, and regulating the use of potentially dangerous

chemicals. Chronic toxicity refers to the adverse effects of repeated or continuous exposure to a chemical over time, such as weeks, months, or years. Chronic toxicity assesses a substance's long-term impacts on health, whereas acute toxicity investigates a substance's immediate consequences. Long-term consequences of exposure at lower doses are typically studied more than acute effects. These impacts could include cognitive deficits, organ damage, the start of cancer, and difficulty conceiving. Different compounds can come into contact with humans through a variety of methods, including ingestion, skin contact, and inhalation. Understanding these exposure routes is critical for assessing health risks and implementing effective risk management methods.

Inhaling airborne pollutants such as solvents, heavy metals, welding or soldering fumes, dust from construction or manufacturing activities and industrial processes or cleaning products exposes people to a wide range of hazardous chemicals, these chemicals have the potential to have negative health effects. The risk of public health is increased when air pollution from vehicles, industries, agriculture, and natural sources occurs outside and is inhaled, including nitrogen oxides, sulfur dioxide, ozone, particulate matter, and volatile organic compounds. Prolonged exposure to outdoor air pollution has been linked to increased mortality, exacerbation of respiratory conditions like asthma, reduced lung function, and respiratory and cardiovascular ailments.

- In addition to immediate symptoms like headaches, nausea, dizziness, and respiratory tract irritation, inhaling these substances can lead to long-term health problems such lung damage, respiratory diseases (like asthma and chronic obstructive pulmonary disease), and headaches.
- Assessments of inhalation exposure generally entail determining the amounts of pollutants in the air in various settings and assessing the possible health effects of those contaminants using epidemiological research and risk assessments. Engineering controls (such as ventilation systems, air filtration), administrative controls (such as workplace regulations, exposure monitoring), and personal protective equipment (such as respirators, masks) are examples of strategies to mitigate inhalation exposure in order to lower exposure levels and safeguard respiratory health. In order to mitigate inhalation exposure and raise air quality standards and protect public health, public awareness, education, and legislative measures are also crucial.

Ingestion exposure occurs when substances are swallowed or consumed through food, water, or other ingestible materials. Pesticides, heavy metals, microbiological infections, and additives are examples of contaminants found in food and water. If these chemicals consumed in dangerous amounts it can be extremely harmful to one's health. Exposure through ingestion raises concerns for both acute poisoning episodes and chronic long-term impacts, such as cancer, neurological diseases, organ damage, and gastrointestinal issues. Exposure to substances through ingestion happens when they are swallowed or eaten through food, water, drinks, or other edible things. Due to its ability to cause the body to absorb a wide range of contaminants, including chemicals, diseases, toxins, and allergens. This pathway of exposure is significant. Ingestion exposure can have a wide range of health consequences, depending on the type of pollutant, the amount, and the duration of exposure. Gastrointestinal symptoms include nausea; vomiting, diarrhea, stomach discomfort, and dehydration are examples of acute outcomes.

Acute intake of poisonous substances can cause poisoning, damage to organs, and even death in extreme circumstances. Some toxins can have more subtle health effects, such as neurological impairments, immune system dysfunction, reproductive problems, developmental disorders, and an increased risk of chronic diseases like cancer, cardiovascular disease, and metabolic disorders if consumed over an extended period of time or through chronic ingestion. In order to prevent exposure by ingestion and safeguard the public's health, food and water quality must be monitored and regulated. To guarantee that ingredients in food and water sources are safe for ingestion, regulatory bodies set safety requirements, upper limits that can be reached, and guidance. The detection and prevention of

contamination episodes, foodborne illness outbreaks, and other health concerns linked with ingesting exposure are facilitated by surveillance systems, food safety inspections, and laboratory testing.

Direct skin contact with contaminated objects, liquids, or materials, as well as submersion in polluted water and contact with dust or dirt can all result in dermal exposure. Workers are especially susceptible to dermal exposure in occupational contexts where they handle chemicals, insecticides, solvents, cleaning agents, and other dangerous compounds. Chemicals that are absorbed through the skin have the potential to cause localized effects including burns, rashes, dermatitis, and allergic reactions when they enter the bloodstream and circulate throughout the body. Systemic effects affecting internal organs, tissues, and physiological functions can also result from skin exposure, depending on the characteristics and toxicity of the chemical. Occupational dermal exposure assessments involve evaluating potential hazards, measuring skin contact with chemicals, conducting exposure monitoring, and implementing preventive measures such as engineering controls (e.g., ventilation, containment), administrative controls (e.g., workplace regulations, hygiene practices), and personal protective equipment (e.g., gloves, protective clothing, barrier creams) to minimize exposure levels and protect workers' skin health. In order to minimize exposure levels and protect workers' skin health, occupational dermal exposure assessments involve evaluating potential hazards, measuring skin contact with chemicals, conducting exposure monitoring, and implementing preventive measures like ventilation, containment, and personal protective equipment (PPE, gloves, protective clothing, and barrier creams). Using gloves and protective clothes, maintaining good hygiene (washing hands after handling chemicals, for example), avoiding close contact with known allergens or irritants, and carefully reading safety instructions and warning labels on consumer products are some strategies to reduce dermal exposure in non-occupational settings.

When drugs are injected into the bloodstream directly by needle punctures, injections, or medical procedures, it is known as injection exposure of toxicants. Depending on the type and toxicity of the injected material, this mode of exposure involves immediate dangers and may result in a variety of harmful health impacts. Injection exposure can happen during medical procedures such immunizations, medicine administration, blood transfusions, intravenous (IV) therapy, and diagnostic tests that use radioactive tracers or contrast agents. Injectable toxicants can be introduced to people receiving medical care as well as healthcare personnel who give injections. Inadequate injection techniques or tainted needles and syringes have the potential to spread blood borne viruses, including HIV, hepatitis B, and hepatitis C. These infections can be fatal and have long-term health effects. Certain people may develop adverse reactions to injectable drugs, such as prescription pharmaceuticals, contrast agents, or vaccine ingredients. Allergy symptoms can vary from minor skin rashes and itching to severe anaphylaxis, which is a potentially fatal disease marked by breathing difficulties, throat swelling, and a drop in blood pressure. Caustic or irritating substances injected into the body have the potential to cause scarring, necrosis, and tissue damage. Chemical irritants or corrosive chemicals may cause tissue degradation, ulceration, discomfort, and localized inflammation; these effects may necessitate medical attention, including surgery. When poisonous materials are injected straight into the bloodstream, the body's defenses and natural barriers are bypassed, resulting in quick absorption and dispersion throughout the body. Organ damage, neurological impairment, cardiovascular effects, respiratory distress, metabolic changes, and even death are examples of systemic effects that can occur from injectable substances, depending on their toxicity. In order to ensure that patients are aware of the potential risks associated with injection exposure medical procedures and to promote patient safety and well-being, healthcare professionals should be trained in safe injection practices, which include proper needle insertion techniques, medication preparation, hand hygiene, and disposal of sharps and medical waste. In addition, patient education and informed consent are crucial.

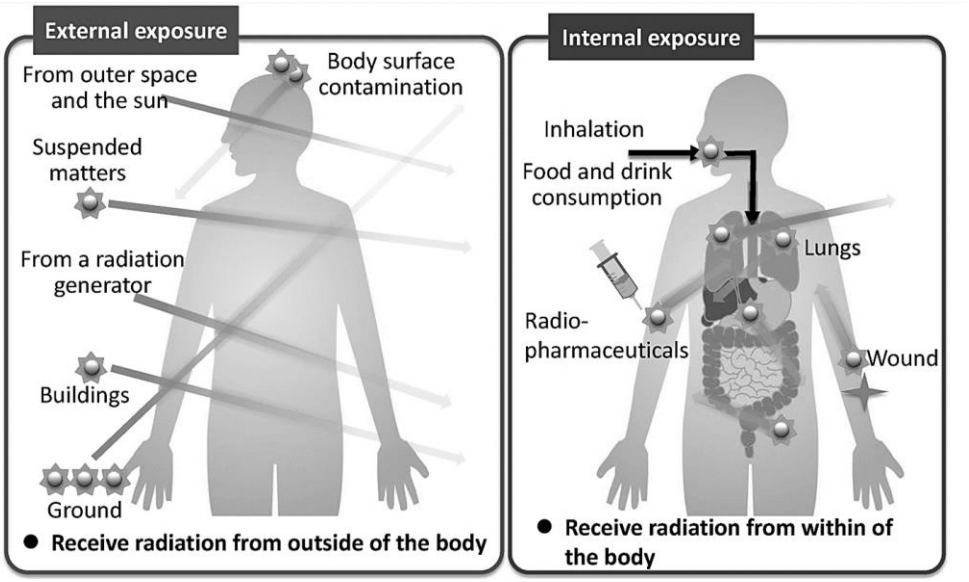
Environmental exposure of toxicants" refers to the presence of dangerous compounds in the environment that humans and other living things can absorb, consume, or inhale. Toxicants can come

from a variety of sources, such as industrial processes, agricultural practices, waste disposal, transportation, and natural processes. They can contaminate soil, water, food, and air. One important way that toxicants are exposed to the environment is through air pollution. Pollutants include particulate matter, nitrogen oxides, sulfur dioxide, volatile organic compounds, and heavy metals are released into the atmosphere by emissions from power plants, automobile exhaust, industrial sites, and wildfires. The inhalation of these airborne toxicants may result in neurological disorders, cardiovascular issues, respiratory ailments, and other health consequences. Exposure to contaminants found in water sources can occur by ingestion, cutaneous contact, and inhalation of water vapor. Surface water and groundwater can get contaminated with heavy metals, pesticides, industrial chemicals, medicines, and microbiological pathogens due to industrial discharges, agricultural runoff, wastewater effluents, and unintentional spills. Reproductive problems, brain impairment, gastrointestinal diseases, and other health issues can arise from recreational activities in polluted water bodies or from consuming contaminated drinking water. Industrial sites, waste disposal sites, agricultural lands, and polluted sites can all contribute to the buildup of toxicants in soil and sediment through leaching, runoff, and deposition. Exposure to soil contaminated by pesticides, heavy metals, hazardous waste, and persistent organic pollutants (POPs) can occur through eating of contaminated crops or soil by inhaling dust particles. Contaminants from soil and sediment can affect ecosystems, human health, and the food chain by bioaccumulation in organisms. Food is a major source of environmental exposure to toxins since pollutants can build up in crops, animals, and shellfish via pathways in the soil, water, and air and along the food chain. During the manufacturing, processing, storage, and distribution of food items, pesticides, herbicides, fungicides, veterinary medications, heavy metals, mycotoxins, and environmental contaminants can contaminate them. Acute poisoning, long-term dangers like cancer, developmental difficulties, and reproductive problems, as well as chronic health consequences and foodborne infections, can all result from consuming contaminated food. Individuals who live or work close to industrial facilities, hazardous waste sites, traffic routes, and agricultural areas are more likely to be exposed to environmental toxins through their home and occupational settings. Various industries, such as manufacturing, construction, agriculture, mining, and healthcare, can result in occupational exposures to chemicals, solvents, dusts, and fumes. There are additional dangers associated with environmental exposure from residential exposures to indoor air pollutants, household chemicals, building materials, and consumer products.

Pollution prevention, environmental monitoring, risk assessment, regulatory controls, public health interventions, community engagement, and sustainable practices are just a few of the comprehensive strategies needed to address environmental exposure to toxicants. These strategies decrease the number of sources of contamination, reduce exposure pathways, safeguard vulnerable groups, and advance environmental sustainability.

3.4 HUMAN EXPOSURE AND ITS TYPES

Toxicants can be exposed to humans through a variety of routes and sources, which poses serious threats to both human health and the environment. Toxicants are a broad category of compounds that include, chemicals, heavy metals, pesticides, and among other things. It is necessary to take into account the sources, routes, and factors influencing exposure levels in order to comprehend human exposure to toxicants and their potential health impacts. There are several types of toxicant exposure have been identified:



3.4.1 Inhalation Exposure

Inhaling airborne pollutants such as solvents, heavy metals, welding or soldering fumes, dust from construction or manufacturing industry and activities have the potential to harmful for natural and human health. Air pollution from automobiles, factories, agriculture, and natural sources, such as nitrogen oxides, sulfur dioxide, ozone, particulate matter, and volatile organic compounds, increases the risk to public health when inhaled outside. Prolonged exposure to outdoor air pollution has been related to higher death rates, worsening of respiratory disorders such as asthma, decreased lung function, and respiratory and cardiovascular problems.

In addition to immediate symptoms like headaches, nausea, dizziness, and respiratory tract irritation, inhaling these substances can lead to long-term health problems such lung damage, respiratory diseases (like asthma and chronic obstructive pulmonary disease), and headaches.

Assessments of inhalation exposure generally entail determining the amounts of pollutants in the air in various settings and assessing the possible health effects of those contaminants using epidemiological research and risk assessments. Engineering controls, administrative controls and personal protective equipment are examples of strategies to mitigate inhalation exposure in order to lower exposure levels and safeguard respiratory health. In order to mitigate inhalation exposure and raise air quality standards and protect public health, public awareness, education, and legislative measures are also crucial.

3.4.2 Ingestion Exposure

Ingestion exposure occurs when substances are swallowed or consumed through food, water, or other ingestible materials. Pesticides, heavy metals, microbiological infections, and additives are examples of contaminants found in food and water, if they consumed in dangerous amounts, can be extremely harmful. Exposure through ingestion raises concerns for both acute poisoning episodes and chronic long-term impacts, such as cancer, neurological diseases, organ damage, and gastrointestinal issues. Ingestion exposes people to substances when they swallow or consume them through food, water, drinks, or other edibles. This route of exposure is essential because it has the ability to cause the body to absorb a wide range of contaminants, including chemicals, diseases, toxins, and allergens. Ingestion exposure can have a wide range of health consequences, depending on the type of pollutant, the amount, and the duration of exposure. Acute gastrointestinal symptoms include nausea, vomiting, diarrhea, stomach discomfort, and dehydration. Acute ingestion of hazardous substances can result in

poisoning, organ damage, and, in extreme cases, death.

Some toxins can cause more subtle health effects, such as neurological impairments, immune system dysfunction, reproductive problems, developmental disorders, and an increased risk of chronic diseases such as cancer, cardiovascular disease, and metabolic disorders, if consumed over time or through chronic ingestion. Food and water quality must be monitored and regulated to prevent exposure through ingestion and to protect public health. To ensure that substances in food and water sources are safe for consumption, regulatory authorities establish safety guidelines, upper limits, and guidance. Surveillance systems, food safety inspections, and laboratory testing all help to detect and prevent contamination incidents, food borne illness outbreaks, and other health risks associated with ingestion exposure.

3.4.3 Dermal Exposure

When substances come into contact with the skin and are absorbed, they may have a negative impact on one's health. This is referred to as dermal exposure. Because the skin is the body's largest organ and may absorb a variety of things, including toxins, chemicals, and allergens, this exposure pathway is critical. Direct skin contact with contaminated items, liquids, or materials, as well as immersion in polluted water and contact with dust or dirt. It can all lead to cutaneous exposure. Workers are especially vulnerable to cutaneous exposure when working with pesticides, insecticides, solvents, cleaning agents, and other hazardous materials. Chemicals absorbed through the skin have the potential to induce localized effects such as burns, rashes, dermatitis, and allergic reactions when they reach the bloodstream and circulate throughout the body. Systemic effects on internal organs, tissues, and physiological functions may also result from skin exposure, depending on the chemical's properties and toxicity. To reduce exposure levels and protect workers' skin health, occupational dermal exposure assessments include evaluating potential hazards, measuring skin contact with chemicals, monitoring exposure, and implementing preventive measures such as engineering controls (e.g., ventilation, containment), administrative controls (e.g., workplace regulations, hygiene practices), and personal protective equipment (e.g., gloves, protective clothing, barrier creams).

To reduce exposure levels and protect workers' skin health, occupational dermal exposure assessments include assessing potential hazards, measuring skin contact with chemicals, monitoring exposure, and implementing preventive measures such as ventilation, containment, and personal protective equipment (PPE, gloves, protective clothing, and barrier creams). Some strategies for reducing dermal exposure in non-occupational settings include wearing gloves and protective clothing, practicing good hygiene (e.g., washing hands after handling chemicals), avoiding close contact with known allergens or irritants, and carefully reading safety instructions and warning labels on consumer products.

3.4.4 Injection Exposure

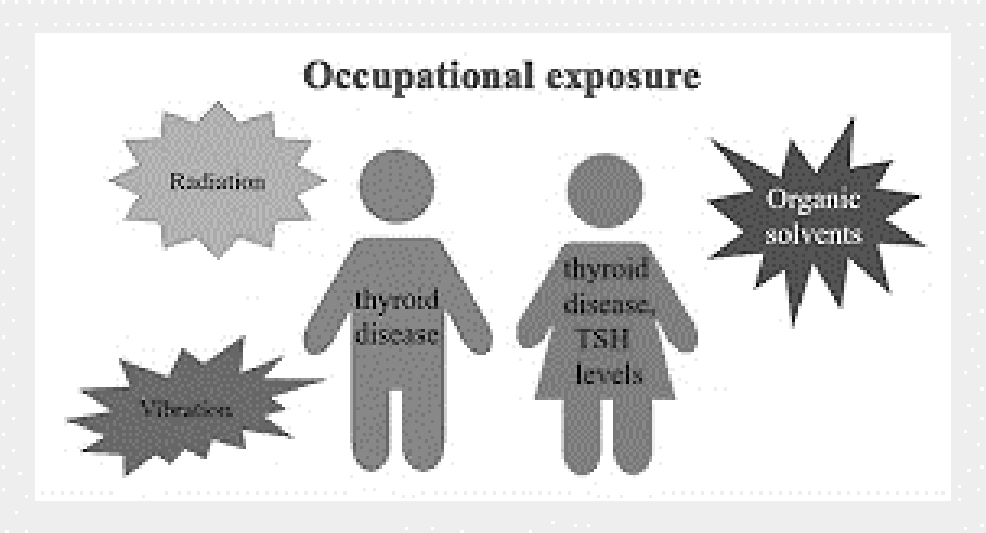
Injection exposure of toxicants occurs when drugs are administered directly into the bloodstream or via injections. It depending on the nature and toxicity of the injected chemical. This mode of exposure poses immediate risks and may have a wide range of negative health consequences. Injection exposure can occur during medical operations such as vaccines, drugs administration, blood transfusions, intravenous (IV) therapy, and diagnostic testing involving radioactive tracers or contrast agents. Injectable toxicants can be administered to both patients and healthcare workers. Inadequate injection procedures or contaminated needles and syringes can spread blood-borne diseases such as HIV, hepatitis B, and hepatitis C.

These infections are potentially deadly and have long-term health consequences. Certain persons may experience adverse responses to injectable drugs, such as prescription pharmaceuticals, contrast agents, or vaccine components. Allergy symptoms range from modest skin rashes and itching to severe anaphylaxis, a potentially fatal disorder characterized by difficulty breathing, throat swelling, and a drop in blood pressure. Caustic or irritating substances injected into the body can induce scarring, necrosis, and tissue damage. Chemical irritants or corrosive substances can cause tissue degeneration, ulceration, discomfort, and localized inflammation, which may demand medical treatment, including surgery. When hazardous compounds are injected directly into the bloodstream, the body's defenses and natural barriers are circumvented, allowing for rapid absorption and dispersion throughout the body. Organ damage, neurological impairment, cardiovascular impacts, respiratory distress, metabolic abnormalities, and even death are all examples of systemic effects that injectable drugs might cause depending on their toxicity. Healthcare professionals should be trained in safe injection practices, which include proper needle insertion techniques, medication preparation, hand hygiene, and sharps and medical waste disposal. In addition, patient education and informed consent are essential.

3.4.5 Occupational Exposure

Workers who are exposed to hazardous products or unsafe working conditions while doing their duties are considered to have had occupational exposure. Physical dangers such as noise, vibration, radiation, and ergonomic stressors can all cause this exposure, as can the ingestion, injection, skin contact, or inhalation of dangerous chemicals. Exposure at work can cause acute injuries, long-term health repercussions, occupational illnesses, and work-related deaths, making it a severe public health concern.

Chemical Exposure: Chemicals such as acids, solvents, pesticides, heavy metals, carcinogens, and industrial chemicals can expose workers in a range of industries throughout the manufacturing, processing, handling, storage, and transportation processes. Chemical exposure can occur from inhaling fumes, vapors, or aerosols, swallowing contaminated food or water, coming into contact with liquids or solids through the skin, or unintentional spills or leaks. Toxic chemical exposure at work can result in cancer, neurological disorders, dermatitis, respiratory ailments, chronic health difficulties, and reproductive issues, in addition to acute poisoning.



Biological Exposure: Healthcare professionals, laboratory technicians, agricultural workers, and people in other occupations may be exposed to biological hazards such as viruses, bacteria, fungi, parasites, and allergies while providing patient care, conducting research, working with animals, or maintaining the

environment. Biological exposure can occur through inhaling airborne illnesses, coming into intimate contact with infected objects or bodily fluids, consuming contaminated food or water, and suffering needle stick injuries or other occurrences involving sharp devices. When exposed to biological substances at work, individuals may develop allergic reactions,gastrointestinal disorders, skin infections, respiratory infections, and infectious diseases.

Physical Exposure: Employees, they work in different environments may be exposed to physical hazards such as vibration, noise, heat, cold, radiation, and ergonomic strains. While extreme heat or cold can cause heat stress, hypothermia, and other thermal-related illnesses, excessive noise can cause hearing loss, tinnitus, and other auditory issues. While exposure to ionizing radiation, ultraviolet (UV) radiation, or electromagnetic fields can cause radiation-related health issues, vibration exposure can cause hand-arm vibration syndrome (HAVS) and whole-body vibration effects. Musculoskeletal disorders (MSDs), which include strains, sprains, and overuse injuries, are frequently induced by ergonomic stressors such as heavy lifting, uncomfortable postures, and repetitive activities.

Psychosocial Exposure: Psychosocial risks such as stress, workplace violence, and bullying, harassment, and employment insecurity are also considered occupational exposure. Workplace demands, organizational concerns, interpersonal conflicts, and job expectations can all contribute to mental health issues in employees, including anxiety, depression, burnout, and post-traumatic stress disorder (PTSD). Psychosocial exposure can have a negative impact on one's overall well-being, morale, productivity, and job performance, resulting in turnover, absenteeism, and poor health outcomes.

A multifaceted approach to occupational exposure prevention must include hazard identification, risk assessment, exposure control measures, engineering controls, administrative controls, personal protective equipment (PPE), training and education, workplace ergonomics, health promotion, surveillance and monitoring, and regulatory compliance. Employers, employees, occupational health professionals, government agencies, and other stakeholders all have important roles to play in ensuring workplace safety, protecting workers' health, and fostering a safety and health culture. Organizations can reduce the incidence of work-related diseases and injuries and promote safer, healthier work environments by addressing occupational hazards, lowering exposure risks, and implementing preventative measures.

3.4.6 Internal Exposure

Internal exposure occurs when toxic substances enter the body and go through physiological processes to be absorbed, distributed, digested, and eliminated. This can have detrimental effects on health. This route of exposure includes a number of entry points, such as injection, ingestion, inhalation, and skin contact. It entails the absorption of pollutants into the bloodstream and their subsequent distribution to the body's organs, tissues, and cells.

- **Ingestion Exposure:** Toxins ingested through food, drink, or other consumable materials can enter the body by bypassing the gastrointestinal tract and entering the bloodstream via intestinal walls. Pesticides, heavy metals, microbiological infections, industrial chemicals, and food additives can cause acute poisoning, long-term health consequences, and systemic toxicity when the liver metabolizes them, circulates them throughout the body, and deposits them in organs such as the liver, kidneys, and brain.

- **Inhalation Exposure:** When airborne toxicants enter the respiratory system, they can pass through the blood-blood barrier in the lungs and enter the circulation, where they are transported to various organs and tissues. Pollutants that can harm the lungs, heart, brain, and other organs can cause respiratory ailments, cardiovascular problems, neurological abnormalities, and

systemic health problems when inhaled. Pollutants include particulate materials, gasses, vapors, aerosols, and biological agents.

Sources of Toxicants-

- **Industrial Activities:** Numerous toxicants, such as heavy metals, volatile organic compounds, and persistent organic pollutants (POPs) like dioxins and polychlorinated biphenyls (PCBs), are released into the environment as a result of industrial activities.

- **Agricultural Practices:** Agriculture-related pesticides, herbicides, and fertilizers can pollute crops, soil, and water, exposing people through eating, breathing, and skin contact.

- **Consumer Products:** Toxicants are found in a wide range of consumer goods, including as electronics, personal care items, flame-retardant furniture, and home cleaners. Exposure can happen through the consumption of contaminated dust or residues, skin contact, or inhalation of volatile chemical compounds.

- **Waste Management:** Hazardous waste must be disposed of properly to avoid contaminating soil and groundwater and endangering public health by exposing people to toxicants that seep from landfills, illicit dumping sites, and facilities that dispose of industrial waste.

Factors Influencing Exposure Levels-

- **Duration and Frequency of Exposure** The likelihood of harmful health impacts rises with prolonged or recurrent exposure to toxicants, particularly when such compounds bioaccumulation over time in the body.
- **Concentration and Toxicity:** Greater health risks are associated with higher concentrations of toxicants, and the severity of potential health impacts is influenced by a substance's toxicity.
- **Route of Exposure:** The body's capacity to absorb and metabolize toxicants is influenced by the route of exposure; inhalation frequently leads to a quicker rate of absorption than ingestion or cutaneous contact.
- **Individual Susceptibility:** An individual's sensitivity to the health impacts of toxicants can be influenced by a number of factors, including age, genetics, pre-existing medical issues, lifestyle choices, and occupational exposures.

3.5 ACCIDENTAL POISONING

Inadvertent consumption, inhalation, or contact with a harmful substance can lead to poisoning. This is a serious condition that must be treated immediately since it could be fatal. Anyone, regardless of age or condition, can be accidently poisoned, and it can happen anywhere, including the home, office, or outdoors. Ingestion of household chemicals is a leading cause of accidental poisonings. Cleaning supplies, pesticides, and laundry detergents are all examples of compounds that might be harmful if swallowed, especially by small children who may mistake them for food or liquids. Inadequate storage of these medications can increase the risk of unintended intake.For example, storing cleaning materials in unmarked containers or placing them within children's reach can lead to confusion and unintended poisoning. Drugs mistakes are a frequent cause of unintended poisoning. Taking the wrong prescription, administering it at the incorrect dosage, or combining pharmaceuticals that are not intended to be used together can all have negative consequences. Confusion and misunderstanding are more likely to occur in households with a large number of prescription medicines. Over-the-counter medications, such as

cough syrups or pain painkillers, can, nevertheless, be toxic if consumed in excess. Ingesting harmful plants or mushrooms is another potential concern, especially for persons who are unaware of the toxicity of specific species. Plants in gardens and outdoor settings may encourage youngsters to try or ingest them, perhaps causing unintentional poisoning.

Carbon monoxide poisoning, which is silent but deadly, can occur in homes with gas appliances, poor ventilation, or malfunctioning heating systems. Carbon monoxide gas, which is colorless and odorless, can build up to dangerous levels indoors, causing symptoms such as headaches, nausea, and dizziness, as well as unconsciousness or death if exposed for an extended period of time. Another risk factor for unintentional poisoning is inhaling harmful fumes or gases in industrial or agricultural settings. Agricultural operations, cleaning procedures, and manufacturing processes may expose employees to chemicals such as ammonia, chlorine, or pesticides, which can cause respiratory distress and other health problems. To avoid unintended poisoning, you must raise awareness, provide information, and take preventative measures. Parents and caregivers should keep medications and household chemicals out of children's reach, ideally by locking cabinets or other storage facilities. Proper chemical identification and communication of medicine dose recommendations can help to avoid errors. People can avoid swallowing dangerous plants and mushrooms in the outdoors by knowing how to identify them. Making a call to a poison control center or local emergency services can help prevent more injury and provide information on correct first aid techniques. In cases of unintentional poisoning, timely treatment can save lives, emphasizing the importance of awareness and preparation in preventing and controlling this serious health risk.

3.6 INTERNAL POISONING

When hazardous substances are consumed, inhaled, or absorbed, the body's internal organs and systems are harmed. This condition is known as internal poisoning. Internal poisoning happens when hazardous substances enter the body through different channels and interfere with internal processes, as opposed to external poisoning, which happens when the body comes into touch with toxic substances from the outside. Many different substances, such as chemicals, medicines, pharmaceuticals, and poisons present in food or drink, can cause internal poisoning. The consumption of hazardous substances or domestic items is a frequent cause of internal poisoning. Internal poisoning can result from unintentionally consuming cleaning supplies, insecticides, or automobile fluids, particularly when these substances are confused for food or liquids. When drugs are taken in excess or when they are combined, the body may not be able to process and get rid of them as quickly, which can have harmful effects. Prescription medications with a narrow therapeutic window i.e., a small difference between a therapeutic and hazardous dose increase this risk. Because many drugs have toxic effects on the body when consumed in large quantities or in combination with other substances, illegal drug use is a leading cause of internal poisoning. Methamphetamine, cocaine, ecstasy, opiates, and other narcotics can be highly hazardous, causing cardiac arrest, respiratory depression, organ damage, and convulsions. Injection medications deliver pollutants and chemicals into the bloodstream, which increases the risk of internal poisoning. If the poisons inherent in hazardous plants or mushrooms are absorbed by the body, consuming them can cause internal poisoning. Compounds found in some plants and mushrooms are hazardous to humans and can cause symptoms ranging from organ failure to gastrointestinal upset. Accidental ingestion of hazardous plants or mushrooms occurs frequently, particularly when people are ignorant of the risks connected to certain species. Internal poisoning can also occur from the consumption of tainted food or drink, leading to food poisoning. During food manufacturing, handling, or storage, bacteria, viruses, parasites, and microbial toxins can contaminate food, resulting in gastrointestinal symptoms such nausea, vomiting, diarrhea, and abdominal discomfort. Severe food poisoning can cause organ damage, electrolyte abnormalities, and dehydration. Vigilance, education,

and appropriate safety precautions are necessary to prevent internal poisoning. Accidental ingestion can be avoided by keeping home chemicals and prescriptions out of children's reach, using child-resistant packaging, and labeling the items correctly. To lower the danger of pharmaceutical overdose, education regarding drugs safety is crucial. This includes instructions on proper dosing and storage.

Internal poisoning from drugs can be avoided by abstaining from illegal drug usage and getting treatment for substance misuse. People can prevent ingesting accidents in outdoor situations by learning how to recognize toxic plants and mushrooms. The risk of food poisoning can be decreased by adhering to food safety precautions, such as washing your hands properly, cooking food to the right temperature, and preventing cross-contamination. The length and intensity of a toxicant's exposure are important factors in determining how severely the substance affects the body. Chemicals, biological agents, or physical elements that negatively impact living things are all considered toxicants. It is crucial to comprehend how exposure length and toxicity are related in order to evaluate risks, put safety precautions in place, and create treatment plans. The amount of time that a person is in touch with a toxicant is referred to as the duration of exposure. Long-term exposure happens over a longer time span, from days to years, whereas short-term exposure happens over a comparatively short period, from seconds to hours. The effects of toxicants can differ based on the duration of exposure acute vs chronic. Symptoms of acute toxicant exposure usually appear right away or very quickly. This may happen after several exposures in a short amount of time or after a single high-dose exposure. Acute poisoning can cause symptoms like nausea, vomiting, headaches, disorientation, respiratory distress, seizures, and in extreme situations, even death. The degree of symptoms and the probability of unfavorable consequences are contingent upon various elements, including the dosage, mode of exposure, drug toxicity, and individual susceptibility.

Effects on human health- There are two types of consequences that exposure to harmful substances can have on human health: immediate and long-term effects. After brief exposures to relatively high concentrations of material, short-term effects, also known as acute impacts, typically manifest between minutes to days (acute exposures). There could be a systemic or local impact. Local effects happen where the toxicant and body come into touch. This site is typically the skin or eyes, although it can also include the lungs in the case of inhaled irritations or the gastrointestinal system in the case of ingested corrosives. The term "systemic effects" refers to the negative consequences that a toxin can have on the body after it has entered via the skin, moved to other areas of the body, and impacted vulnerable organs. Long-term effects, often known as chronic consequences, occur when exposure and harm occur years apart. These consequences could manifest following an apparent recovery from acute exposure, or they could be the consequence of years of repetitive exposure to low concentrations of the compounds (chronic exposure).

The chemicals involved and the organs they affect determine the health effects that arise from either acute or chronic exposure. The toxicity of most substances varies depending on the organ. Typically, one or two organs will exhibit the majority of a chemical's effects. These organs are referred to as target organs since they are more susceptible than other organs to that particular toxin. The following is a list of the body's organs along with instances of consequences from chemical exposure.

3.7 SUMMARY

The distribution of toxicants inside the body and the degree of exposure are greatly influenced by the route of exposure. Exposure through inhalation can cause toxicants to enter the bloodstream quickly, which can have systemic effects. Toxins consumed orally have the potential to enter the body through the gastrointestinal system and find their way to different organs and tissues. Depending on the characteristics of the toxin and the length of contact, dermal exposure, which happens when skin comes

into touch with it can have either localized or systemic effects. The degree of exposure to toxicants can also be influenced by environmental variables such temperature, humidity, ventilation, and the presence of other chemicals. For instance, a lack of ventilation and high temperatures can increase the amount of airborne contaminants that people inhale, and certain compounds might react negatively or positively to change their toxicity. Determining the time and degree of toxicant exposure is critical for assessing risks, implementing preventative measures, and selecting the best treatment options. To protect the public's health and safety, regulatory agencies and health organizations develop exposure limits and guidelines based on scientific evidence. Surveillance and monitoring programs help to identify and reduce toxins in the public, workplace, and environment. Public awareness campaigns, education, and training are critical for promoting safe behavior and reducing the risks associated with toxicant exposure.

3.8 TERMINAL QUESTIONS

Q. 1. What is toxicant exposure, discuss the toxicant exposure.

Answer:----------

Q. 2. Discuss about acute toxicity and acute exposure and its prevention.

Answer:----------

Q. 3. Discuss about chronic toxicity and chronic exposure and its prevention.

Answer:----------

Q. 4. What is human exposure? Discuss the types of human exposure.

Answer:----------

Q. 5. What are the internal and external exposure and its role on human health?

Answer:----------

Q. 6. Discuss the Occupational exposure and its sources and effects.

Answer:----------

Q. 7. Discuss the Environmental exposure and its effects.

Answer:----------

3.9 FURTHER SUGGESTED READINGS

1. Environmental Toxicology, Kees van Gestel, Vrije University, Amsterdam, Environmental Toxicology.
2. Environmental Toxicology, Third Edition, Sigmund F. Zakrzewski, oxford university press
3. A Textbook of Modern Toxicology: Ernest Hodgson A John Wiley & Sons, Inc., Publication
4. Principles of Environmental Toxicology, I. Shaw, J. Chadwick, CRC Press
5. Occupational Toxicology, Chris Winder, Neill H. Stacey, CRC Press.

Uttar Pradesh Rajarshi Tandon Open University

PGBCH-117N

Environmental Toxicology and Occupational Health Hazards

BLOCK

2

TOXICITY AND PUBLIC HEALTH

UNIT-4

Fate of Toxicant in Human Body

UNIT-5

Chemical Toxicity in Human

UNIT-6

Public Health

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BLOCK INTRODUCTION

The following three units are included in the second block of environmental toxicology & occupational health hazards are as:

Unit 4: The absorption of toxicants is covered in this unit. This article discusses the many assortative mechanisms, including distribution, binding, and storage of toxicant in human bodies. There is additional discussion of the excretion, active, and passive transfer of toxicant

Unit-5: This section covers a variety of toxicity types, including the toxicity of alcohol, the toxicity of ketenes, the toxicity of minerals (sodium, potassium, iodine, iron, nitrogen, calcium, zinc, copper, selenium, and manganese), and the toxicity of dioxins.

Unit-6: Public health and toxicologists are the subjects of this unit. This unit discusses epidemiological approaches to toxicants as well as the laws and regulations that control them. But this article also covers car emissions, pesticides, and hazardous compounds that are on the blacklist.

UNIT-4 : FATE OF TOXICANT IN HUMAN BODY

Structure

4.1 INTRODUCTION

ADME is the study of how toxicants are absorbed, distributed, metabolized, and eliminated. It is critical to understand the path of a toxicant in the human body. Toxicants can enter the body via a

variety of routes, including the skin, food, or inhalation. Once inside, they may pass through biological barriers present in the skin, respiratory system, or gastrointestinal tract. Absorption rates are affected by the chemical properties of toxicant, the route of exposure, and the physiological condition. After absorption, the toxin enters the bloodstream and goes to various organs and tissues. However, the blood flow, lipid solubility, and affinity for specific tissues all influence dispersion of toxicant. The body biotransforms a huge variety of toxicants, primarily in the liver, but other organs may be implicated. Enzymatic activities convert the toxin into metabolites during the process, typically enhancing their water solubility for easier excretion. Not only can metabolism activate or detoxify poisons, but it can also produce toxic reactive intermediates. A toxicant's ultimate fate is elimination from the body. This can happen through breast milk, breath, sweat, excrement and urine. Even the bile secretion helps to excrete certain toxicants through feces, inadditon, the kidneys play an important role in the excretion of water-soluble chemicals through urine. Furthermore, the lungs can be employed to eliminate volatile toxins. Modern society relies on thousands of chemicals, and the majority of us are exposed to a wide range of substances in a variety of settings. Predicting the effect of these compounds is thus extremely challenging. Chemical substances interact in a number of ways, which complicates this process even more. Some chemical substances, for example, combine to produce an additive reaction, which is the sum of the separate responses (for example, 2 + 2 = 4). Others may cause a super additive effect, also known as a synergistic reaction, which is more than the sum of the individual responses (2 + 2 = 6). One of the most well-known examples of synergism is the combination of barbiturate tranquilizers and alcohol; while neither is hazardous in modest amounts, the combination can be fatal. Pollutants can also combine. For example, inhaling sulfur dioxide gas and particulates (minute airborne particles) simultaneously can restrict airflow through the lungs' narrow airways. The cumulative reaction is significantly greater than the sum of the individual responses. The synergistic effects of smoking and asbestos are explored later.Another intriguing interaction is potentiating, which occurs when a molecule with no toxic impact mixes with a poisonous chemical, making the toxicant even more harmful. This reaction is represented by the equation 0 + 2 = 6. For example, isopropyl alcohol (rubbing alcohol) has little effect on the liver, but when mixed with carbon tetra chloride, it significantly increases its toxicity. Antagonism occurs when certain compounds counteract each other's effects. In some circumstances, specific combinations of potentially dangerous compounds decrease the negative effect. This can be expressed as the equation 2 + 4 = 3. Mortality in mice exposed to nitrous oxide gas is significantly reduced when particles are present. Scientists are uncertain about the reasons for this phenomenon.

Objectives

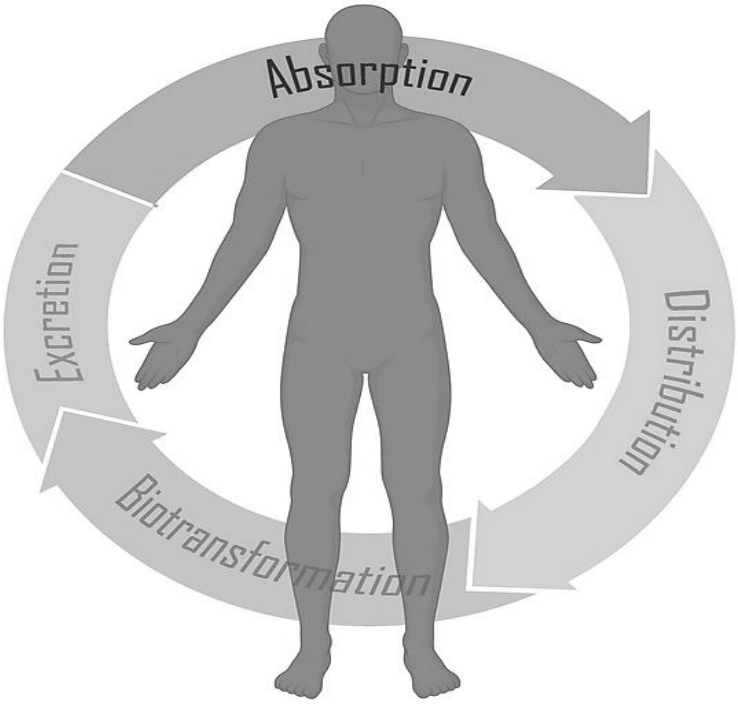
After reading this unit the learner will be able to known the

- Toxicant and its absorption, distribution in human body
- Binding storage and excretion of toxicants
- Transport mechanism of toxicant in human body
- Factors effecting distribution and transport of toxicant

4.2 TOXICANT AND ITS ABSORPTION

Toxin buildup in the human body, especially in adipose tissue, can have detrimental effects on health. Lipophilic toxicants, such as heavy metals, certain insecticides, and persistent organic pollutants (POPs), are stored in adipose tissue. Because these compounds are slowly metabolized and eliminated by the body. Once the toxicant storage in the human body, these toxins can damage different organ

systems by chance in hormonal balance that cause chronic illnesses like cancer, heart problems, and neurological damage. Therefore, it is essential to minimize the toxicants buildupin the body. Protect human health by changing one's lifestyle, limiting one's exposure to dangerous substances, and disposing of them properly. Adipose tissue, due to its lipophilic nature, stores a portion of the toxicants.



The toxicants can enter the body through a variety of channels, including ingestion, inhalation, and dermal absorption. Once absorbed, they can spread throughout the body. Adipose tissue can store a variety of toxicants, such as the following:

Persistent Organic Pollutants (POPs): These are man-made substances that withstand deterioration and endure extended durations in the environment. Dioxins, polychlorinated biphenyls (PCBs), and specific pesticides like DDT are a few examples. POPs have the ability to biomagnified via the food chain and build up in fat tissue.

Heavy Metals: The body's fatty tissues can become accumulated with metals like lead, mercury, cadmium, and arsenic. They can be harmful to several organ systems and are frequently present in tainted food, water, and air.

Volatile Organic Compounds (VOCs): A number of lipophilic VOCs, including benzene, toluene, and styrene, can build up in adipose tissue due to their exposure through inhalation or skin contact. Unfavorable health effects have been linked to long-term VOC exposure.

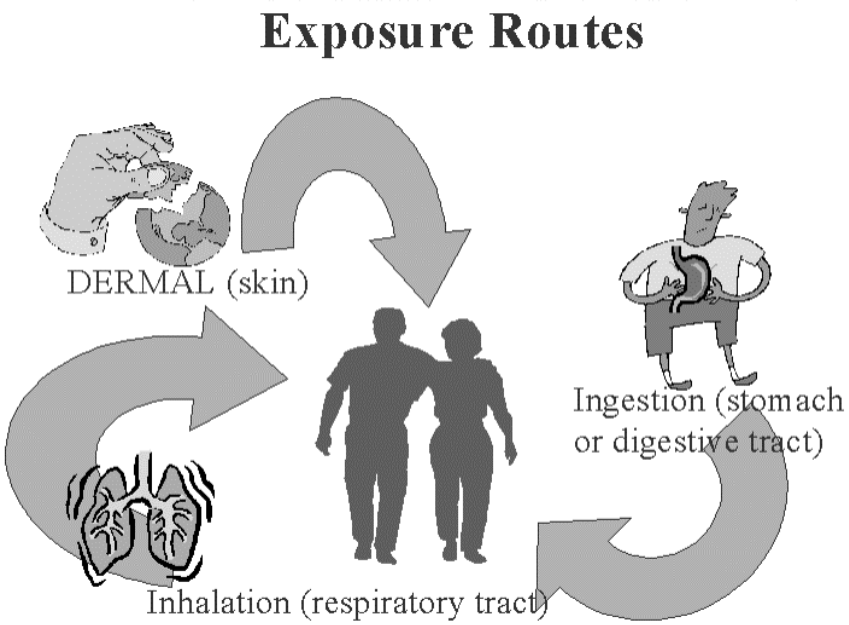
Polycyclic Aromatic Hydrocarbons (PAHs): The term "polycyclic aromatic hydrocarbons" (PAHs) refers to a class of organic molecules that are produced when organic materials burn partially. They are known carcinogens, connected to cancer and other health problems, and can build up in adipose tissue.

Phthalates: These are substances that are frequently present in food packaging, personal hygiene items, and plastics. Phthalates may affect hormonal balance and reproductive health since they can seep into food and drink items and accumulate in adipose tissue, according to certain research.

4.3 ROUTES OF EXPOSURE

Toxicants enter the body through absorption. Materials that are swallowed or inhaled by the body are

not considered to be part of it until they pass through the cellular barriers of the respiratory system or gastrointestinal tract. Internal organs must be affected by a drug through absorption; however local toxicity such as irritation may also happen.



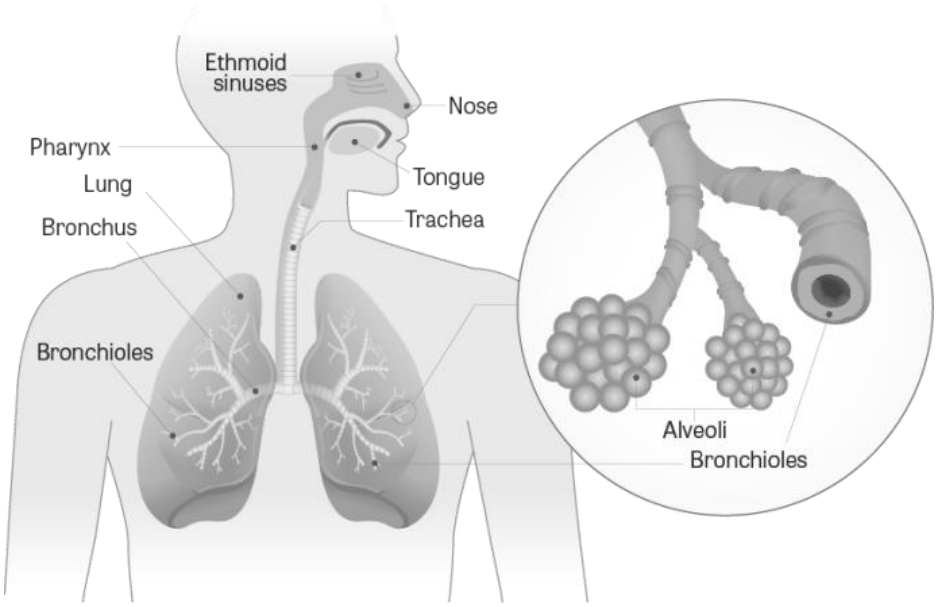
The following are the main pathways via which xenobiotics can enter the body:

Respiratory tract: The alveoli in the lungs are the primary absorption sites in the respiratory system. The vast alveolar area, strong blood flow, and proximity of the blood to the alveolar air all contribute to gaseous contaminants' ease of absorption. In the gaseous stage, the inhaled substance is transferred into a liquid layer that lines the route. The transfer of balls via diffusion via this layer is determined by

- Gas diffusion coefficient layer thickness
- Gas concentration at boundaries of this layer

The rate of absorption of toxicant is depends on the solubility in the gas of the blood. The more soluble toxicant occurs in the faster the absorption. However, equilibrium between the air and the blood is more soluble chemical such as chloroform complex to less soluble chemical such as ethylene. In addition to gases and bypass liquid aerosols, airborne particles may also be absorbed. In general, particles larger than 10 microns do not enter the respiratory tract; when they do, they are deposited in the more and dispersed by wiping, blowing, and sneezing. Every small particle smaller than 10 microns is likely to be exhaled.

Smaller particles are deposited in the trachea, bronchi, and bronchioli, where they are either respired by mucocilliary aspirators or engulfed by phagocytes. Larger particles are likely to be deposited in the nosapharynx and absorbed either through the epithelial region or through the gastrointestinal tract epithelium after being swallowed along with mucous.



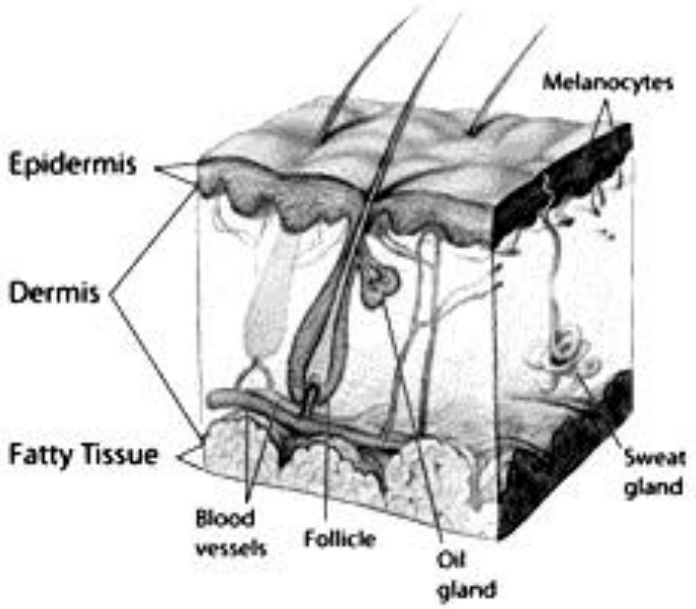
The particles carried up by aspirators will be coughed up or swallowed and phagocytes with engulfed particles will be absorbed into lymphatics. Estimate that 25% of inhaled particles are expelled, 50% are deposited in the upper respiratory tract, and the remaining 25% in the lower respiratory tract. The relative rates of deposition and clearance dictate particle retention in the body.

- **Gastrointestinal (GI) tract:** Absorption of toxic substances occurs along the entire length of the GI track, but it differs in the stomach due to the lower PH in the stomach. The stomach is a significant site of absorption, particularly for weak acids that exist in diffusible non-ionized lipids soluble from. Wear base, on the other hand, is highly ionized in acidic gastric secretions and thus difficult to absorb.

  The differential in absorption is amplified by the presence of circulating plasma beak acids, which are primarily in ionized form and are hence less readily absorbable. Intestinal absorption is further enhanced by the long contact time and the large surface area provided by the and microbial in the intestine. There are especially career-mediated transport systems that are responsible for the absorption of nutrients such as iron calcium sodium, monosaccharide, and amino acid, but a few toxicants, such as thallium and lead, are known to be absorbable by active transport systems. Furthermore, particle materials, such as azidyes and polystyrene, can be absorbed by intestinal cells by pinocytosis.

- **Skin:** In general, the skin is very impermeable and so serves as an effective barrier between the organism and its environment. But in some substances can pass through the skin in sufficient quantities to create a systemic effect. A chemical may be absorbed through the hair follicles or sweat gland cells. However, because minor roots account for only a small portion of the skin's surface area, percutaneous absorption of chemicals is mostly required through the epidermis and dermis. The initial phase of percutaneous abortion is the diffusion of the toxicant through the epidermis, which particularly yields the stratum corneum that is the most significant barrier. The stratum corneum is made up of multiple layers of cohesive dead cells that retain chemicals. Small amount of polar substances appear to diffuse through the outer surface of protein filaments of the hydrated stratum corneum whereas non polar substances dissolves in and diffused through the lipid Matrix between protein filaments. The second phase of percutaneous abortion is diffusion of the toxicants through the dermis which contains a pores, non selective aqueous diffusion medium and therefore it is much less selective or effective as a barrier than the stratum

corneum and as a consequence removal in the percutaneous absorption acids alkali and some gases will also increase the absorption of dimethyl sulphoxide increase dermal permeability.



Other routes of exposure – used primarily for specific medical purposes:

- **Ingestion:** Eating or drinking the contaminated food, water, or other liquids is a common way to come into contact with harmful substances. Foods can be ingested accidently or on purpose, and the gastrointestinal tract absorbs the substance.
- **Inhalation:** Breathing in contaminated air can result in the inhalation of airborne toxicants. This path is especially important for chemicals and pollutants found in indoor and outdoor air pollution, as well as industrial settings.
- **Dermal Absorption:** Toxins can be absorbed via the skin when they come into contact with polluted surfaces, soil, water, or objects containing hazardous compounds. Skin integrity, exposure period, and chemical properties are some of the factors that influence dermal absorption.
- **Injection:** Toxicants are administered directly through injection, bypassing natural barriers, whether on intentionally (drug abuse, for example) or by accident (needle stick injuries).

4.3.1 Role of Cell Membranes in Absorption

Xenobiotics must pass through cell membranes (also known as cell walls) before entering, travelling through, and exiting the body. Cell membranes are robust barriers that act as a critical line of defence for the body, preventing chemicals or external invaders from accessing bodily tissues. Normally, materials cannot pass through the densely packed cells that make up solid tissues such as skin or the mucous membranes that line the intestines and lung.

Even in cell membranes the xenobiotic compound is passed through it. To go from one part of the body to another, it must also pass through many membranes. To pass through a single cell, a material must first cross the membrane, then enter the cell and depart by crossing the membrane again. This is true whether the cells are present in the epidermis, blood vessel lining, or an inside organ such as the

liver. A medication frequently must pass many membrane barriers before reaching the site of harm. Certain toxicants find it difficult or impossible to get through a membrane barrier, whereas others do so with relative ease. Those who are able to breach the membrane employ two basic strategies: 1) passive transfer and 2) aided transport.

4.3.2 Mechanisms of Absorption

Toxicants are absorbed by the body via complex physiological systems that are influenced by the material's chemical composition and the circumstances surrounding the exposure route. The primary pathways of absorption include:

1. **Passively Transport:** Passive transfer is the most common route by which xenobiotic infiltrate cell membranes. A wide range of toxicants can passively diffuse through biological membranes, including those lining the skin, respiratory system, and gastrointestinal tract. This mechanism is driven by concentration gradients as well as the hydrophilicity or lipophilicity of the toxicants.

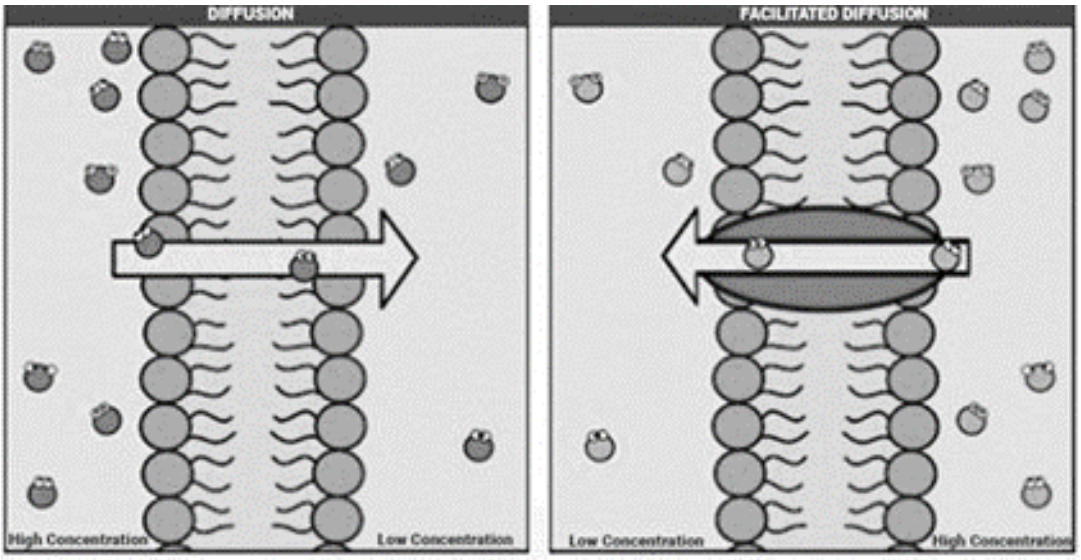


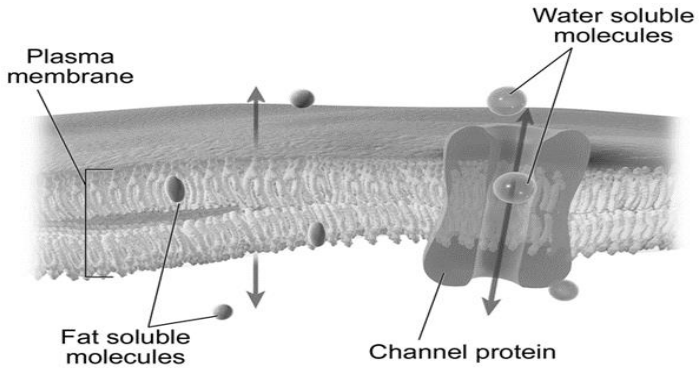
Fig.4.1: Active transport mechanism

The rate of passive transmission is influenced by two factors:

a) When a substance moves from a high to a low concentration, its concentrations vary on both sides of the membrane. Diffusion will continue until the concentrations on both sides of the membrane equalize.

b) The substance's ability to pass through the membrane's small pores or its lipophilic interior. The properties listed below determine a chemical substance's capacity for passive transmission.

- Lipid solubility
- Molecular size
- The degree of ionization



High lipid solubility compounds can permeate through the phospholipids membrane. Small water-soluble compounds, as well as normal intracellular water flow, can penetrate across membranes via aqueous holes. Although some may slowly permeate through the membrane's lipid component, big water-soluble substances frequently fail to enter through the small holes. The majority of aqueous pores have a diameter of 4 Angstroms (Å) and can accommodate molecules with molecular weights of 100 to 200. The renal glomeruli and capillary membranes are the exception. These membranes have relatively wide pores (about 40 Angstrom [Å]) that allow molecules with a molecular weight of up to 50,000 (which is slightly less than albumin's molecular weight of 60,000) to pass through.

1. **Active Transport:** Certain molecules are too large to pass via aqueous channels, cannot dissolve in the lipid layer, and cannot move via diffusion. Several of these compounds have active transport pathways, which mean they can flow across the membrane in the opposite direction of the concentration gradient, i.e. from low to high concentrations. This necessitates the cellular energy given by adenosine triphosphate (ATP).

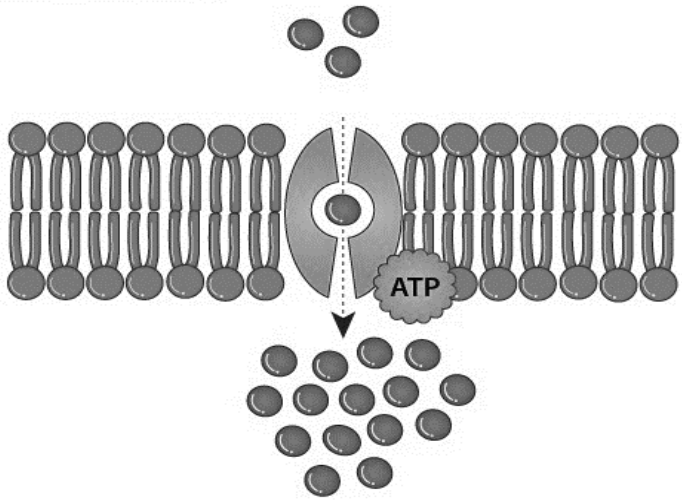


Fig. 4.2: Passive transport mechanism

Using this energy mechanism, the transported material can move from one side of the membrane to another. In addition to maintaining nutritional and electrolyte balance, active transport is required for foreign chemicals to enter the liver, kidney, and central nervous system. Active transport, which may be inhibited or saturable by other molecules, allows for selective uptake of certain medications.

2. **Facilitated Diffusion:** Harmful chemicals travel through membranes using carrier proteins and do not require energy input. Certain chemicals that are too large or too polar to diffuse easily can

be delivered using this mechanism. Certain transport proteins implanted in the cell membrane facilitate the passage of molecules across the membrane via the carrier-mediated transport process. The outcome is similar to passive transport, but it occurs faster and can transfer larger molecules through the membrane more easily when a carrier is present. Facilitated diffusion can be seen in the ability of the central nervous system and red blood cells to absorb sugar and amino acids.

3. **Endocytosis:** This is the mechanism by which cells swallow external substances, forming vesicles that are internalized and pass past cellular barriers. Endocytic pathways are one way whereby toxicants, such as large compounds or nanoparticles, might enter cells. The two basic types of endocytosis are 1) phagocytises and 2) pinocytosis.

   - **Phagocytosis:** Phagocytises, sometimes known as "cell eating," is the process by which large particles caught in extracellular fluid are ingested and either transported or eliminated within cells. For some liver, spleen, and lung phagocytes, this is a critical procedure.
   - **Pinocytosis:** A comparable process known as "cell drinking," or pinocytosis, entails absorbing liquids or minuscule particles suspended in extracellular fluid.

4.3.3 Absorption Variability

Many factors, including as the toxicant's physicochemical properties, the exposure site, and the presence of specific transporters or receptors in the target tissues, impact how essential each of these routes is in comparison to others. The absorbed dose via epidermal, oral, or respiratory exposure is only a fraction of the exposure dose (external dose). The exposure dose for medications that are physically injected or implanted in the body is the same as the internal or absorbed dose. A variety of factors influence how well toxicants are absorbed, how much enter the body, and whether they end up in the bloodstream.

1. **Chemical Properties:** A toxicant's ability to infiltrate biological barriers and enter tissues is controlled by its physicochemical qualities, which include molecular size, lipophilicity, solubility, and ionization state.

2. **Exposure Route:** The kinetics and efficiencies of absorption differ depending on the exposure route. For example, due of the respiratory tract's large surface area and thin epithelial barriers, inhalation typically results in rapid absorption, but cutaneous absorption may be slower but nonetheless significant, particularly for some drugs with high permeability.

3. **Dosage and Concentration:** Toxicology and absorption kinetics are strongly impacted by the toxicant's dose and concentration. Higher concentrations or doses may saturate absorption systems, resulting in harmful effects at lower concentrations or with nonlinear kinetics.

4. **Biological Factors:** Individual differences in physiology, metabolism, and genetic makeup may have an impact on toxicant absorption. Age, sex, health, and nutritional status can all influence the distribution and absorption of toxicants in the body, affecting enzymatic activity, skin permeability, and gastrointestinal motility.

5. **Interactions with Food or Matrix**: Toxicants' interactions with food or other matrices can have an impact on their metabolism, bioavailability, and absorption. For example, some compounds can alter their fate in the body by attaching to food ingredients, altering chemically, or being trapped in tissues.

6. **Co-exposure and Synergistic Effects**: Co-exposure to diverse toxicants or environmental stressors can influence absorption rates and toxicity via additive, synergistic, or antagonistic

interactions. Complicating matters is the likelihood that complicated mixtures absorb more or less than individual chemicals.

Various routes of exposure allow for the body to absorb a multitude of chemicals with hazardous effects.

- **Heavy Metals:** Heavy metals such as lead, mercury, cadmium, and arsenic can contaminate food, water, air, and consumer products. These metals can accumulate in tissues and cause systemic toxicity as well as long-term health impacts when ingested, inhaled, or come into contact with the skin.
- **Organic Pollutants:**Persistent organic pollutants (POPs) are lipophilic compounds that can accumulate in adipose tissue and be biomagnified in the food chain. Examples include pesticides, dioxins, and polychlorinated biphenyls (PCBs). POP exposure has been linked to issues with human development, reproduction, and cancer in both humans and wildlife.
- **Volatile Organic Compounds (VOCs):** Benzene, toluene, formaldehyde, and other volatile organic compounds are common indoor and outdoor air pollutants emitted by a range of industrial and consumer sources. The primary mode of exposure is inhalation, and volatile organic compounds (VOCs) can easily enter the bloodstream, affecting multiple organ systems and worsening respiratory, neurological, and cardiovascular diseases.
- **Medications and Personal Care Products:** Ingestion, inhalation, or skin contact can all result in the absorption of certain medications, such as hormones, psychotropic drugs, and antibiotics, as well as compounds found in personal care products like parabens and phthalates. Prolonged exposure to these substances may impact reproductive health, cause endocrine disruption, or increase antibiotic resistance.
- **Herbicides and Pesticides:** Organophosphates, glyph sate, and chlorpyrifos are examples of agricultural pesticides that can be hazardous to human health through environmental contamination, occupational contact, or dietary exposure. These substances can affect the brain system, respiratory system, or reproductive systems in an acute or long-term manner. They can also be absorbed through a variety of pathways.

4.4 DISTRIBUTION OF TOXICANTS

Toxicants are absorbed into the body and then distributed throughout the body, reaching different tissues and organs from their point of entrance. Comprehending the dispersion of toxicants is imperative in evaluating their systemic impacts, capacity to accumulate in specific organs, and overall toxicity. The body's dynamic distribution of toxicants is impacted by a number of physiological, chemical, and environmental variables. Toxin distribution pathways and factors must be understood in order to predict exposure risks, forecast target organ toxicity, and develop effective therapeutics to mitigate negative health consequences. Scientists and public health specialists can design strategies to decrease exposure and protect human health by better understanding the complex interplay between biological systems and toxicants. To get a comprehensive understanding of toxicant dispersion and its implications for the environment and public health, additional study is needed to investigate newly identified pollutants, improve risk assessment approaches, and build predictive models.

After absorption, the toxicant enters the bloodstream, and where it enters the vascular system is primarily determined by its size. For example, if a toxicant enters the body via the skin, it enters the peripheral blood supply. If it passes through the gastrointestinal tract, it will partially feed the urine; if it goes through the lungs, it will enter the pulmonary circulation. The rate of toxicant distribution to the tissue is determined by the amount of blood flow through the organ and the ease with which the toxicant

penetrates the capillary wall and reaches the cell of a specific tissue. The toxicant enters the bloodstream after absorption, and the area of the vascular system into which it enters relies mostly on its size. For example, if a toxicant enters the body through the skin, it will enter the peripheral blood supply. If it passes through the gastrointestinal tract, it will partially feed the urine; if it passes through the lungs, it will reach the pulmonary circulation. The blood flow through the organ and the ease with which the toxicant crosses the capillary wall and enters the cell of a specific tissue dictate the rate of distribution of toxicants to the tissue. The distribution of the toxicant into different tissues and the target organ is reflected in the concentration of the toxicant in plasma, which is highly significant. The concentration of lipid-based toxins, which are widely dispersed throughout tissues and extremely soluble, is low in plasma. Distribution value may be expressed as quantity using the following formula:

$$V_D(l) = \frac{Dose(mg)}{Plasmaconcentration(mg/l)}$$

A tissue or organ may become concentrated with the toxicant during dissemination; these tissues and locations are referred to as storage depots.

4.4.1 Processes of Distribution

1. Toxicants, in addition to proteins, can target diverse tissues throughout the body based on their physicochemical qualities and distribution. Lipophilic chemicals, for example, may concentrate in fatty tissues, whereas water-soluble molecules may primarily damage high-flow organs like the liver and kidneys. Toxicants, once sequestered in tissues, can cause localized inflammation, oxidative stress, or cell death by directly interacting with biological components.
2. **The Placental and Blood-Brain Barriers:** BBB and placental barrier restrict barriers prevent some chemicals, such as toxins, from entering the fetal circulation and the brain, respectively. Small molecular weight or lipid-soluble toxicants, however, have the ability to get through these barriers and have neurotoxin or developmental consequences. The placenta functions as a barrier between the circulations of the mother and the fetus during pregnancy, allowing only the transfer of vital nutrients and preventing the entry of several toxins. The placental barrier shields the growing, delicate fetus from the majority of toxins found in the mother's bloodstream. The placenta's barrier, which separates the fetal and maternal blood vessels, is made up of many cell layers. Water-soluble toxicants are prevented from diffusing by lipids in cell membranes. Nonetheless, the placental barrier allows for the passage of the developing fetus's waste products, gasses, and nutrients. Similar to the blood-brain barrier, the placental barrier efficiently slows down the majority of toxicants from the mother into the fetus but is not totally impenetrable. Certain toxicants, however, can still pass through the placenta and affect embryonic growth and neurodevelopment or perhaps result in developmental defects. Most chemicals, including toxicants, are prevented from entering the brain by the blood-brain barrier. Its highly specialized structure, made up of densely packed endothelial cells, actively carries vital nutrients while blocking dangerous substances and restricts the diffusion of chemicals. When toxicants cross the blood-brain barrier, they have the potential to cause neuroinflammation, impair neuronal function, or even worsen neurological conditions. Determining the hazards of neurotoxicity and prenatal exposure requires an understanding of the mechanisms by which toxicants interact with the placenta and blood-brain barrier. Studying the sensitivity of these barriers to toxicants and how they work might help develop targeted remedies for linked health disorders as well as methods to reduce exposure and safeguard sensitive groups.

4.4.2 Factors Influencing Distribution

The distribution of toxicants within the body is influenced by a number of factors, such as:

- **Chemical Properties:** The toxicant's affinities for different tissues, as well as its distribution behaviour, are governed by its physicochemical properties, which include molecular size, lipid solubility, ionization state, and protein binding.
- **Blood Flow:** Blood flow dynamics and tissue perfusion rates determine how toxicants are distributed and administered to different organs. Compared to organs with lower perfusion rates, those with higher blood flow rates get more circulating toxicants.
- **Protein Binding:** The amount of binding to plasma proteins influences the free fraction of toxicants that can be absorbed by tissues and the distribution equilibrium. Compounds with high affinity for proteins may have delayed tissue penetration and prolonged dispersion kinetics.
- **Tissue Structure and Permeability:** Differences in tissue composition, permeability, and structure influence how toxicants are dispersed. Lipophilic compounds tend to concentrate in adipose tissue, whereas hydrophilic molecules may be better distributed in watery compartments.
- **Metabolic Activity:** The distribution and kinetics of toxicant elimination can be altered by enzymes in organs such as the liver, kidneys, and lungs that degrade toxicants. Metabolites' distribution patterns and toxicity profiles may differ from those of their parent medicines.
- **Age, Sex, and Genetics:** Individual variables such as age, gender, genetic differences, and health can all have an impact on distribution.

4.4.3 Compartments of Distribution

The body can contain toxicants in a number of different compartments, such as:

1. **Bloodstream:**Toxins are initially disseminated throughout the bloodstream after absorption, where they interact with plasma proteins, cells, and blood components.
2. **Extracellular Fluid (ECF):**Toxins can enter the extracellular fluid (ECF) that surrounds cells and tissues from the bloodstream. This generates concentration gradients, which direct the dispersion of poisons into intracellular compartments.
3. **Adipose Tissue:**Because adipose tissue is predominantly constituted of lipids, lipophilic toxicants have a significant affinity for it. Lipophilic chemicals can be stored and released gradually in adipose tissue.
4. **Organs and Tissues:**Toxicants target certain organs and tissues based on blood flow, tissue perfusion, metabolic activity, and affinity for cellular targets, among other factors. Buildup in the designated organs may cause localized toxicity or impair organ performance.
5. **Barrier Systems:**Specialized barrier systems, such as the gastrointestinal mucosa, placental barrier, and blood-brain barrier (BBB), regulate the flow of toxins between compartments and protect delicate tissues.
6. **Intracellular Fluid (ICF):**Toxicants may split into compartments within the cell, where they can interact with biomolecules, organelles, and cellular structures, causing detrimental effects or metabolic alterations.

4.5 BINDING AND STORAGE OF TOXICANTS

Toxicants' distribution, bioavailability, and toxicity are all heavily controlled by how they bind and store in the body. Toxicants can bind and accumulate in specific tissues or compartments in a reversible or irreversible manner via interacting with proteins, lipids, nucleic acids, cellular structures,

and other molecular targets. Understanding the mechanisms and variables governing toxicant binding and storage is essential for determining exposure risks, anticipating toxicological findings, and developing effective therapies to reduce negative health effects.

4.5.1 Mechanisms of Binding

Toxicants can bind to biological molecules and structures in a variety of ways, including:

1. **Covalent Binding:**Certain toxicants bind to lipids, proteins, and DNA in the cell, causing chemical changes and cellular damage. Covalent binding can have long-term ramifications for cellular integrity and function, as well as permanent damage.
2. **Non-Covalent Binding:**Toxins can interact with biological molecules by non-covalent interactions such as hydrophobic, van der Waals, electrostatic, and hydrogen bonding. Non-covalent binding might include transient interactions with biological targets and is typically reversible.
3. **Receptor Binding:**Some toxicants bind to specific receptors or enzyme active sites by simulating natural ligands, interfering with normal physiological activities and communication pathways. Receptor binding can cause pharmacological effects, receptor desensitization, and undesirable physiological consequences downstream.
4. **Metal Binding:**When metal toxicants such as lead, mercury, cadmium, and arsenic bind to proteins' sulfhydryl groups (-SH), they can replace essential metals and disrupt cellular signaling pathways, redox processes, and enzyme function. Metal binding can cause organ damage, protein dysfunction, and oxidative stress.
5. **Chelation:** Metal ions can be confined by chelating agents, which create stable complexes that lower the metals' toxicity and bioavailability. Chelation therapy is used to treat metal toxicity and flush the body of dangerous metals through feces or urine.

4.5.2 Storage Sites In The Body

Toxins can sometimes be accumulated in bodily tissues. When a poison enters the bloodstream, it may first attach to plasma proteins. Toxins attached to proteins are classified as a sort of storage because they do not increase the chemical's toxicity potential. The most common plasma protein that binds toxins is albumin. Typically, the toxicant binds to albumin for a short amount of time. Adipose tissue, bone, the liver, and the kidneys are the principal storage sites for toxicants.

- **Adipose Tissue:** Due to its high lipid content and wide surface area, adipose tissue is a primary storage location for lipophilic toxicants. Certain pesticides, polychlorinated biphenyls (PCBs), and persistent organic pollutants (POPs) are examples of lipophilic chemicals that can partition into adipose tissue. There, they undergo sequestration and eventual slow release.
- **Bone Tissue:** Metals such as lead, mercury, cadmium, and fluoride can accumulate in bone matrix and eventually mineralize, using bone tissue as a reservoir. Although bone remodeling and the release of stored pollutants into circulation can cause re-exposure, bone storage also acts as a long-term sink for toxicants.The hydroxyapatite-calcium matrix incorporates calcium and hydroxyl ions during normal bone-forming activities. In the bone matrix, a number of substances, mostly elements, can take the place of calcium and hydroxyl ions because they have similar kinetics.
- **Liver:** The liver is an essential organ for the metabolism of xenobiotics and detoxification, as it is the site of the metabolism of toxicants. Some toxicants are stored in the liver. Its hepatocytes, or liver cells, have a high blood flow and proteins that bind to many substances, including toxins.

- **Kidneys:**Similar to the liver, the kidneys have a high blood flow, which exposes them to large amounts of toxins preferentially. Through filtration, reabsorption, and secretion mechanisms, the kidneys assist in the excretion of metabolites and water-soluble toxicants. On the other hand, a number of toxins, including nephrotoxic substances and heavy metals, can build up in renal tissues and damage the kidneys by reducing renal function.
- **Brain and Nervous System:**Drugs, neurotoxins, and lipophilic toxicants can cross the blood-brain barrier (BBB) and accumulate in the brain and central nervous system (CNS), causing neurotransmitter imbalances, neuronal dysfunction, and neurotoxic effects. The blood brain barrier protects the brain from the majority of poisons. The countless tiny branches of specialized cells known as astrocytes form a wall that separates the brain's neurons from the capillary endothelium. Water-soluble substances can only pass through highly tight junctions between nearby endothelial cells and lipids found in astrocyte cell walls. Toxicant accumulation in the brain may contribute to behavioural issues, cognitive decline, and ne.

4.6 EXCRETION OF TOXICANTS

Toxins must be excreted from the human body in order for the body to be healthy and to help rid it of dangerous toxins. There are several ways that toxicants might be expelled, but the main ones include perspiration, feces, urine, and breath. A number of variables affect the effectiveness of excretion, such as the chemical makeup of the toxin, how the body metabolizes it, renal function, level of hydration, and the person's general health. Reducing the body burden of toxicants and promoting effective excretion can be achieved through maintaining a balanced diet, getting regular exercise, staying hydrated and limiting exposure to environmental contaminants. However, a number of conditions can affect excretory processes, resulting in toxic buildup and detrimental health effects. These conditions include genetic predispositions, continuous exposure to high amounts of toxicants, kidney or liver disease, and genetic disorders. To reduce the dangers of toxicant buildup in the body, it is crucial to monitor exposure levels, encourage healthy lifestyle choices, and seek medical assistance when needed.

- **Urinary Excretion:** Urine is the primary means of excretion; however the lungs and liver are also significant organs for the elimination of some substances. The kidneys remove a lot of toxins from the body through urine, particularly metabolites and water-soluble substances. This covers medications, organic pollutant metabolites, and heavy metals like lead and mercury. Urine is the body's way of excreting waste and poisons that the kidneys have filtered out of the circulation. Weak abases are easier to eliminate from the body due to urine's acidic composition. Toxins are eliminated from the body by the kidney using the same process, glomerular filtration, tubular diffusion, and tubular excretion that is used to eliminate end products from regular metabolism. By passive diffusion, a toxicant can also be eliminated from the body through the tubules and into the urine. The excretion of organic basis is aided by this mechanism because urine is generally acidic. Nonetheless, weak acids frequently undergo metabolism to become stronger acids, increasing the proportion of ionic forms that are ejected by some toxicants from the proximal tubular cells and are not reabsorbed through the tubular cells. As long as the binding is reversible, toxicants attached to proteins can also be released. There are two different secretary mechanisms: one for organic acid and the other for organic basis.
- **Fecal Excretion:** The excretion of certain toxicants occurs through feces, especially those that are not absorbed in the gastrointestinal system or move through enterohepatic circulation. Toxins from food, unabsorbed medications, and certain metals are examples of this. These toxins are

eventually expelled from the body through bowel movements, and the liver's produced bile is a vital part of this process.

- **Respiratory Excretion:** As part of the respiratory process, exhaling can be used to get rid of volatile or gaseous toxicants. This covers gases such as carbon monoxide as well as volatile organic compounds (VOCs). By trading these chemicals for oxygen during breathing, the lungs provide as a pathway for their removal.
- **Lungs Excretion:** those toxicants which adjust in the gaseous phase at body temperature are escalated mainly by the lungs. Volatile liquids do also radley has created by the expired air highly soluble liquid such as chloroform are slowly is created because of their storage in the lady post tissue. Excretion of the toxicant from the lungs is a placed by the simple diffusion for sale membrane.
- **Mother milk:** it is not an important excretory root as for as the host organism is concentrated however it may be significant for the nursing child or from cow and buffaloes to human. The excretion through milk take place by a simple diffusion since milk is slightly acidic basic compounds will reach a higher in the milk then in the plasma. Compound such as DDT and PCB is also reach a higher level in milk because of its height count.
- **Sweat Excretion:** The skin's sweat glands have the ability to expel trace levels of toxins. While sweating is not a significant method of excretion for the majority of toxicants, it can aid in the removal of some chemicals, especially those that are low in molecular weight or extremely lipophilic.

4.7 ACTIVE TRANSPORT OF TOXICANTS

Active transport of toxicants" refers to the energy-intensive process of actively moving toxicants across biological membranes against their concentration gradient. Active transport systems facilitate the body's absorption, distribution, and removal of toxins. Active transport is a fundamental biological process that maintains cellular homeostasis and regulates the movement of ions, nutrients, and signalling molecules across cell membranes.

Active transport routes facilitate the absorption, efflux, and intracellular trafficking of toxicants, hence influencing their bioavailability, distribution, and toxicity profiles. Understanding the physics and control of active transport is crucial to understanding the kinetics of toxicants, predicting the toxicity of target organs, and developing treatments that mitigate detrimental effects on health.

4.7.1 Mechanisms of Active Transport

Toxicants are transported actively by a variety of pathways, each with distinct chemical constituents, energy needs, and substrate selectivity:

- **ATP-Dependent Pumps:** ATP-binding cassette (ABC) transporters are essential membrane proteins that move a variety of substrates, including toxins, across cell membranes by utilizing the energy of ATP hydrolysis. ABC transporters are a functional unit that may bind and translocate substrates. They are made up of two transmembrane domains (TMDs) and two nucleotide-binding domains (NBDs). P-glycoprotein (P-gp), multidrug resistance-associated proteins (MRPs), and breast cancer resistance protein (BCRP) are a few examples of ABC transporters involved in toxicant transport.
- **Ion Pumps and Exchangers:**In order to provide the ion gradients and membrane potentials required for cellular activity. The ion transporters actively pump ions against their electrochemical gradient. H^+-ATPase, Ca^{2+}-ATPase, and Na^+/K^+-ATPase are a few examples of

these transporters. These pumps indirectly influence the transport of charged toxicants by preserving ion gradients and controlling membrane potential across cell membranes.

- **Cotransporters and Antiporters**: The mechanism of coupled transport of substrates across membranes is facilitated by cotransporters, also known as symporters, and antiporters. This process is triggered by the electrochemical gradient of one or more ions. One example of a transporter of glucose and sodium ions is the sodium-dependent glucose transporter (SGLT), whereas the sodium-calcium exchanger (NCX) exchanges sodium ions for calcium ions. Cotransporters and antiporters can modify ion gradients and membrane potential, which can have an indirect effect on the transport of toxicants.
- **Vesicular Transport:**Exocytosis and endocytosis involve the fusion, internalization, and formation of membrane-bound vesicles that allow for the uptake and release of macromolecules, nanoparticles, and vesicles carrying cargo. Exocytosis, caveolae-dependent endocytosis, and clathrin-mediated endocytosis are examples of vesicular transport processes that can carry toxins across cells and enclose them in vesicular compartments.

4.7.2 Regulation of Active Transport

Active transport systems' cellular homeostasis and ability to react to physiological and environmental signals are maintained by strict regulation of their activity at several levels:

1. **Gene Expression and Transcriptional Regulation**: The transcriptional expression levels of transporters involved in active transport can be influenced by a range of transcription factors, nuclear receptors, and signalling pathways. Transcriptional regulation modifies transporter amount and activity in response to developmental, metabolic, or pathological conditions.
2. **Post-translational Modifications:** Phosphorylation, glycosylation, ubiquitination, and palmitoylation are examples of post-translational changes that can control transporter activity, subcellular localization, and turnover. Reversible changes in transporter activity in response to environmental stimuli, metabolic state, or cellular signalling are known to control it dynamically.
3. **Substrate-Induced Regulation:** A substrate's binding to an active transporter results in allosteric regulation and conformational changes. Because of substrate-induced regulation, which modifies transporter kinetics, substrate affinity, and transport capacity, cells are able to adapt to changing substrate concentrations and metabolic demands.
4. **Cellular Signaling Pathways:** Transporter activity can be altered by intracellular signaling pathways, including those involving G-proteins, protein kinases, phosphatases, and second messengers, through direct phosphorylation, cAMP-mediated activation, or calcium-dependent regulation. Cellular signaling networks that combine internal and extracellular inputs dynamically control transporter activity and trafficking. Active transport mechanisms are essential for the toxicity and disposal of xenobiotics and environmental toxicants.

- **Drug Absorption and Distribution:** The absorption, distribution, and elimination of medications and xenobiotics are influenced by active transporters located in the gastrointestinal tract, liver, kidney, and blood-brain barrier (BBB). Drug bioavailability, effectiveness, and toxicity profiles can be impacted by polymorphisms, genetic differences, and transporter-mediated drug interactions.
- **Drug Resistance and Multidrug Resistance**: By effluxing cytotoxic substrates from cancer cells or microbial infections, overexpression of ABC transporters, such as P-gp, MRPs, and BCRP, can impart resistance to chemotherapeutic medicines and antimicrobial agents. Active

transporter-mediated multidrug resistance (MDR) is a major obstacle to antimicrobial therapy and cancer treatment.

- **Toxicant Elimination and Detoxification**: By moving toxicants and metabolites into bile, urine, feces, and other bodily fluids, active transporters in the liver, kidney, intestine, and excretory organs help in the removal and detoxification of these substances.
- **Environmental Exposures and Risk Assessment:** Environmental toxicants can interfere with active transporters and impair cellular functions related to detoxification, metabolism, and elimination. Examples of these toxicants include heavy metals, pesticides, industrial chemicals, and persistent organic pollutants (POPs). Comprehending the function of active transport in the kinetics and disposition of toxicants is crucial for evaluating exposure hazards, forecasting toxicological consequences, and developing risk mitigation tactics.

4.7.3 Examples of Active Transport of Toxicants

- P-**glycoprotein (P-gp):**P-gp is a well-researched ABC transporter that is expressed in several organs such as the kidney, liver, intestine, and blood-brain barrier. By effluxing a variety of substrates, including opioids, antibiotics, chemotherapeutic medications, and environmental toxins, P-gp lowers the intracellular accumulation of these substances, hence enhancing drug resistance in microbial pathogens and cancer cells.

- **Multidrug Resistance-Associated Proteins (MRPs):**Multidrug Resistance-Associated Proteins (MRPs) are a family of ABC transporters that facilitate the exit of conjugated metabolites, organic anions, and xenobiotics from cells. Drug detoxification and elimination are aided by MRPs, specifically MRP2 and MRP4, which assist the excretion of glutathione conjugates, glucuronide conjugates, and other toxicants through the biliary and renal system.

- **Breast Cancer Resistance Protein (BCRP):**BCRP is an ABC transporter that is expressed in the epithelial cells of the intestine, liver, kidney, and blood-brain barrier. It helps metabolites and foreign substances to exit the body.

4.8 PASSIVE TRANSPORT OF TOXICANTS

In the human body, toxins are moved across biological membranes using a simple process known as passive transport, which happens without needing the use of energy. Passive transport mechanisms like diffusion and aided diffusion have a major impact on the body's ability to absorb, distribute, and excrete toxins. In this in-depth analysis, we will go over the mechanisms, influencing factors, importance in toxicology, instances, and consequences for human health of the passive transport of toxicants. Passive transport is the basic mechanism by which molecules, ions, and other substances travel across biological membranes as a result of concentration gradients. Toxins can more easily diffuse across cellular walls thanks to passive transport systems, which also help the body absorb them from the environment, distribute them throughout, and excrete them through excretory channels. This has to do with toxicity. Understanding the processes and factors influencing passive transport of toxicants is essential for deciphering toxicant kinetics, predicting target organ toxicity, and creating treatments to mitigate detrimental health effects.

4.8.1 Mechanisms of Passive Transport

There are two primary methods by which toxicants are passively transported: increased diffusion and diffusion. These non-energy-intensive techniques, which depend on concentration gradients, are how toxins are transported across biological membranes:

1. **Simple Diffusion:** Simple diffusion is the passive movement of molecules across biological membranes along a concentration gradient, from regions of greater concentration to areas of lower concentration. Lipophilic or hydrophobic toxicants, such as nonpolar chemicals and lipid-soluble drugs, can readily diffuse through lipid bilayers and cross cell membranes without the assistance of specialized transport proteins. The factors influencing diffusion rates include molecular size, lipid solubility, membrane permeability, and concentration gradient.
2. **Facilitated Diffusion:** Channels or carrier proteins enable chemicals to move passively across membranes. Facilitated, as opposed to simple, diffusion requires a specific kind of transporter protein that binds to toxicants and aids in their movement across membranes along their concentration gradient. Subsequent to substrate concentration and transporter availability, selective and saturable diffusion is promoted. Cells require facilitated diffusion to take in or release certain polar or charged toxicants, such as ions, glucose, and amino acids.

4.8.2 Factors Influencing Passive Transport

The passive transport of toxicants across biological membranes is influenced by a multitude of factors, including the physicochemical properties of the toxicant, membrane characteristics, ambient conditions, and cellular parameters.

1. **Chemical Properties of Toxicants:**The physicochemical features of toxicants, such as their polarity, solubility, ionization state, and molecule size, influence their passive transit across biological membranes. Lipophilic or nonpolar toxicants have higher permeability and faster diffusion rates than hydrophilic or charged substances; hence, they may require assisted diffusion or active transport processes.
2. **Membrane Permeability and Composition:**Chemicals that are soluble in lipids have an easier time passing across biological membranes than those that are hydrophilic because of the lipid bilayer, which prevents these compounds from diffusing through. Membrane fluidity, thickness, lipid content, and the presence of membrane proteins (such as transporters and channels) all affect permeability and selectivity for toxicants. Changes to the membrane's properties, such as fluidization or the breaking down of lipid bilayers by solvents or detergents, can raise the rates of passive transport.
3. **Concentration Gradient:**A biological membrane's concentration gradient of the toxicant determines the direction and rate of passive transport. Higher concentration differences between intracellular and extracellular compartments lead to accelerated diffusion and greater inflow or effluxes of toxicants. Concentration gradients are influenced by various factors such as metabolic activity, excretory clearance, exposure concentration, and tissue distribution.
4. **Temperature and Physical State**:Temperature affects diffusion coefficients, membrane fluidity, and molecular kinetic energy, all of which are related to passive transport rates. High temperatures increase the mobility and diffusion velocities of molecules, which increases the entry or exit of toxic compounds via membranes. Melting and freezing of lipid bilayers can alter their physical states, which can affect the kinetics of passive transport and change the permeability of the membrane.
5. **pH and Ionization State:** A toxicant's pH and ionization state determine how it partitions between the aqueous and lipid phases, which has an impact on the permeability and diffusion behavior of membranes.Because of their electrostatic interactions with membrane phospholipids, charged or ionized molecules may show lower permeability, whereas uncharged versions can diffuse more easily. The distribution and toxicity of weak acids and bases can be affected by the passive transport of these substances across membranes due to pH gradients.

6. **Surface Area and Thickness of Membranes:**The surface area and thickness of biological membranes affect passive transport rates by changing the available surface area and diffusion path length for molecule exchange. Thinner barriers or larger area membrane surfaces promote greater penetration and diffusion of toxicants. Large membrane surfaces on cellular structures, such as alveoli in the lungs and microvilli in the colon, enhance the exchange and absorption of toxicants.

7. **Cellular Metabolism and Energy Status:** Passive transport rates can be indirectly influenced by cellular metabolic activity, ATP levels, and energy status through the preservation of ion gradients, membrane potential, and transporter activity. ATP-generating metabolic processes like glycolysis, oxidative phosphorylation, and ATP-dependent pumps supply the energy required for active transport mechanisms. The dynamics of passive transport are also impacted by these mechanisms in an indirect way.

8. **Carrier proteins and channels:** Certain toxicants are facilitated in crossing membranes by carrier proteins and channels via increased diffusion. The availability, specificity, and saturation kinetics of carrier proteins or channels dictate the rate and capacity of passive transport for each substrate. Subcellular localization, post-translational modifications, and carrier protein expression regulation are ways to modify the kinetics of passive transport.

4.9 SUMMARY

The complex process of toxicant absorption is influenced by several factors, including the individual, the exposure route, and the chemical composition of the toxin. Understanding how toxicants enter the body is essential for assessing exposure risks, developing effective preventive strategies, and reducing the harmful health effects associated with environmental contaminants. Passive transport systems are essential to the absorption, distribution, and elimination of toxicants. They impact their pharmacokinetics, tissue distribution, and toxicity profiles. Passive diffusion is one of the main ways that toxins from the environment, such as pollution of the air and water, toxins in food, and skin exposures, are absorbed. Lipophilic or volatile toxicants can penetrate biological membranes and enter the bloodstream by passive diffusion, putting the body at risk for health problems. Passive transport is the mechanism by which toxins are moved throughout the body and influences the distribution of toxins among different tissues, organs, and cellular compartments.

4.10 TERMINAL QUESTIONS

Q. 1. What does the term "toxicant" means? Addressed the four categories of toxicants?

Answer:----------

Q. 2. What is the absorption of toxins? Which pathways lead to the intake of toxicants?

Answer:----------

Q. 3. What are the major routes of absorption of poison?

Answer:----------

Q. 4. Distribution elucidates the mechanism of toxicant absorption and distribution.

Answer:----------

Q. 5. Talked about how to store and bind toxicants.

Answer:----------

Q. 6. Active and toxicant transmission was discussed.

Answer:----------

4.11 FURTHER SUGGESTED READINGS

1. Environmental Toxicology,Kees van Gestel, Vrije University, Amsterdam, Environmental Toxicology
2. Environmental Toxicology, Third Edition, Sigmund F. Zakrzewski, oxford university press
3. A Textbook of Modern Toxicology: Ernest Hodgson A John Wiley & Sons, Inc., Publication
4. Principles of Environmental Toxicology, I. Shaw, J. Chadwick, CRC Press
5. Occupational Toxicology, Chris Winder, Neill H. Stacey, CRC Press

UNIT-5 : CHEMICAL TOXICITY IN HUMAN

Structure

5.1 INTRODUCTION

Chemicals can enter the body by direct contact with the skin, ingestion, or inhalation. The degree and kind of reported toxicity can be influenced by the exposure route. The phrase "chronic toxicity" refers to the long-term, progressive effects of frequent or prolonged exposure to a chemical, whereas "acute toxicity" refers to the adverse effects that occur shortly after a single encounter. Chemicals can be carcinogenic (cause cancer), mutagenic (alter DNA), neurotoxic (affect the neurological system), hepatotoxic (damage to the liver), nephrotoxic (damage to the kidneys), and reproductive (affect fertility or pregnancy outcomes). When the body absorbs too much of a specific mineral, it can lead to mineral toxicity. When exposed to chemicals, cells and tissues can be harmed via a wide range of events,

including direct injury, disruption of biochemical pathways, interference with hormone signaling, formation of reactive oxygen species, which leads to oxidative stress, and manipulation of gene expression. A person's sensitivity to chemical toxicity may be influenced by a variety of factors, including age, gender, heredity, pre-existing medical conditions, and lifestyle choices. Chemical exposure's harmful repercussions may be more likely to affect certain populations, such as small children, pregnant women, the elderly, and those with compromised immune systems. It is crucial to evaluate and control the dangers connected to chemical exposure in order to safeguard human health. Regulatory authorities conduct risk assessments to analyse the potential hazards of chemicals and establish safety measures and exposure limits to mitigate risks. To reduce exposure and avoid negative health impacts, chemical risk management solutions include implementing environmental controls and occupational safety measures. In general, knowledge of the causes and consequences of chemical toxicity in humans is necessary for risk assessment and mitigation, public health protection, and the promotion of safer chemical use and management techniques.

Objectives

After reading this unit, learner will able to know

- Alcohol toxicity of alcohol and its effects
- Toxicity of ketenes and its effects on human beings
- Toxicity of Minerals such as Sodium, Potassium**,** Iodine**,** Iron
- Also the toxicity of Nitrogen**,** Calcium**,** ZincCopperand Manganese
- Toxicity of dioxins, its sources, symptoms and effects on human being

5.2 ALCOHOL TOXICITY

Alcohol poisoning, or alcohol toxicity, occurs when excessive alcohol consumption leads to fatal and severe bodily impairments. Alcohol, a central nervous system depressant, affects breathing, heart rate, coordination, and brain processes. Large intakes exceed the body's capacity to metabolize and excrete the substance, making them hazardous. Moderate alcohol consumption is generally considered safe for most adults. The degree of alcohol toxicity is determined by a variety of factors, including the amount and frequency of alcohol consumption, personal tolerance levels, age, gender, body weight, and overall health. Ethyl alcohol depresses the central nervous system in an uneven, descending pattern from cortex to medulla. It first depresses the higher centers that control judgment and Mol behavior (stage of excitation), then the motor centers (stage of incoordination), and ultimately the vital centers in the medulla (stage of narcosis). The difference between a dose that causes narcosis and one that inhibits crucial functions is tiny. Thus, a dose that induces stupor is perilously close to a lethal level.

- Alcohol poisoning symptoms include:
- Confusion.
- Vomiting.
- Seizures.
- Slow breathing, which are fewer than eight breaths a minute
- Breathing that's not regular.
- This is when there is a gap of more than 10 seconds between breaths.
- Skin that looks blue, gray or pale.

- Low body temperature, also known as hypothermia.
- Trouble staying conscious or awake.

The risk of alcohol poisoning is considerably enhanced by binge drinking, which is defined as consuming a large amount of alcohol in a single sitting. Alcohol poisoning symptoms may arise quickly and include the following:

Depression of the central nervous system: Alcohol depresses the central nervous system, causing symptoms such as disorientation, loss of consciousness, slurred speech, and impaired coordination. In extreme cases, respiratory depression caused by alcohol intoxication might result in a coma or even death.

Respiratory depression: Excessive blood alcohol concentrations may impede the brain's respiratory centre, resulting in shallow or irregular breathing. Severe respiratory depression needs immediate medical intervention due to the risk of hypoxia (low oxygen levels) and respiratory failure.

Hypoglycemia: Alcohol reduces blood sugar levels by preventing the liver from producing glucose. Hypoglycemia can worsen symptoms including loss of consciousness, weakness, and confusion, making it more difficult to treat alcohol poisoning.

Gastrointestinal distress: Alcohol upsets the digestive tract, causing symptoms such as abdominal pain, nausea, and vomiting. Vomiting can worsen electrolyte imbalances and dehydration, exacerbating these diseases further.

Effects on the cardiovascular system: Drinking alcohol can alter heart rate, rhythm, and blood pressure. Common signs of alcohol poisoning include bradycardia (slow heart rate) and hypotension (low blood pressure), which in extreme situations can result in cardiovascular collapse.

Cognitive impairment: Drinking impairs one's judgment, decision-making, and cognitive function, increasing the risk of accidents, injuries, and risky behaviour. Patients suffering from alcohol poisoning may be unable to recognize the severity of their condition or seek immediate medical attention.The primary objectives of treatment for alcohol poisoning are to keep vital bodily functions going, prevent the patient from absorbing more alcohol, and stabilize the patient's mood. In mild cases, supportive care such as oxygen therapy, intravenous fluids, and vital sign monitoring could be adequate. Advanced life support techniques like hemodialysis, mechanical breathing, and the delivery of countermeasures like glucose or thiamine might be necessary in severe situations.

Moderation, awareness of personal limits, and responsible drinking practices are required to avoid alcohol poisoning. To reduce the risk of toxicity, drink moderately, avoid binge drinking, and switch between alcoholic and non-alcoholic beverages. To avoid potentially fatal effects, raise awareness of the warning signs and symptoms of alcohol poisoning, as well as the importance of seeking medical assistance as soon as possible. Avoiding alcohol during pregnancy, as well as combining it with other drugs or therapies, may lower the risk of alcohol poisoning and the associated health problems. Unlike food, which takes hours to digest, alcohol is absorbed by the body quickly and usually before most other nutrients. Furthermore, the body takes much longer to remove alcohol. The liver is responsible for the majority of alcohol metabolism. The danger of alcohol poisoning grows as you consume more alcohol. This is the meaning of a single drink.

- **Beer:** 12 fluid ounces (360 milliliters) with about 5% alcohols.
- **Malt liquor:** 8 to 9 fluid ounces (240 to 270 milliliters) with about 7% alcohol.
- **Wine:** 5 fluid ounces (150 milliliters) with about 12% alcohol.

- Liquor such as gin, rum, vodka or whiskey: 1.5 fluid ounces (45 milliliters) of an 80-proof drink, which has about 40% alcohol.

However, a single drink may contain significantly more alcohol than those on the preceding list. For example, some artisan beers can have four times the alcohol concentration of regular beers. The alcohol content is stated on the label. Alternatively, ask the server about the alcohol content. Recognize the amount of alcohol in the beverages you're drinking and adjust your consumption accordingly.

Acute Poisoning: This could happen if you consume any alcohol-containing preparation in little amounts at regular intervals or all at once. While a few cases of intoxication via inhaling vapours have been documented, this route cannot be considered toxicologically significant.

Symptoms and signs: The symptoms of acute alcoholism might vary greatly. Its depressing effect on the central nervous system is the only thing responsible for the effects. Alcohol often produces three stages: (1) exhilaration, (2) incoordination, and (3) narcosis. Those who are mentally or physically weary, epileptics, people with head injuries, and those who have taken barbiturates or other CNS depressants are more likely to experience the effects early on.

Stage of excitement: There is a sense of well-being and pleasure caused by inhibition of the higher centers. As a result, the first signs of drunkenness are behavioral changes. As a result, the social usefulness of alcohol in moderation is based on its ability to paralyze inhibitions that display as shyness, resulting in the drinker conversing better, laughing and smiling more readily, or becoming furious more quickly. Because of a lack of typical restraint, he may act obscenely and/or speak in filthy terms. This stage is also known as the flippant stage. His face is flushed, the conjunctivae are injected, the pupils are dilated and react slowly to light and accommodation, his breath smells of alcohol, and his pulse is racing. This stage is characterized by a blood alcohol content of 0.05 to 0.1 percent (50-100 mg %). At this point, some people retain a high degree of mental clarity despite their intoxication. Small effects are seen at alcoholic concentrations less than 0.05 percent (50 mg %). When a person's blood alcohol content is between 0.05 and 0.1 percent (50-100 mg %), they are typically considered gay and vivacious; when their blood alcohol content is 100 mg% or above, they should not drive. In the UK, 80 mg% is the legal limit for driving while inebriated.

Stage of incoordination: There is a lack of coordination in thought, speech, and action. Incoordination of thought causes confusion, which is why this condition is frequently referred to as the stage of confusion. The memory for recent events is impaired Speech becomes slurred and nonsensical due to lack of coordination, and consonants are difficult to pronounce. Muscle incoordination results in a staggered walk. Skilled movements are impaired, and reaction time increases. A one-tenth-second increase in reaction time means that an automobile traveling at 80 km/h requires an extra 2.3 meters of road to draw up. The eyes are suffused, with dilated pupils that react slowly to light and accommodation. The vision is blurry, and there is a possibility of temporary double vision. The mouth is dry, the tongue is furry, and the breath smells strongly of alcohol. Nausea and vomiting are common, and the latter can be dangerous; nonetheless, vomiting can remove alcohol from the stomach and have a sobering impact. He may have hiccups and present an unkempt appearance. Depending on his underlying feelings, the individual may become depressed, homosexual, or irritable.

At this stage, the percentage of alcohol in the blood is between 0.1 and 0.3 percent (100-300 mg %). This is an important stage in the medical legal process when an offense is committed. An individual in charge of a vehicle may cause an accident. An ordinary moral person may indulge in sexual excesses.

Stage of narcosis: Also known as coma. At this stage, the percentage of alcohol in the blood is 0.3% (300 mg %) or higher. The patient falls into a deep sleep and only responds to powerful stimuli. Dryness of the mouth and tongue is common, and the latter can be furred. Sometimes there is excessive

salivation.The pulse is quick, the temperature is subnormal, and the pole may be concentrated. A fine lateral typically promotes Symptoms of medullary paralysis is shown by such symptoms as slow, stertorousrespirationcold clammy cyanotic skin, dilated pupils, abolished reflexes, and almost imperceptible pulse If this stage lasts for more than twelve hours, death invariably ensues from paralysis of the cardiac of respiratory centre of later from the effects of pulmonary cedema.

Death from acute alcoholism is uncommon. In general, unless huge volumes are absorbed in a short period of time. Recovery begins with severe sadness and gastrointestinal irritation, which last for 24 hours. Headache can also occur as an aftereffect (hangover effect) of cerebral edema.

Fatal dose: The fatal dose will vary depending on the patient's age and habits, as well as the strength of the liquor consumed. Alcohol concentrations of 0.4-0.5 percent (400-500 mg %) or more in the blood can be fatal. Prolonged alcohol-induced coma can result in irreparable hypoxic brain damage, which can ultimately to death. In such circumstances, the blood alcohol level is typically low, as one would expect after a prolonged period of survival. Death is frequently caused by taking a huge amount of something in a short period of time. Children have developed serious symptoms after consuming 1 ml/kg of denatured alcohol containing 5% methyl alcohol.

Fatal period: The usual fatal period is 12 to 24 hours though death may be delayed for 5 to 6 days.

Cause of death: The respiratory center becomes depressed, resulting in death. Alcohol can be deadly at lower blood levels when mixed with other central nervous system agents such as barbiturates, carbon monoxides, morphine, or in the presence of certain underlying cardiac disorders. Excessive alcohol use causes irreparable brain and liver damage that can eventually prove fatal. Alcoholics can die from poisoning caused by several poisonous chemicals found in cheap industrial alcohol mixtures. Alcoholics may bleed to death from relatively small damage. Peripheral blood tests for alcohol may come up negative in people who sustain head injuries with subdural or epidural haemorrhages and survive for hours or days.

Analysis of a brain blood clot, which is not part of the circulation detoxifying cycle, may disclose the initial blood alcohol level at the moment of damage. The drunken person may harm himself by falling. Exposure to heat or cold, drug overdose, fire burn, attempting to swallow an excessively big bolus of food (cafe coronary), drowning, aspiration, etc.

Treatment of Alcohol poisoning: Emetics may soil the air passages with the vomit and should preferably be avoided. The stomach should be lavaged with care and the contents preserved. The patient C should be kept warm. Vitamin B is said to accelerate the metabolism of alcohol. Its intravenous administration, in dosage of 50 to 100 mg may effect a rapid recovery of may restore a comatose patient to a near conscious state. In a proportion of cases, coramine 3 to 5 ml can be given slowly intravenously, with amazing results. Isotonic saline with 5 per cent glucose (preferably fructose) may be required to deal with symptoms of hypoglycaemia, if present.

The increase in intracranial pressure which often occurs can be treated with saline purges and intravenous hypertonic glucose solution. When there is dangerous respiratory depression, artificial respiration may be necessary along with oxygen inhalation.Acidosis (common with methyl alcohol poisoning), if present, will require administration of sodium bicarbonate by mouth in a dose of 2 gms (½ teaspoonful) in 250 ml (1 cup) of water every two hours to maintain neutral or slightly alkaline urine. If oral therapy is not possible, 50 gms of sodium bicarbonate dissolved in 1 litre of 5% dextrose solution can be given intravenously along with 10-15 units of insulin. The plasma bicarbonate level should preferably be checked frequently to avoid over-treatment. Very serious cases will require haemodialysis or peritoneal dialysis.

Postmortem appearances: On external examination of a case dead due to acute alcoholic poisoning,

the clothes are generally in a disorderly/torn condition. Stains due to vomit or blood are present. The eyes are suffused and the pupils dilated. The mouth is dry and tongue furred. Rigor mortis lasts longer than usual. Bruises are generally found on various parts of the body. Other injuries may be present.

Chronic Poisoning (Alcoholic Addiction): This is caused by continuous alcohol use and is characterized by progressive physical, moral, and mental decline (alcoholic dementia). Physical degeneration is marked by poor personal cleanliness and loss of appetite. Chronic gastroenteritis, wasting, and peripheral neuropathies. Impotence, infertility, and fatty abnormalities in the liver and heart. Alcohol is a hepatotoxic substance. Cirrhosis of the liver is prevalent. Moral decay is marked by widespread societal consequences. Dementia is one of the three most prevalent clinical symptoms caused by prolonged alcoholism: (1) delirium tremens. (2) Korsakoff's psychosis; and (3) acute hallucinations.

5.3 TOXICITY OF KETENES

Ketones are organic compounds with a carbonyl group attached to two extra carbon atoms. Some are naturally occurring and necessary for the body's metabolic operations, while others can be harmful. Understanding the toxicity of ketones requires examining specific chemicals and their effects on human health. Acetone, well-known ketones, is used as a solvent in industrial applications and produced by the body as a by-product of fat metabolism. It is relatively safe and is eliminated from the body through sweat, urine, and breath. Acetone vapors can cause skin, eye, and respiratory irritation, leading to headaches, nausea, dizziness, and tiredness. Methyl ethyl ketone (MEK), a solvent in paints, adhesives, and coatings, can also cause skin and respiratory irritation, fatigue, headache, nausea, and dizziness. Long-term exposure to MEK can cause neurological side effects like memory loss, cognitive impairment, and liver and kidney damage. Both ketones can be toxic when breathed or applied topically.Furthermore; there are substantial health risks linked with the synthesis of ketones in the body under conditions such as diabetic ketoacidosis (DKA). When there is a large insulin shortage, ketones accumulate in the blood and urine, resulting in diabetic ketoacidosis (DKA). Increased fat breakdown for energy production produces ketones such as acetoacetate and beta-hydroxybutyrate. While small amounts of ketones are normally created after prolonged fasting or exercise, excessive levels can induce organ malfunction, metabolic acidosis, and electrolyte imbalances. The symptoms of diabetic ketoacidosis (DKA) include abdominal pain, nausea, vomiting, lethargy, fruity-smelling breath, severe thirst, frequent urination, and confusion. If medical assistance is not received promptly, DKA can progress to a coma and, ultimately, death. Ketones are produced when the body breaks down fat for energy due to a lack of carbs, such as during hunger or fasting. Chronic hunger can cause ketosis, characterized by elevated blood and urine ketones. Severe ketosis can cause electrolyte imbalances and metabolic acidosis, causing symptoms like nausea, headaches, weakness, and fatigue.

5.4 MINERALS TOXICITY

Mineral toxicity is a serious health issue caused by excessive mineral consumption. Minerals are essential for various physiological activities, including neuron and bone health and enzyme activity. Lead poisoning is a well-known case of mineral toxicity, a heavy metal used in paints, pipes, and gasoline. It can be caused by ingestion of tainted food or water, inhalation of lead dust or fumes, or direct contact with lead-containing objects. Lead poisoning is particularly dangerous for children, whose developing bodies and brains are more susceptible to its effects.Lead poisoning, a harmful heavy metal found in dental fillings, industrial operations, and some fish species, can cause neurological damage, kidney damage, and reproductive issues. Symptoms include abdominal pain, fatigue, headaches,

irritability, learning difficulties, and developmental delays. Mercury poisoning, on the other hand, can cause kidney failure, cardiovascular problems, and brain impairment. These effects can disrupt prenatal development and cognitive function, making pregnant women and young children more vulnerable. Consuming too much of a mineral through supplements or fortified foods can lead to toxic effects. High iron supplementation can cause iron overload, causing symptoms like nausea, vomiting, constipation, and stomach pain. Chronic iron overload can also increase the risk of diabetes and cardiovascular disease. Similarly, excessive calcium supplementation can cause hypocalcaemia, characterized by excessive blood calcium levels, causing symptoms like nausea, constipation, tiredness, confusion; kidney stones, bone pain, and cardiac arrhythmia.To avoid mineral toxicity, take the necessary precautions and are aware of potential exposure sources. To avoid consuming too many minerals, consumers should exercise caution when taking supplements or eating meals fortified with nutrients. They should also follow dosing recommendations. Those with underlying medical conditions, young children, and pregnant women should consult with their doctors before starting any supplement regimen. Furthermore, reducing the environmental sources of heavy metals such as lead and mercury can reduce the population's risk of toxicity. In general, one can protect against the negative effects of mineral poisoning on health and well-being by being aware of the risks and taking the required precautions.

5.4.1 Sodium Toxicity

Sodium is a vital mineral that is required for numerous physiological activities, including nerve transmission, muscle contraction, and fluid balance. Hypernatremia, or excessive salt ingestion, can cause sodium toxicity, which is defined as an abnormally high blood sodium concentration. Sodium poisoning can be caused by dehydration, certain medical conditions, prescription medication, or an excessive intake of sodium in the diet. Sodium chloride, popularly known as table salt, is a prominent preservative and flavor in food preparation, as well as one of the primary sodium sources in the human diet. Many packaged and processed meals contain high levels of salt as a flavor enhancer and stabilizer. Chronic salt poisoning from a high-sodium diet can increase the risk of hypertension, heart disease, and stroke, and kidney damage. The American Heart Association recommends that most adults, particularly those with high blood pressure, kidney disease, or other risk factors, limit their sodium consumption to no more than 2,300 milligrams per day, with an ideal limit of 1,500 milligrams per day. Acute sodium poisoning is characterized by a sudden spike in blood sodium content following severe dehydration or considerable water loss. Prolonged vomiting, diarrhea, excessive perspiration, or a lack of fluid intake is all examples of when this might happen. Acute sodium toxicity symptoms include thirst, dry mouth, weakness, confusion, irritability, seizures, coma, and possibly death if not treated.To avoid sodium poisoning, use salt in moderation and stay hydrated. People should make an effort to eat a well-balanced diet rich in whole grains, fruits, vegetables, and lean proteins while limiting their intake of salty packaged and processed foods. Reading food labels and picking low- or no-sodium alternatives can help you reduce your salt intake. Furthermore, staying hydrated throughout the day by drinking plenty of water might help you maintain electrolyte balance and avoid salt toxicity from dehydration. The underlying cause and degree of sodium poisoning dictate how the condition should be managed. In cases of acute sodium poisoning, intravenous fluid rehydration and electrolyte balance correction may be required.To regulate salt levels and avoid complications in chronic cases, dietary changes, medication adjustments, and lifestyle changes may be recommended. To ensure the best possible health and well-being, consult with a healthcare expert about the proper assessment, diagnosis, and treatment of salt poisoning.

5.4.2 Potassium Toxicity

Potassium is an essential mineral that is required for various physiological activities, including neuron and muscle function and fluid balance maintenance. Although excessive potassium consumption can lead to potassium poisoning, also known as hyperkalemia, potassium is still necessary for optimal

health in general. Kidney failure, medication use, medical problems, and eating habits can all contribute to potassium toxicity. Fruits, vegetables, and legumes are some of the most potassium-rich foods. Eating a potassium-rich diet is generally seen as good, with a lower risk of cardiovascular disease and hypertension. However, due to low potassium excretion by the kidneys, persons with specific medical conditions, such as chronic kidney disease or renal failure, may be more vulnerable to acquiring potassium poisoning. Potassium supplements and potassium-containing medications can cause potassium overdose if used improperly or excessively. Angiotensin-converting enzyme (ACE) inhibitors, potassium supplements, and potassium-sparing diuretics are a few medications that may raise blood potassium levels and increase the risk of hyperkalemia. Those taking these medications must regularly monitor their potassium levels and follow their doctor's recommendations for dosage adjustments. Potassium toxicity symptoms may vary depending on the severity of the sickness and individual circumstances. Mild hyperkalemia can induce nonspecific symptoms such as weakness, nausea, fatigue, and muscle cramps, or it might be asymptomatic. As potassium levels rise, more serious symptoms may emerge, including palpitations, an irregular heartbeat, chest pain, breathing difficulty, and paralysis. If severe hyperkalemia is not treated soon once, it can lead to cardiac arrest, sudden death, and potentially lethal arrhythmias. Blood tests are commonly used to identify potassium levels and assess renal function in the diagnosis of potassium intoxication. Electrocardiography (ECG) can be used to evaluate heart function and detect hyperkalemia-related anomalies such as excessive T waves, enlarged QRS complexes, or absent P waves. In some cases, additional testing, such as imaging examinations, renal function tests, or urine tests, may be necessary to determine the underlying cause of hyperkalemia. Treatment for potassium poisoning aims to lower blood potassium levels while also regulating cardiac function. This could include modifying one's diet to ingest less potassium, discontinuing or reducing medications that cause hyperkalemia, and taking pharmaceuticals that improve potassium excretion or transfer potassium into cells. To prevent potentially fatal cardiac arrhythmias, severe cases of hyperkalemia may necessitate the administration of intravenous calcium, insulin, glucose, or sodium bicarbonate. To prevent potassium toxicity, it is vital to be aware of the dietary sources of potassium, to carefully monitor potassium levels in those who are at risk, and to treat underlying medical illnesses and medicines. Developing a tailored plan to reduce potassium levels and avoid hyperkalemia complications necessitates close consultation with a healthcare provider.

5.4.3 Iodine Toxicity

Iodine is a brown flaky compound with soft, scaly crystals that have a metallic sheen and an unpleasant taste. It is soluble in alcohol but only marginally so (0.03%) in water. At all temperatures, iodine emits a violet-colored vapor with a distinctive odor. Iodine solubility is considerably increased in the presence of iodide. Sodium and potassium iodides are white crystals that dissolve in water. Iodine acts directly on the cells by precipitating proteins. The consequences are so comparable to those generated by acid corrosives, and the primary symptoms of poisoning include vomiting, collapse, and coma. The fumes of iodine are extremely irritating to the respiratory system.Iodine, an essential mineral, is required for thyroid function and the production of thyroid hormones, which regulate growth, development, and metabolism. Iodine poisoning, also known as iodine-induced hyperthyroidism can result from an excess of iodine intake, whereas iodine deficiency can cause thyroid diseases such as goiter and hypothyroidism. Iodine poisoning can occur due to various factors such as high iodine consumption, exposure to iodine-containing medications, or environmental contamination. Although rare in areas with adequate intake, it can occur in individuals who consume significant amounts of iodine-containing supplements or have iodine-based contrast agents used in medical procedures. Acute toxicity symptoms include mouth, throat, stomach burning, nausea, vomiting, diarrhea, abdominal pain, and metallic taste. Severe toxicity can lead to shock, respiratory difficulty, and electrolyte imbalances.

On the other side, prolonged exposure to high iodine levels produces chronic iodine toxicity,

which develops gradually over time. Chronic iodine overdose can cause thyroid malfunction, such as hyperthyroidism and thyroiditis. Chronic iodine poisoning can result in palpitations, tremors, weight loss, sweating, heat intolerance, weariness, and insomnia. Chronic excessive iodine exposure increases the risk of thyroid cancer, autoimmune thyroid disorders, and thyroid nodules. Blood tests are frequently used to monitor thyroid hormone levels and assess thyroid function in order to diagnose iodine toxicity. Imaging techniques such as ultrasonography may be used to examine the thyroid gland and detect any abnormalities, such as thyroid nodules or enlargement. In some cases, further tests such as fine-needle aspiration or thyroid uptake scans may be required to study thyroid function and architecture in greater detail. Treatment options for iodine poisoning include thyroid dysfunction management, supportive care, and symptomatic treatment, depending on the severity of the disease. To treat acute iodine toxicity, the patient may be given electrolytes, fluids, and supportive medicines to alleviate and stabilize symptoms. To avoid iodine poisoning, it is vital to understand the sources of iodine exposure, consume iodine-containing foods and supplements in moderation, and constantly monitor iodine levels in high-risk populations. Controlling iodine consumption and preventing iodine toxicity need ongoing consultation with a healthcare provider.

Symptoms and signs: When iodine is eaten, the symptoms resemble those of a caustic and irritating toxin. Brownish discoloration of the lips and oral mucosa, pain in the mouth with an unpleasant taste, and extreme thirst Its irritating action on the stomach and bowels is characterized by acute abdominal discomfort, vomiting, and diarrhea, both of which are black. Yellow, brown, or blue, having a distinctive iodine odor. The maturation process is unpleasant, and urine can be repressed or sparse. When evacuated, it is dark brown and smells strongly of iodine. In addition to irrigative symptoms, it produces severe depression, a weak pulse, delirium, and collapse. Injection of iodine compounds can result in a rapid lethal collapse due to hypersensitivity. Iodine vapour inhalation causes glotticoedema and mortality due to asphyxiation. Iodism is caused by the prolonged intake of iodine or iodine derivatives. This term is frequently used to describe unique reactions to iodides or iodine. Classic symptoms include headache, acute coryza, bronchial catarrh, conjunctivitis, and oedema of the face and eyelids, which resolve when the medicine is discontinued. Severe cases may include collapse.

- **Fatal dose**: Although the deadly dose of iodine is thought to be around 2 gms, even 20 mg may create toxic symptoms, and 100 mg may result in death. 8-10 mL of iodine tincture may be considered a lethal dose. However, 5 ml of the tincture resulted in death, whereas 150 ml led to recovery. Iodides have been administered in high dosages over long periods of time without ill effect, while distressing symptoms have been reported with a single dose of less than one gram.

- **Fatal period**: The average fatal period is twenty-four hours. Rapid death may occur from anaphylaxis.

- **Treatment:** The stomach should be washed with a 1% starch solution containing 5% sodium thiosulphate. Demulcents such as starchy foods, eggs, milk, and oils are advantageous. In cases of intolerance, the drug should be discontinued immediately and an antihistamine given. If necessary, 4 to 10 mg of hydrocortisone can be administered intravenously until the symptoms decrease. While these medications can alleviate oedema, a tracheostomy is sometimes required. Sodium thiosulphate is useful because it transforms free iodine into harmless iodide. 100 mL of a 5% solution should be given orally. The remainder of the treatment should adhere to conventional principles. In cases of chronic poisoning, iodine or iodides should be discontinued.

- **Postmortem appearances**: Skin rashes and oedema of the eyes and face may develop. Mucous membranes and lips may be stained yellow or brown. The mucous membranes in the mouth, esophagus, and stomach might become excoriated and corroded. There could be glotticoedema,

acute pulmonary oedema, and fluid effusion into the pleural and pericardial sacs. The kidneys exhibit glomerular and tubular necrosis.

- **Medicolegal aspects**: Suicidal people frequently use iodine tincture. Iodine preparations are not suitable for homicidal applications since they tint farinaceous foods blue. However, because iodine is caustic in strong solutions, it has been used as vitriolage to throw on people. Injecting iodine compounds can result in a sudden deadly collapse. Acute poisoning is typically accidental. Children may be drawn to its vibrant colour and consume it. The alcoholic iodine solution may be inadvertently consumed or used excessively as an external application. A dilute iodine solution, 15 drops of the tincture to a tumblerful (200 ml) of water, may be useful in the absence of potassium permanganate, as a chemical antidote against any oxidisablepoisions

5.4.4 Iron Toxicity

Iron, an essential mineral, is involved in a variety of physiological activities such as energy production, oxygen transport, and DNA synthesis. Although iron deficiency is a severe health concern, iron poisoning, also known as iron overload, can be induced by taking excessive amounts of iron. Iron poisoning can be caused by a variety of factors, including accidentally taking iron supplements, consuming a lot of iron-rich or fortified foods, or having hereditary illnesses that affect iron metabolism, such as hemochromatosis. While iron deficiency anemia is typically treated or prevented with iron supplements, taking too much iron can be hazardous since it overburdens the body's ability to regulate iron levels. Iron toxicity symptoms often appear six hours to several days after taking an excessive amount of iron. Early signs include abdominal pain, vomiting, diarrhea, and gastrointestinal bleeding. As iron levels rise, more serious symptoms may appear, including weakness, lethargy, dizziness, hypotension (low blood pressure), tachycardia (rapid heart rate), confusion, convulsions, coma, and death if left untreated. Iron poisoning can harm a range of systems and organs, including the gastrointestinal tract, liver, heart, and brain. Severe iron poisoning can result in potentially fatal consequences such hemorrhagic shock, metabolic acidosis, and multiple organ failure. Children, particularly those under the age of six, are especially vulnerable to iron poisoning due to their tiny stature and limited ability to metabolize iron. Iron poisoning is frequently detected with blood tests that evaluate transferrin saturation, total iron-binding capacity (TIBC), and serum iron concentrations. Imaging studies, such as computed tomography (CT) scans or abdominal X-rays, can be used to determine the quantity of iron in the gastrointestinal system and detect abnormalities like intestine blockage or perforation. In some situations, an endoscopy may be necessary to detect and remove iron tablets or shards from the stomach or intestine. The goals of iron toxicity treatment include removing excess iron from the body, stabilizing the patient, and managing symptoms. Pumping the stomach or inducing vomiting may be required to eliminate undigested iron from the digestive tract. Chelating medications, such as deferoxamine, can be used to bind and eliminate excess iron from tissues and blood. Supportive care, including as blood transfusions, intravenous fluids, and medicine to treat complications and symptoms, may be provided as needed. When utilizing iron supplements and fortified foods, vigilance must be exercised to avoid iron toxicity, particularly in children and individuals who are already at risk of iron overload. To avoid iron overload, drugs and iron supplements must be kept out of children's reach and doses must be strictly followed. People with inherited disorders that impact iron metabolism should collaborate with healthcare providers to successfully treat iron overload and monitor iron levels. In general, iron poisoning can be avoided and treated by seeking immediate medical assistance and becoming aware of the condition's warning indications.

5.4.5 Nitrogen Toxicity

Nitrogen toxicity, also known as nitrate poisoning or nitrite poisoning, occurs when there is an

excessive buildup of nitrates or nitrites in the body, which can be harmful to one's health. Although nitrogen is a common element in the environment and essential for plant growth, there are times when large quantities of nitrates and nitrites can arise, endangering both human and animal health. Soiled food or water is a leading cause of nitrogen toxicity. Nitrates and nitrites, two forms of nitrogen molecules, can enter groundwater via septic systems, industrial contamination, or agricultural runoff. Nitrate-containing fertilizers used in agriculture can potentially contaminate soil and water.Furthermore, nitrates and nitrites could be added to or used as preservatives in some foods like green leafy vegetables, root vegetables, and cured or processed meat. In the human body, microbes in the mouth and gastrointestinal tract can convert nitrates to nitrites.The blood's hemoglobin can then react with nitrites to form methemoglobin, an inefficient type of hemoglobin that cannot transport oxygen.Methemoglobinemia, or having too much methemoglobin in the blood, can induce tissue hypoxia, or oxygen shortage, with symptoms such as cyanosis (blue skin coloring), tiredness, disorientation, and shortness of breath. Severe methemoglobinemia can cause unconsciousness, convulsions, breathing problems, and even death if left untreated. Because of their small size and immature enzyme systems, babies are particularly vulnerable to nitrate toxicity. Babies that ingest formula or water contaminated with high nitrate levels may develop methemoglobinemia, sometimes known as "blue baby syndrome." Blue newborn syndrome can lead to cyanosis, rapid breathing, tiredness, and poor feeding. To treat methemoglobinemia in neonates and minimize consequences such as brain damage or death, urgent medical attention is required. Nitrogen toxicity can be avoided by limiting exposure to nitrate and nitrite-containing products, as well as providing clean drinking water and food supplies. This could include testing for nitrate pollution in water sources, implementing agricultural measures to limit nitrogen runoff, and refraining from using nitrate-containing fertilizers in close proximity to water sources.Furthermore, lowering the intake of foods rich. Foods high in nitrates or nitrites, such as prepared meals and cured meats, can help reduce the risk of nitrate poisoning. Methylene blue, a medication that aids in the conversion of methemoglobin back into functional hemoglobin and restores the blood's ability to transport oxygen, is often used to treat nitrogen toxicity. In extreme cases, supportive care such as oxygen therapy, intravenous fluids, and blood transfusions may be necessary to stabilize the patient and reduce symptoms. To avoid serious complications and ensure the best possible outcome, those who show signs of methemoglobinemia should seek medical attention as soon as possible, especially babies and young children.

In general, protecting human and animal health requires awareness of the causes and consequences of nitrogen toxicity, as well as the implementation of preventative measures.

5.4.6 Calcium Toxicity

Calcium is a mineral required for blood coagulation, muscle contraction, nerve transmission, and strong bones. While adequate calcium consumption is required for good health, eating too much of it can cause hypocalcaemia, or calcium poisoning. Calcium poisoning can be caused by a variety of circumstances, including an excessive diet, the use of calcium supplements, certain medical conditions, or drug abuse. One of the most prominent causes of calcium toxicity is the over intake of calcium supplements or fortified foods. Although calcium supplements can help prevent or treat osteoporosis and other bone problems, taking too much calcium can overtax the body's ability to control calcium levels, leading in hypercalcemia. When taken without medical supervision, high-dose calcium supplements, particularly those containing calcium carbonate, may raise the risk of calcium poisoning. Calcium poisoning symptoms vary according on a person's medical history and severity of the ailment. In moderate situations, hypercalcemia may produce no symptoms at all or vague symptoms such as fatigue, nausea, vomiting, constipation, and stomach pain. When calcium levels rise, more severe symptoms may develop, such as disorientation, weariness, sadness, irritability, kidney stones, and heart arrhythmias. Drugs and diseases can raise the risk of calcium toxicity. Hyperparathyroidism, which is characterized by hyperactive parathyroid glands, can result in increased bone resorption and intestinal calcium

absorption, leading to hypercalcemia. Several medications, including lithium, thiazide diuretics, and vitamin D analogs, can raise the risk of hypercalcemia by increasing blood calcium levels. Blood tests are commonly used to monitor blood calcium levels and measure kidney function in order to diagnose calcium toxicity. Electrocardiography (ECG) may be used to evaluate heart function and detect any hypercalcemia-related anomalies, such as arrhythmias or decreased QT intervals.

Imaging tests such as X-rays or bone densitometry are occasionally used to examine bone density and detect anomalies such as osteoporosis or bone cancer. Treatment for calcium poisoning aims to lower blood calcium levels while also addressing symptoms. This may require discontinuing or adjusting calcium supplements or medications that exacerbate hypercalcemia. Intravenous fluids, diuretics, and medications such as calcitonin or bisphosphonates can all be used to promote calcium excretion or inhibit bone resorption. In extreme circumstances, hemodialysis or other extracorporeal therapies may be required to eliminate excess calcium from the bloodstream and restore calcium levels to normal. To prevent calcium poisoning, limit your intake of calcium-rich foods and supplements, particularly if you are predisposed to hypercalcemia. When taking calcium supplements, it is critical to stick to the specified dose and avoid taking too much without first visiting a doctor. Patients who are using calcium metabolism-altering medications or have underlying medical issues should consult with healthcare professionals to ensure the best possible management of hypercalcemia and calcium levels. Overall, treating and preventing this potentially lethal sickness necessitates understanding the warning signs and symptoms of calcium overdose and seeking medical help as soon as possible.

5.4.7 Zince Toxicity

Zinc is an essential trace mineral that is necessary for a variety of physiological tasks such as cell division, DNA synthesis, wound healing, and immune function. Zinc overdose, also known as zinc poisoning or zinc toxicity, results from taking an excessive amount of zinc. Zinc deficiency can lead to immune system dysfunction, poor development, and other health problems. Zinc poisoning can result from a variety of factors, including increased dietary consumption, excessive use of zinc supplements, or exposure to zinc-containing settings or goods. Zinc supplementation improves immunity, cures colds, and speeds up wound healing, but too much zinc can be problematic because it surpasses the body's ability to regulate zinc levels. Zinc toxicity symptoms may vary depending on the severity of the sickness and individual circumstances. Mild zinc poisoning can result in abdominal discomfort, nausea, vomiting, diarrhea, and other gastrointestinal symptoms. When zinc levels rise, more severe symptoms may emerge, including headaches, dizziness, weakness, lethargy, and a metallic taste in the mouth. Because excessive zinc can impair the body's ability to absorb and use copper, chronic zinc poisoning can lead to copper deficiency. Copper deficiency symptoms include anemia, neutropenia (a low white blood cell count), and neurological disorders such as tingling and numbness in the extremities. Pregnant or nursing women, neonates, and people with pre-existing medical conditions may be particularly susceptible to zinc poisoning.Increased zinc intake during pregnancy and nursing is necessary to support fetal growth and development, but too much zinc can be hazardous to both the mother's and the fetus' health. Similarly, due to their tiny size and developing metabolic systems, newborns are more vulnerable to the negative consequences of zinc overload. Zinc overconsumption in newborns can cause immunological dysfunction, developmental delays, and gastrointestinal difficulties. Blood tests are commonly used to identify zinc toxicity by measuring blood zinc levels and assessing kidney and liver function. Imaging examinations such as X-rays or ultrasounds may be employed. In some circumstances, further testing, such as hair or urine analysis, may be required to determine zinc status and monitor treatment efficacy. The goals of treating zinc toxicity are to eliminate excess zinc from the body, stabilize the patient, and alleviate symptoms. This could entail stopping or altering zinc supplements or prescription drugs that worsen zinc toxicity.

5.4.8 Copper Toxicity

Copper alone is not dangerous, but some of its salts are. The two most prevalent copper salts are sulfate or blue vitriol (Nilatutia) and subacetate or verdigris (Zangal). Copper sulfate is a crystalline salt with a blue color and a metallic taste. In tiny dosages of 0.5 g, it functions as an emetic, but in bigger amounts, it acts as an irritating toxin. Copper subacetate is a blue green salt generated when vegetable acids react with copper cooking utensils that have not been properly tinned. Copper is a powerful enzyme inhibitor. Copper is a trace mineral that is necessary for a number of physiological functions, including connective tissue development, iron metabolism, and enzyme functioning. Even if too much copper is required for good health, enough copper can cause copper toxicity, also known as copper overload or poisoning. Copper poisoning can be caused by a number of circumstances, including excessive consumption, ingesting polluted water or food, using copper-containing supplements or medications, or working in an area with copper dust or fumes. Rare hereditary disorders, such as Menkes or Wilson's disease, can alter copper metabolism and raise the risk of copper poisoning. Copper toxicity symptoms may vary depending on the severity of the ailment and particular circumstances.Mild copper intoxication may cause abdominal pain, nausea, vomiting, diarrhea, and other gastrointestinal symptoms. As copper levels rise, more serious symptoms may appear, such as headaches, dizziness, weakness, lethargy, a metallic taste in the mouth, and jaundice. Chronic copper poisoning can cause neurological disorders like tremors and seizures, renal failure, liver damage, and psychological issues like anxiety and depression. Infants, pregnant or nursing women, and anyone with pre-existing medical disorders may be particularly vulnerable to the harmful effects of copper poisoning. Nursing and pregnant women require greater levels of copper to promote fetal growth and development, but too much copper can be harmful to both the mother's and the baby's health.

Similarly, due to their small stature and underdeveloped metabolic systems, babies are especially prone to the harmful effects of copper intoxication. Excessive copper consumption in newborns can result in growth retardation, developmental delays, and gastrointestinal problems. To detect copper poisoning, blood tests are used to assess serum copper levels as well as liver and kidney function. Imaging tests, such as ultrasound or MRI, can be used to evaluate the liver and detect problems such as cirrhosis or hepatotoxicity. In some cases, additional testing, such as hair or urine analysis, may be required to evaluate copper status and follow therapy effectiveness. Treatment for copper toxicity aims to manage symptoms, stabilize the patient, and remove excess copper from the body.

This may require discontinuing copper supplements or modifying prescription medicines that exacerbate copper toxicity. Chelating medicines, such as trientine or penicillamine, can be used to promote copper excretion while reducing toxicity. To alleviate gastrointestinal symptoms and avoid dehydration, supportive treatment such as intravenous fluids, electrolyte replenishment, and antiemetic may be administered.

Acute Poisoning

Symptoms and signs: These begin within 15 to 30 minutes. Salivation and thirst produce a metallic taste in the mouth. There is a burning sensation along with abdominal pain (colic), vomiting, diarrhea, and collapse, all of which are common side effects of any irritating toxin. Vomited substance is green or blue in color and must be recognized from bile or bilious vomit. The addition of ammonium hydroxide causes the vomit to turn bright blue, while the bile remains unaffected. The stools are liquid and brown, not bloody. The urine is inky in color, little in quantity, and contains albumin and casts. Uremia can arise in some instances. There may be a significant headache, and breathing may become difficult. Jaundice is prevalent in severe cases, along with extremity spasms. Cold perspiration implies a cardiovascular breakdown. Convulsions and coma occur before death. If the patient's symptoms are minor after the first six hours, they will most likely recover. A woman was admitted to the hospital with severe, bluish green vomiting, which was suspected to be caused by copper sulphate poisoning. The

addition of ammonium hydroxide established the biliary character of the vomit. When asked, it was discovered that she was pregnant, with very terrible pregnancy vomiting!

5.4.9 Manganese Toxicity

Manganese toxicity can be caused by excessive manganese exposure from a range of sources, such as contaminated water, particular foods, or industrial environments. It is less common than manganese insufficiency. The body requires manganese, an important trace mineral, for a variety of physiological functions such as metabolism, bone formation, and antioxidant defence mechanisms. However, excessive doses can have a harmful impact on one's health. Manganese poisoning is believed to be produced by oxidative stress, mitochondrial dysfunction, and alterations in neurotransmitter levels in the brain. The actual processes causing this toxicity remain unknown. Manganese can accumulate in a variety of organs, but it is particularly problematic for the brain's neurotransmitter and neuronal systems.

Manganese poisoning symptoms might vary depending on the duration and severity of exposure. People may first experience neurological symptoms such as headaches, irritability, and mood swings. Long-term manganese exposure can lead to more serious neurological issues, such as Parkinsonism, which is defined by stiffness, tremors, and difficulty moving and coordinating. Additional symptoms may include respiratory issues, cognitive deterioration, and reproductive difficulties. One of the most well-known incidents of manganese poisoning occurred in the Louisiana hamlet of Leeville, when a neighbouring manganese mining operation contaminated the town's drinking water, exposing the people to high quantities of manganese.

As a result, numerous inhabitants developed neurological symptoms, highlighting the dangers of excessive manganese exposure. To avoid manganese toxicity, exposure to manganese-rich environments must be limited. Some strategies include avoiding polluted drinking water, ensuring enough ventilation in industrial situations with high manganese concentrations, and exercising caution while using manganese supplements. Regulations can also help to decrease the amount of manganese discharged into the environment as a by-product of mining and industrial processes. The primary therapy for manganese toxicity is to remove the affected person from the source of exposure while providing supportive care to control symptoms.

In extreme cases, chelation therapy, which involves administering chelating chemicals to the body in order to bind and eliminate excess manganese. It may be considered, but its efficacy has not been fully demonstrated.

5.5 FOOD POSIONING AND POISONOUS FOODS

Food poisoning is a vague term. It may be used in a general (wider) sense or in a special (restricted) sense. When the term is used in its general or wider sense, it includes all illnesses resulting from ingestion of foods containing non-bacterial or bacterial products. When the term is used in a specific or limited sense, it indicates that only bacterial compounds are to blame for the poisoning. Inorganic compounds and toxins arising from plants and animals are among the non-bacterial products. By convention, foods containing these items are referred to as poisonous foods. The poisons produced by the bacteria are among the bacterial products. Conventionally, the poisoning that results from this is referred to as bacterial food poisoning. The ailment is typified by: (1) multiple people attacking simultaneously; (2) all victims having previously consumed a common food; and (3) most cases having comparable signs and symptoms.

BACTERIAL FOOD POISONING- This is of three types, namely (1) infection type (2) toxin kind; (3) botulism. Ptomaine toxicity caused by extensive breakdown of food is uncommon.

- **Infection type**: This kind of food poisoning is caused by consuming live bacteria, such as those in the salmonella group, which proliferate in the digestive tract and cause a real infection.
- **Toxin type**: Enterotoxin, which is created by the staphylococcus bacteria, is one example of the toxic compounds that cause this sort of food poisoning. These substances are produced by multiplying organisms that have gotten access to the cooked food.
- **Botulism:** This type of food poisoning is caused by ingesting prepared botulinum toxin in preserved foods. The toxin is produced by Clostridium botulinum.
- **Infection Type:** In this type of food poisoning, germs grow in the gut, resulting in gastroenteritis. The Salmonella group of organisms is responsible for the attack, which includes S. typhimurium (Aertrycke), S. enteritidis (Gaertner), S. suipestifer (cholera suis), S. Thompson, and S. newport. Occasionally, the shighella group of organisms, specifically Sh. sonnei and Sh. flexneri, may be involved. Certain birds, animals, and reptiles serve as natural reservoirs for salmonella germs. Food may be contaminated by infected excreta of mice or rats, or infection may be transmitted by flies or human carriers employed in food processing. Shighella infection occurs when food or water supplies are contaminated with the feces of people who either have the disease or, less commonly, are asymptomatic carriers of the bacterium.

The types of foods which are particularly likely to be infected are twice cooked meat meals, fish dishes, soups, custards, milk, cream, ice-cream, and canned goods which, though originally sterile, may become infected if not promptly consumed once the tin has been opened. Occasionally but not always, there may be a perceptible alteration in the character of the dish.

The outbreak of salmonella food poisoning is likely to occur whenever large amounts of food are prepared and the unconsumed food is kept for future meals. Accordingly, such food poisoning is reported far more frequently from canteens, restaurants, hospitals and other institutions than from private houses.

Symptoms and signs: Individual susceptibility to salmonella food illness varies significantly. As a result, while some people may not experience any symptoms, others may suffer greatly. The sickness is more than simply toxemia; it also includes gastroenteritis caused by bacterial infection. The incubation period is longer than that with Staphylococcus food poisoning. The organisms proliferate in the colon, and symptoms often appear after at least 12 hours. The symptoms begin abruptly, with a shiver, followed by headache, nausea, vomiting, severe abdominal cramps, and intense prostration.

Three symptoms separate this from staphylococcal enterotoxin poisoning: (1) muscle weakness, (2) fever, and (3) persistent, foul-smelling diarrhea. Before making a diagnosis, the causative organism must be isolated from the patient as well as any questionable food items.

Treatment: If there is no diarrhea, cleanse the stomach with gastric lavage and empty the bowels with a cathartic. Most patients recover rapidly with bed rest and warmth. No eating is permitted until the acute symptoms have subsided. The rest of the treatment is symptomatic. Chloramphenicol is the preferred antibiotic, with a daily dose of up to 2 g for adults and a maximum of 7 days.

Postmortem appearances: These are symptoms of gastroenteritis and generalized toxemia. The mucosa of the stomach and small intestine exhibits variable degrees of inflammation and ulceration. In severe situations, lesions may spread to the large intestine. The liver, spleen, kidneys, and lungs are all clogged.

Toxin type: This type of food poisoning is caused by poisons that develop in the food before to intake. The majority of cases are caused by staphylococci strains that generate enterotoxin, including Staphylococcus aurous and Staphylococcus albus (coagulase positive strain). This enterotoxin is an exotoxin that is relatively stable to heat and will not boil. Staphylococcus aureus can be found in

humans' noses, throats, and skin lesions. Cows with mastitis carry Staphylococcus albus (a coagulase-positive strain). Other toxin-producing organisms that can cause food poisoning include Proteus vulgaris, Streptococcus viridans (milk streptococci), B. coli, and Clostridium welchii when present in significant quantities. Even salmonella can cause toxin-based food illness. The bacteria may be eliminated during the cooking process, but the enterotoxic compounds they create are heat resistant and may remain in the meal.

To cause this type of poisoning, (1) food must be contaminated by a strain of organism that produces enterotoxins, (2) the type of food must be suitable for the growth of this organism, and (3) the infected food must be kept at a temperature suitable for bacterial growth for an adequate period of time to produce an appreciable quantity of enterotoxins. Staphylococcal food poisoning is most commonly caused by milk, custard, cream (cake filling), and pre-prepared meats. The infected food is tasty and not visibly contaminated.

Symptoms and signs: The toxin is already present in the food and therefore the symptoms develop rapidly within one to four hours. The first symptom is salivation followed by gastroenteritis. The gastroenteritis is sharp and severe and is usually over in twenty-four hours. Recovery is the rule.

Unlike salmonella food poisoning, this condition is not an infection. But like botulism, it is the result of ingesting preformed toxins contained in the food. However, staphylococeal food poisoning differs considerably from botulism in that symptoms appear rapidly and are mainly gastrointestinal, they are of short duration, and recovery is usually prompt and complete.

Treatment: This is largely symptomatic and on the same lines as in salmonella poisoning. In children, dehydration may be severe, and intravenous fluids may be necessary.

Postmortem appearances: These are the same as those found in salmonella poisoning.

Botulism: Botulism, a rare disease in India, is caused by an anaerobic spore-forming bacillus, Clostridium botulinum, which produces an exotoxin. The organism and its spores are heat-resistant and commonly found in soil. The toxin is likely present in soil-contaminated undercooked or canned foods, which should be discarded immediately. The most common culprits are meat, fish, and vegetables. A rancid butter odor is often noticeable in affected food. The toxin is destroyed by heat at 80°C for thirty minutes, so adequate cooking provides protection. The toxin paralyzes muscles by blocking nerve impulses at the myoneural junction, and adequate cooking provides protection against the toxin.

- **Symptoms and signs:** The symptoms of a contaminated food are mainly nervous and typically begin within 12 to 36 hours. The initial symptom is diplopia, affecting both internal and external ocular muscles. The pharynx and larynx may become involved, leading to faulty articulation and bulbar palsy. Respiratory paralysis and breathing center extension are common. In rare cases, nausea, vomiting, abdominal pain, and diarrhea may occur. The victim is usually conscious until the end, and the fatal dose may be less than 5 grams. Death may occur within 24-48 hours or may be delayed for a week.
- **Treatment**: The patient's stomach should be washed out and bowels emptied with saline purges. Intravenous fluids may be needed. Anti-botulism serum (type A and B) is urgently administered, with a dose of 20 ml intramuscularly in suspected cases and 30 to 50 ml intravenously in 5 percent glucose for treatment. If the organism is typed, monovalent serum can be given at six or twelve hourly intervals. Management of bulbar and respiratory failure follows poliomyelitis management.
- **Postmortem appearances:** Pathological changes include congestion and hemorrhages in all organs, particularly the central nervous system, and degenerative changes in the liver and kidneys.

5.6 POISONOUS FOODS

This term refers to food poisoning caused by toxic principles, metallic contamination, or food allergies, excluding conventional bacterial and toxins. Examples include poisonous food grains, infected rye, adulterated oil, and poisonous mushrooms.

Food Grains, Rye, Oil and Mushrooms

Food Grain Contamination

- Lathyrussativus is the most common affected grain.
- Other affected grains include loliumtemulentum, stigmata maides, and paspalamscrobiculatum.
- Symptoms include neurological issues like spastic paraplegia and polyneuritis.
- Contaminated rye can cause gangrenous or convulsive ergotism.
- Contaminated mustard oil can cause dropsy
- Poisonous mushrooms can cause irritant or neurotic poisoning

Lathyrussativus:

KesariDal: A Drought-Resistant Pulse in Indian Diet

- Also known as kesari dal, a staple in some Indian regions.
- Excessive consumption can cause lathyrism.
- Blended with wheat, it appears harmless but cooks like a poison.
- Neurotoxic, preferring the pyramidal tract.
- Lathyrism can occur suddenly, with back pain and leg stiffness causing back pain.

Loliumtemulentum: Darnel Plant Poisoning

- Darnel, also known as darnel, grows in wheat fields.
- Poisoning caused by tumuli, a pyridine base in fungi.
- Symptoms include giddiness, headache, tremors, muscle weakness, gastrointestinal discomfort, pupil dilation, stupor, and coma.
- Death has not been recorded.

Stigmata maides: Maize in India: A Potential Pollagra Inducer

- Grown throughout India.
- Induces pellagra due to nicotinic acid shortage.
- Low in tryptophan, essential aminoacid for nicotinic acid synthesis.
- Majority of nicotinic acid is bonded, unabsorbed.

Paspalamscrobiculatum: This maize, also known as kodra, is frequently consumed by the underprivileged. The poison is said to dwell in the grain's husk and can be eliminated by boiling. Kodra poisoning symptoms are remarkably similar to those of darnel, including giddiness, headache, tremors, muscle weakness, gastrointestinal discomfort, dilated pupils, stupor, and even coma. The poisoning could end fatally. According to common opinion, there are two types of grains: sweet and bitter, with only the latter being poisonous. The actual nature of the toxin is unknown. The similarity of the symptoms suggests that the symptoms of kodra poisoning are caused by an inadvertent mixing of darnel and grain.

Rye: The parasitic fungus is known as Clavicepspurpurea. The symptoms associated with ingesting infected rye flour can be local, such as vasomotor constriction and even extremity gangrene, or generalized in the nervous system, such as formication and paroxysmal convulsions. Ergotism is a type of poisoning that can spread rapidly. The amount of ergot consumed determines the sort of poisoning that occurs. If bread contains 10% ergot or less, convulsive poisoning predominates. If ergot concentrations exceed 10%, the gangrenous form predominates. LSD is derived from rye ergot. It is possible that infected rye flour can cause hallucinations similar to LSD under certain settings.

Oil: Mustard oil, used in food preparation, is sometimes contaminated with argemone oil, a plant derived from the seeds of argemonemexicana, also known as sialkanta, darudi, satyanashi, bharamdandi, and piladhatura. Other edible oils may also be falsified.The coxicity is caused by two alkaloids found in the oil: sanguinarine and dihydrosanguinarine, with the former being more toxic. The adulteration has caused a large number of cases of epidemic dropsy. Ten percent of cases develop glaucoma. The most common cause of death is heart damage. Treatment involves removing polluted oil, taking appropriate steps, and administering prednisolone.

Mushrooms*:* Certain mushroom species are harmless and can be eaten as food, while others are dangerous and can cause unintentional poisoning when mistaken for edible ones. People often mistake dangerous mushrooms for edible ones due to the inability to remove toxic skin, color changes, darkening spoons, or cooking destroys toxins. These distinction criteria are not always accurate.In Europe, the species most commonly encountered include Amanita phalloides and Amanita mascaras. Poisonous mushrooms are also found in India, however their classification does not appear to have been determined yet. Amanita phalloides, often known as death cap, has a beat-stabilized polypeptide principle that harms cells throughout the body. The liver, kidneys, brain, and heart are particularly damaged. The poisonous principle immediately binds to the tissues. Amanita muscaria is used to kill flies. It contains variable amounts of a heat-labile atropine-like alkaloid, which causes narcosis, convulsions, and hallucinations, as well as a heat-stable alkaloid, muscarine, which stimulates smooth muscles and organs that supply the parasympathetic nervous system, similar to the action of acetylcholine on those structures. Ingestion of merely a portion of one mushroom from a deadly species can result in death within three to six days. The standard treatment for mushroom poisoning is symptomatic. Atropine reduces the cholinergic effects of poisonous mushrooms. Corticosteroids may be useful and should be tried. Pathologic observations in fatalities from mushroom poisoning include considerable postmortem lividity, reduced rige mortis, gastrointestinal mucosal inflammation, fat degeneration of the liver, kidneys, heart, and skeletal muscles, and meningeal hyperemia. Petechial hemorrhages into serous membranes are common. Mushroom spores can be collected from the victim's intestine. Each mushroom has distinct spores.

Metallic Contamination: This is likely more common than hazardous. Arsenic contamination of iron pyrites, which were used to prepare sulphuric acid for the conversion of starch to sugar, poisoned beer, confectionery, and baking powder enriched with acid calcium phosphate. Fruits sprayed with arsenic have also produced problems. The varnish used to lacquer tinplate containers also contained the toxin. Lemonade and other acidic liquids have been known to damage and dissolve antimony-containing enamels, causing sickness. Copper is sometimes added to peas to keep their colour, and cooking with copper equipment on a daily basis may seldom be harmful. Cider, beer, lemonade, and other plumbo-solvent liquids stored in lead tanks or bottled in siphons with lead connections may cause poisoning from this metal. Tea, cheese, and other tin foiled-wrapped commodities may also become contaminated. Peaty waters may acquire enough lead as they flow through supply pipes. Lead-glazed containers may release metal to dishes cooked in them. Lead solder in home cooking equipment may cause lead poisoning. Tin poisoning is mainly caused by acid fruits or shellfish contacting the metal in unlacquered tinplate containers.

Aluminum has no harmful properties and hence has become acknowledged as a standard premium metal for cooking equipment. It is now largely replacing tin in the fabrication of wrapping foils. Zinc is rarely toxic, however consumers of dessert fruits like apples cooked in zinc receptacles have occasionally received an emetic dose. Various metallic poisons were previously used in food products as colors, preservatives, or coloring agents. Cases of cadmium poisoning from refrigerator fittings have recently been recorded. Other examples of chemical food poisoning include illness caused by using silverware cleaned with cyanide plate powder, as well as ginger paralysis caused by the adulteration of ginger fluid extract with triorthocresylphosphate.

Food Allergy: This is a condition characterized by sensitivity to specific dietary proteins, resulting in symptoms like nausea, vomiting, diarrhea, joint aches, and articaria. It can also cause glottis oedema and asthmatic seizures from shellfish like tomatoes, strawberries, and mussels. Diagnosis is straightforward, and antihistaminic medications are helpful.

Medicolegal Aspects: Pathological alterations in lathyrism are irreversible. Patients grow impoverished and pose a significant social concern. It is important to recognize the situational character of poisoning caused by other causes. Any cases of food poisoning from a hotel must be reported to public health authoritiesof copper sulphate or verdigris is fatal.

Fatal period: This varies from 12-24 hours. It may be delayed for 3-5 days or even a week.

Treatment: This is similar to poisoning by mercury. Stomach should be washed with I per cent solution of potassium ferrocyanide which forms an insoluble compound, cupric ferrocyanide. Albumins form an insoluble albuminate of copper and are very valuable. Demulcent fluids are also necessary. Penicillamine, BAL or calcium EDTA are helpful and may be given in the usual dosage.

Postmortem appearances: The skin may be yellow owing to jaundice. Greenish blue froth may be coming out of the mouth and nostrils. The most striking appearance is the bluish or greenish coloration imparted to the gastric mucosa. The mucous membrane is congested and injected and occasionally shows eroded patches. The intestinal mucous membrane may share the same appearances.

Chronic Poisoning: This may result among workers who handle this metal or its salts. It may result from the continued use of copper vessels for preparing and preserving food. The poison enters the system by absorption from the alimentary canal, by the lungs in the form of dust, and partly by the skin in handling the metal or its salts.In chronic poisoning, the main symptoms and signs are allied to poisoning with lead. The usual symptoms consist of a metallic taste in the mouth; a green line on the gums at the base of the teeth; gastrointestinal symptoms, such as nausea, vomiting, colic, diarrhea or constipation; and general signs of progressive emaciation, viz, anaemia, malaise and debility. The evidences of implication of nervous system are also very similar, viz, peripheral neuritis, with wrist drop or foot drop in some cases. Wilson's disease may possibly occur. Bronzed diabetes may be present. The treatment is similar to that of chronic poisoning by mercury.The chief postmortem appearances consist of parenchyma- tous injury to the heart, the liver, and the kidneys. Mallory has described haemochromatosis (bronzed diabetes) from chronic copper absorption.

5.7 TOXICITY OF DIOXINS

One class of chemical pollution that is very harmful to the environment is dioxins. The majority of the time, they are created as by-products of industrial operations such chemical synthesis, trash incineration, and paper bleaching. Dioxins can also be spontaneously released by forest fires and small-scale volcanic eruptions. The most hazardous dioxin is 2, 3, 7, 8-tetrachlorodibenzo-p-dioxin (TCDD), a persistent organic pollutant (POP). These compounds, which come from three closely related families, number in the hundreds.

- polychlorinated dibenzo-p-dioxins (PCDDs)
- polychlorinated dibenzofurans (PCDFs)
- certain polychlorinated biphenyls (PCBs)

There are hundreds of PCDDs, PCDFs, and PCBs, but only a tiny number of them, those with chlorine atoms in specific locations are toxic. Hazardous carbon rings contain chlorines at locations 2, 3, 7, and 8 (see figure 1). Because the two biphenyl rings of dioxin-like PCBs are in the same plane and seem flat, they act in the body similarly to dioxins. PCDDs and PCDFs are by-products of human activity, such as rubbish burning in the backyard; they are not intentionally produced. Forest fires and other organic processes also produce PCDFs and PCDDs. Although they are manufactured commodities, PCBs are no longer produced in the United States.

In the United States, dioxin is not produced or utilized commercially. It is a contaminant produced when chlorinated organic compounds, such as herbicides like Silvex, are manufactured. The EPA and industry have worked together over the last decade to drastically reduce dioxin production and release into the environment. Dioxins are extremely persistent and breakdown slowly, despite a reduction in environmental levels over the last 30 years. In fact, decades-old releases from fires and pollutants account for a large share of present dioxin exposures in the United States.

Dioxins are pollutants in the environment. They are among the harmful compounds known as persistent organic pollutants (POPs), also called the "dirty dozen." Dioxins are a source of concern due to their potential for high toxicity. According to studies, they affect a variety of organs and systems. Dioxins are persistent once within the body due to their chemical stability and tendency to be absorbed by adipose tissue, where they are stored. It is estimated that their half-life in the body ranges between 7 and 11 years. Dioxins tend to accumulate in the food chain and environment. The concentration of dioxins rises with the animal's position in the food chain.

Because of their proclivity for bioaccumulation throughout the food chain, dioxins are most typically found in animal fats, notably those found in fatty fish, meat, and dairy products. People are more likely to be exposed to dioxins through eating or drinking contaminated food or water, as well as breathing in airborne particles from waste incinerators or industrial sites. Furthermore, skin contact with polluted soil or water can bring dioxins into the body. Dioxins are exceedingly toxic and can have a wide range of severe effects on human and animal health. When exposed abruptly, high concentrations of dioxins can cause skin blemishes, liver damage, and even death. However, because dioxins have the potential to cause long-term health consequences, sustained exposure to lower. Dioxin's most well-known adverse health effects are related to the disruption of the hormonal balance and disruption with hormone signaling. Dioxins and other hormone disruptors have been connected to anomalies in development and reproduction, including low fertility, birth defects, and hormonal imbalances. Moreover, dioxins are carcinogenic and have been linked, among other illnesses, to a higher incidence of lung, breast, and lymphoma malignancies. Additionally, they might affect immunity, making a person more vulnerable to infectious infections and autoimmune disorders. Dioxins' bioaccumulative qualities and enduring presence in the environment make them a serious threat to both the environment and public health. The attempt to reduce dioxin exposure includes enacting regulations that limit emissions from industrial operations, improving waste management practices, and monitoring for dioxin contamination in environmental and food samples.

Humans exposed to high amounts of dioxins for short periods of time may develop liver dysfunction, as well as skin lesions such as chloracne and uneven skin pigmentation. Extended exposure has been linked to weakened immune responses, neurological, endocrine, and reproductive system problems. Dioxins are produced as a by-product of combustion activities, such as the use of wood, coal,

or oil. Bleaching: The use of chlorine to bleach pulp and paper, as well as other industrial operations, can release minor amounts of dioxins into the environment.

Smoking: Cigarette smoke also contains small amounts of dioxins.

Drinking Water: Dioxin can get into drinking water from:

- Air emissions from waste incineration and other combustion, with subsequent deposition to lakes and reservoirs
- Deposition from air to soils that erode into surface waters used for drinking water
- Discharges into water from chemical factories.

Only a small number of labs globally have access to extremely complex techniques required for dioxin quantitative chemical analysis. More and more biological screening techniques, like those based on cells or antibodies, are being created and approved for use with food and feed ingredients. If a screening test produces positive results, additional, sophisticated chemical analysis is required to confirm the results, and these screening processes enable more analyses at a reduced cost.

5.8 SUMMARY

Chemical toxicity is the damaging effect of chemicals on humans and other living things. These effects can be influenced by a variety of factors, including the type of chemical, the method of exposure, the dosage, and the duration of exposure. When exposed to a variety of compounds, including as pesticides, heavy metals, industrial chemicals, and pollutants, they may become chemically poisonous. Chemicals can come into touch with the skin, consumed, or inhaled. The type and severity of toxicity detected can be influenced by the exposure route. Chemicals can cause a variety of toxicities, including mutagen city, which alters DNA, neurotoxicity, which affects the nervous system, hepatotoxicity, which damages the liver, nephrotoxicity, which damages the kidneys, and reproductive toxicity, which affects fertility or pregnancy outcomes. When the body collects an excessive amount of a specific mineral, it can produce mineral toxicity, which can have serious health consequences. Although minerals are essential nutrients for a variety of physiological functions such as bone health, neuron function, and enzyme activity, taking excessive amounts of particular minerals can disrupt normal biological processes and induce toxicity. Dioxins are very dangerous environmental toxins that can cause cancer, immune system malfunction, and endocrine disruption. To protect the environment and public health, dioxin exposure must be reduced through laws and pollution control programs.

5.9 TERMINAL QUESTIONS

Q. 1. What is toxicity? Define alcohol toxicity and its effects on human beings.

Answer:----------

Q. 2. How acetone is toxic, define its toxicity and its effects on human beings.

Answer:----------

Q. 3. What are minerals, discuss its effects on human beings.

Answer:----------

Q. 4. Write toxicity of nitrogen and iron and its effects on human beings.

Answer:----------

Q. 5. Write toxicity of copper and manganese and its effects on human beings.

Answer:----------

Q. 6. Write toxicity of dioxins and its effects on human beings.

Answer:----------

5.10 FURTHER SUGGESTED READINGS

1. Environmental Toxicology,Kees van Gestel, Vrije University, Amsterdam,Environmental Toxicology
2. Environmental Toxicology, Third Edition, Sigmund F. Zakrzewski, oxford university press
3. A Textbook of Modern Toxicology: Ernest Hodgson A John Wiley & Sons, Inc., Publication
4. Principles of Environmental Toxicology, I. Shaw, J. Chadwick, CRC Press
5. Occupational Toxicology, Chris Winder, Neill H. Stacey, CRC Press

UNIT-6 : PUBLIC HEALTH

Structure

6.1 INTRODUCTION

Public health is the science for the protection of health and treatment. and improving population health By promoting healthy lifestyles it improve health quality and through prevent theillness, injury and also managing infectious diseases. It also develops interventions and policies that protect the health of families and communities, such as immunization programs and education on the risks of alcohol and tobacco uses. However, the public health experts evaluate the impact of diseases also diagnose the environmental variables that have potential to alter human health. According to the American Public Health Association, "public health reduces human suffering, saves money, enhances our quality of life, and helps children thrive. Unlike clinical professionals, such as doctors and nurses, who primarily treat patients after they become ill or injured, public health professionals use educational programs, policy recommendations, service administration, and research to try to prevent problems from arising or recurring. Public health initiatives help to reduce health disparities. Promoting access, equity, and high-quality healthcare is an important aspect of public health.

Objectives

After readings to this unit the learner will be able to know

- The toxicologists and public health impact
- The laws and regulations governing toxicants

- The epidemiological approaches to toxicants
- The blacklisted toxic chemicals and Pesticide

6.2 PUBLIC HEALTH OVERVIEW

The science developed the process how to protect and enhancing the health of individuals and their communities is known as public health. This can we do by changing their lifestyles and illness management through after treating infectious diseases. However, the main purpose of public health is reduce diseases and to protect the health of the entire population. These populations can vary in size from a small neighbourhood to a whole country or continent. Medical professional such as doctors and nurses, always should be ready to treat patients. In contrast, public health professionals work to prevent issues from arising or repeating by implementing educational programs, policy proposals, service management, and research. Another purpose of public health is reducing health.

Environmental illness is influenced by dietary, social, and behavioural factors. These impacts are covered in public health classes. A thorough investigation of the various causes of sickness, including those usually highlighted in public health, is essential to understand disease etiology and choose the best course of treatment for patients. To establish integrative theories of illness that take into account behavioural, social, dietary, molecular, physiological, and environmental aspects, both medical and public health perspectives must be merged.

Public health alleviates human suffering, promotes child development, improves our quality of life, and saves money. The field of public health works tirelessly every day to keep people safe and healthy, often in the background. As an example, public health is responsible for:

- Monitoring disease outbreaks and immunizing populations to stop the spread of illness.
- Establishing safety guidelines to safeguard employees.
- Establishing school nutrition initiatives to guarantee children have access to wholesome food.
- Pushing for safety-related laws, such as those requiring seatbelts and smoke-free interior environments.
- Discussing how or heath is affected due to change in climatic local and regional level.
- Identifying racism as a threat to public health.

Because it is not amenable to direct measurement, the World Health Organization's definition of health cannot be regarded as an operational definition. To addresses this gap, a WHO panel developed an operational definition of health. This notion distinguishes two stages of health. In a broader sense, health can be defined as "a condition or quality of the human organism expressing the organism's adequate functioning in given conditions, genetic or environmental". The WHO definition assumes three separate dimensions (physical, mental, and social), while other dimensions such as spiritual and emotional may also be considered.

Physical health: The physiology of body and anatomical integrity is considered under the physical health. It has ability to perform to daily task without any physical limitation. It signifies the ability to perform daily tasks without physical limitations. To make physically fit and active it should be do daily workout and keep walking from one location to another necessitates

Mental Health: Mental health refers to the ability to learn and think effectively and rationally. For example, a person who is not mentally fit (retarded) will be unable to learn something new at the same rate as a normal person.

Social health: The ability to create and maintain proper social interactions is referred to as social health. For example, to commemorate significant occasions, mourn the loss of a close relative, form and maintain intimate relationships, and so forth.

Emotional health: The capacity to express feelings appropriately, such as fear, happiness, and anger, is known as emotional health. The stimulus and the body's reaction should match each other.

Emotional health: Emotional well-being is linked to mental well-being and includes emotions. It also includes remaining genuine to oneself in the face of difficult situations such as stress, sorrow, or anxiety.

Spiritual Health: Some people relate health with religion; for others it has to do with personal values, beliefs, principles and ways of achieving mental satisfaction, in which all are related to their spiritual wellbeing.

6.3 HISTORY OF PUBLIC HEALTH

Examining the evolution of public health principles over time highlights how the field started in antiquity. The middle Ages saw the isolation of leprosy patients, and the 14th century saw attempts to enhance sanitation in the wake of plague outbreaks. As Europe's population grew, so did awareness of newborn fatalities and the number of hospitals in the region. However, with the aim of managing the supply and distribution of medications as well as controlling disease within communities. Many scientific advances during the 16th and 17th centuries were the result of centuries of technological advancement. Knowledgeable leaders at the time understood that maintaining good health was essential to the state's political and economic viability. But neither in England nor on the Continent was national health programs created because the governments lacked the administrative framework and expertise necessary to implement them. Like a result, just like in the middle Ages, local communities continued to tackle public health issues. The development of science during the 16th and 17th centuries established the fundamentals of anatomy and physiology. The ability to classify and observe allowed for the more accurate diagnosis of illnesses. The notion that infectious diseases could be caused by microscopic organisms was starting to take shape. Movements to enhance sanitation in the nineteenth century were found between 1750 and 1830 and took place concurrently in numerous European countries. As Europe's population grew rapidly around 1750, people became more conscious of the high new-born mortality rate and the deplorable circumstances found in jails and mental health facilities. The General Board of Health was founded by the Public Health Act of 1848 to advise and help local governments on sanitation issues. Their prior attempts had been hampered by the lack of a central authority. The board could create local health boards and look into the state of sanitation in certain areas. Since then, several public health laws have been passed to regulate the dumping site of waste and sewage; the housing of animals; the water supply; the registration and also inspection of private nursing homes and hospitals.

Even though Germany's public health trends were similar to those in England and France, there were some notable variances because there was no centralized government in Germany until after the Franco-German War. A coordinated public health unit was established following that war's conclusion and the establishment of the Second Reich. The advent of hygiene as a science of experimentation in laboratories was another step. The first chair in experimental hygiene was established in Munich in 1865, marking the beginning of scientific research in the subject of public health. Public health interests have also broadened to cover disorders such as arthritis, lung ailment, thrombosis, cancer, and cardiovascular disease. There is emerging evidence that environmental factors contribute to the onset of several of these diseases. For example, there is clear evidence that cigarette smoking leads to the development of heart and lung diseases. If the environment can be altered, these illnesses may be avoided. Health education is critical, and it is the responsibility of local and national governments, as well as nonprofit groups. It is particularly focused on sickness prevention. In nearly every nation that has

taken action to lower the prevalence of avoidable sickness, life expectancy has grown.

6.4 PUBLIC HEALTH TOXICOLOGY

The term "public health toxicity" describes how dangerous drugs or environmental elements can negatively impact a population's health. It covers a broad spectrum of risks, such as physical risks, biological agents, chemical pollutants, and social determinants of health. A multidisciplinary strategy including toxicology, environmental science, toxicology, policy-making, and community involvement is needed to address public health toxicity. The field of Public Health Toxicology encompasses two main domains of public health concern: firstly, the identification of possible health risks associated with exposure to specific chemical or biological agents; secondly, the evaluation and subsequent suggestions to mitigate or lessen any ensuing health consequences. The public's health is seriously endangered by chemical contaminants.

Pesticides, heavy metals, and air pollutants such as particulate matter and volatile organic compounds are among the many hazardous substances released into the environment as a result of industrial processes, automobile emissions, and agricultural practices. These contaminants have the potential to enter the food chain, water supplies, and airways, resulting in widespread exposure and health problems such as cancer, respiratory ailments, developmental disorders, and neurological damage. Infections and viruses can potentially have toxicological consequences on public health. Infectious agents such as bacteria, viruses, and parasites spread more easily in filthy living circumstances, without access to clean water, and in overcrowded dwellings. Diseases such as influenza, cholera, malaria, tuberculosis, and tuberculosis can have devastating consequences on populations when they spread, especially in locations with limited access to healthcare resources. Extreme weather, noise pollution, radiation, and other physical hazards exacerbate the threat to public health. Exposure to ionizing radiation from sources such as nuclear accidents and medical procedures increases the risk of developing cancer and genetic changes. Noise pollution from traffic, industrial machinery, and building operations can cause hearing loss, sleep issues, and cardiovascular problems. Climate change-related occurrences such as heat waves, floods, and storms can all offer health hazards, including heat-related illnesses, injuries, and infectious disease transmission. Public health toxicity is also caused by socioeconomic determinants of health such as poverty, prejudice, and unequal access to healthcare. The majority of environmental dangers fall on marginalized people, who typically face barriers while attempting to acquire required services and resources. Economic disparity, bad housing, and a lack of education exacerbate health disparities, putting vulnerable groups at a higher risk of sickness and premature death. To address public health toxicity, coordinated local, national, and international responses are required. Developing policies to limit pollutant emissions, promoting sustainable practices, increasing access to healthcare, and promoting social justice and equity are some examples of initiatives. Toxic exposures have a negative impact on public health, making it critical to strengthen communities through involvement, education, and participatory decision-making. By concentrating on prevention, mitigation, and equality, society may aim to create environments that are healthy for everyone. Toxicologists and public health specialists work together to assess hazards, develop remedies, and design policies that protect individuals from dangerous exposures. Toxicologists research hazardous compounds' properties, behaviors, and effects on living creatures. They investigate the various ways in which chemicals interact with organisms, ranging from cellular reactions to whole-body responses. Toxicologists detect dangerous compounds, determine their mechanisms of action, and assess the risks to human health by conducting tests, analyzing data, and interpreting results. The assessment and management of environmental health hazards clearly highlight the link between toxicology and public health. Toxicologists' knowledge and abilities are useful in identifying potentially dangerous substances and evaluating their toxicological profiles, which include exposure pathways, dose-response

relationships, and probable health consequences. Using this data, public health experts may evaluate how environmental exposures affect the population as a whole and create plans to reduce risks and safeguard vulnerable populations. Toxicologists and public health specialists collaborate on projects such as assessing air pollution and its impact on respiratory health. Toxicologists investigate the components of air pollutants such as nitrogen oxides, ozone, and particulate matter to determine how damaging they are to the respiratory system. Public health experts conduct epidemiological studies to determine the link between air pollution exposure and respiratory outcomes such as lung cancer, respiratory infections, and asthma exacerbations. They work together to develop emission reduction plans, establish air quality standards, and lobby for legislation that reduces the harmful health effects of air pollution on local communities. Another collaborative effort is to assess and control chemical contaminants in food and water. Toxicologists evaluate the safety of pesticides, food additives, and environmental pollutants by conducting risk assessments to determine acceptable exposure levels. Using this data, public health groups may develop guidelines, track adherence, and ensure the security of the food and water supply. In addition to providing guidance on correct food handling procedures to avoid health hazards, they also educate. In addition to providing advise on correct food handling procedures to avoid health hazards, they educate the public on the potential dangers of chemical exposure.Several public health organizations have been established to support national and international efforts to monitor and manage disease in societies. The Public Health Act of 1848 in the United Kingdom established a specialized public health ministry for England and Wales. The Centers for Disease Control and Prevention (CDC) conducts research across the country and is the primary source of information on public health issues. The World Health Organization (WHO) plays an analogous role on a worldwide scale. WHO has a specific responsibility to play in assisting less developed countries around the world in developing administrative and organizational solutions to manage health and disease-related concerns. When developing health-care systems in these countries, health concerns, resource restrictions, medical staff education, and other factors must be considered.

Essential Public Health Services: The ten Essential Public Health Services should serve as a foundation for public health by protecting and advancing the health of every individual in every community. To achieve equality, Essential Public Health Services actively endeavor to reduce structural and systemic barriers that have contributed to health disparities, as well as to promote policies, practices, and overall community circumstances that support everyone's right to optimal health. Ableism, racism, poverty, gender discrimination, and other forms of oppression are among the challenges. Everyone deserves an equal and fair chance to achieve their optimal level of health and well-being.

1. Evaluate and monitor community needs, resources, health indicators, and overall population health.
2. Investigate, diagnose, and address health problems and hazards affecting the population.
3. Effective communication is essential for educating and informing people about health, its determinants, and how to improve it.
4. Bolster, encourage, and galvanize partnerships and communities to enhance health.
5. Create, champion, and implement policies, plans, and laws that impact health.
6. Make use of the legal and regulatory measures intended to safeguard and enhance public health.
7. Ensure the implementation of an efficient system that permits fair access to the specific services and care required for well health.
8. Create and maintain a trained, diversified staff in public health.
9. Improve and innovate public health operations by ongoing review, investigation, and quality enhancement.
10. Create and preserve a robust organizational framework for public health.

Social determinants of health (SDOH): The "social determinants of health" (SDOH) refers to the non-medical variables that affect health outcomes. These include the environments in which people are born, raise, work, reside, and age, as well as the larger group of structures and factors that affect day-to-day living circumstances. Examples of such variables and systems are racism, social norms, political systems, development objectives, and economic policies and systems. Public health practitioners can be reformed and strengthened in their ability to promote health equity. According to the idea of health equality, everyone should have a fair and equal chance to live as healthily as possible.

Distinctions between public health and medicine: People often find it difficult to distinguish between public health and medicine due to their similar concern for the well-being of humans. The truth is that lifestyle, social networks, genetics, and the environment all have a significantly bigger impact on a person's health than medical care. These are some specific ways that medicine and public health are not the same.

Public health	Medicine
Main emphasis on populations	Main emphasis on individuals
A focus on illness prevention and community-wide health promotion	A focus on illness prevention and community-wide health promotion
Predominant focus on encouraging settings and activities that are healthful	A strong focus on health care
Specialties arranged, for instance, according to population and place (occupational health, global health); analytical approach (toxicology, epidemiology); and substantive health issue (nutrition, environmental health)	Organ systems (cardiology, neurology), patient groups (obstetrics, pediatrics), etiology and path physiology (infectious illness, cancer), and technical skill (radiology, surgery) are a few examples of how specializations are arranged.
Primarily focused on diseases that pose a hazard to public health, like no communicable diseases and epidemics, biological sciences research is conducted in both lab and field settings.	Research in biological sciences is conducted in both laboratory and bedside settings, driven by patient requirements.
A crucial component of public health education is the study of social and public policy.	Social sciences are typically offered as electives in medical school.

6.5 PUBLIC HEALTH LAW

Public health law is the study of the legal obligations and powers that the state has, in collaboration with its partners, to ensure the conditions required for people to be healthy, as well as the limitations placed on the state's ability to restrict an individual's autonomy, privacy, liberty, proprietary rights, and other legally protected interests for the benefit of the general public. The primary functions of public health are generally governed by public health law.

Law helps governments create new laws and regulations through assistance with legislative

writing, reviewing and commenting on draft legislation and regulations, and offering advice on other countries' experiences and ways to reduce the risk of litigation. Regarding certain health initiatives or bodies of law, LAW offers capacity building and training specifically designed for attorneys and policy focal points.

Law improves public health in at least two ways: To begin, the infrastructure of public health involves the law. "Infrastructure" public health laws are those passed by legislatures that allow for the establishment of governmental public health agencies, as well as other laws that give them broad legal authority, such as the ability to collect information, conduct inspections, issue licenses, impart knowledge, and develop interventions. Interventional or category public health legislation are more narrowly focused and seek to prevent or mitigate the harm caused by specific health hazards.

Some of these regulations include the capacity to quarantine people exposed to communicable diseases, restrict minors' access to cigarettes, chlorinate public drinking water, and require child safety seats in cars. There are components of both dimensions that overlap with the topics covered in this work. The major reasons for our incapacity to respond correctly to public health emergencies are a lack of legislative authority and the reality that many health department roles are staffed by people with insufficient training and knowledge in public health regulations.

Constitutional Design of Public Health Law: The Constitution of India enumerates the separate and shared legislative powers of Parliament and State Legislatures in three separate lists under Schedule VII: the Union List, the State List and the Concurrent List. On the Concurrent List, this covers topics like mental health, medications, food safety, labor safety and welfare, including maternity, population stabilization and family planning, and health-related economic and social planning. The State legislatures and the Parliament share jurisdiction for social security, employment, benefits, and education. The legislation also regulates the legal and medical professions, the prevention and control of infectious diseases and the vectors that spread them, the recording of births, deaths, and other vital health information. The state legislation is superseded by laws passed by Parliament when it comes to issues on the Concurrent List.

The Parliament naturally has complete and absolute authority over matters under the Union List, which include signing and carrying out foreign treaties and accords, with the exception of those matters expressly pertaining to health, such as port quarantine associated hospitals, seafaring and maritime hospitals, labor laws, and safety regulations in mining and oilfields.

Legislation on items from the State List, such as public health, water and sanitation, hospitals, and dispensaries, is typically outside the scope of Parliament. However, if it is judged "necessary or expedient in the national interest," two-thirds of the RajyaSabha can vote to authorize the parliament to pass legally binding legislation on any state topic.

Furthermore, on a subject ordinarily reserved for the States, two or more States may request that Parliament enact legislation. The resultant legislation may then be adopted or modified by other states. Under Articles 14, 15, and 21 (basic right to life, equality, and non-discrimination), as well as Article 23, the Indian Constitution imposes duties on the State to guarantee the protection and fulfillment of everyone's right to health, without any discrimination (prohibition of forced labor and human trafficking). The Article 24 (prohibition of hiring minors for industrial work, etc.) exhorts the State to endeavor to ensure that everyone has access to certain essential public health conditions, such as the right to employment, education, and public assistance in certain circumstances (Article 41). It also improved nutrition and living standards, as well as to enhance public health (Article 47). The fair and humane working conditions and maternity relief (Article 42); and safeguard and enhance environment and preserve forests and wildlife (Article 48) is also established. It also outlines some related basic obligations, such as the need for each citizen to preserve and enhance the natural environment (Article

51). An inventory of the laws that have been passed in India since its independence that directly affect health is included in Annexure 2.

EXISTING PUBLIC HEALTH LEGISLATIONS IN INDIA AND NEED FOR A NEW BILL

There are currently few states in India as mentioned blew are follows the public health laws or that make draft and policy. Many of these laws have been ineffective for a variety of reasons, and some states have revised their laws to address the issue of implementation. Tamil Nadu, for example, revised their act with thirteen amendments after it was first promulgated in 1939. Over time, parliaments (both central and state) have enacted legislation in the field of public health. Since "Public Health" was a state subject, the enactment was essentially by the states.

Meanwhile, some States also produced updated public health legislation drafts. The sectors that are typically believed to be governed by public health legislation are covered by all of the Acts, including water supply, drainage, buildings and lodging houses, hygienic conditions at fairs and festivals, parks, markets, slaughterhouses, burial sites, diseases that need to be reported, etc. The more recent drafts of the legislation have mostly adopted a "rights based approach," whereas the majority of the earlier iterations have taken a "coercive based approach." Each enactment's scope is listed in Annexure 1. India's public health laws, which now exist in State and Central versions, need to be rethought in order to address contemporary issues in public health. The Act's scope must also account for advancements that will occur over the course of the following few decades. As the Individual endeavors must now be brought together by a shared goal, set of values, and strategy. There has to be a new, focused legislative intervention that addresses public health as it exists today and as it is likely to exist in the future.

In Uttar Pradesh, like in other states of India, public health legislation plays a crucial role in safeguarding the health and well-being of the population. While specific laws may vary, several overarching legislations are pertinent to public health in the state. Here's an overview of some key public health legislations in Uttar Pradesh:

1. **The Epidemic Diseases Act, 1897**: Enacted during the British colonial era, this act grants special powers to the state government to take preventive and control measures during outbreaks of dangerous diseases. It empowers authorities to enforce measures such as quarantine, inspection of travelers, and establishment of temporary hospitals to manage epidemics effectively.
2. **The Public Health Act, 1936**: This legislation addresses various aspects of public health, including sanitation, communicable disease control, vaccination, and the maintenance of essential public health services. It provides the legal framework for the state government to oversee public health initiatives, ensuring the provision of safe drinking water, proper waste disposal, and disease surveillance.
3. **The Food Safety and Standards Act, 2006**: This act establishes standards for food safety and hygiene to ensure the quality and safety of food products consumed by the public. It regulates the manufacture, storage, distribution, sale, and import of food items, aiming to prevent foodborne illnesses and protect consumers from adulterated or unsafe food.
4. **The Clinical Establishments (Registration and Regulation) Act, 2010**: This legislation governs the registration and regulation of clinical establishments such as hospitals, clinics, and diagnostic centers. It sets standards for infrastructure, equipment, and staffing to ensure the quality and safety of healthcare services provided to the public. The Act also mandates the display of rates for various medical procedures and services to promote transparency and prevent overcharging.

5. **The Mental Healthcare Act, 2017**: This recent legislation focuses on protecting the rights of individuals with mental illness and promoting mental health services. It mandates the establishment of mental health services at various levels of healthcare delivery and prohibits discrimination against people with mental health conditions. The Act also regulates the admission, treatment, and discharge procedures for psychiatric patients, emphasizing the need for informed consent and dignity in care.

6. **The Drugs and Cosmetics Act, 1940**: This act regulates the import, manufacture, distribution, and sale of drugs and cosmetics in the state. It aims to ensure the quality, safety, and efficacy of pharmaceutical products and cosmetics available to the public. The Act empowers drug regulatory authorities to inspect manufacturing facilities, test product samples, and take enforcement actions against violations of regulations.

These legislations form the backbone of public health governance in Uttar Pradesh, providing the legal framework for the implementation of various health interventions and services. However, effective enforcement and implementation of these laws require coordination among different government departments, adequate resources, and community participation. Regular monitoring, evaluation, and updates to existing laws are essential to address emerging public health challenges and safeguard the health of the population.

ANNEXURE-1

PUBLIC HEALTH LAWS (INCLUDING CENTRAL / STATE DRAFTS)

There are 5 State Acts, 4 State Bills and 3 Modal Acts made by various agencies / task force at Central level. There was also a public health regulation issued prior to independence. These documents are given in chronological order of development/enactment.

1. **Public Health (Emergency provisions) Ordinance, 1944:** This is an ordinance released by way of the powers conferred by section 72 of the Government of India Act, 1935 to make special provisions in regard to public health in India. The purpose of this ordinance was to ensure the provision of adequate medical services, of preventing the spread of human disease, of safeguarding the public health and for providing or maintaining services essential to the health of the community. This ordinance gives the government to supersede the local authority if the latter fails to comply with any rule or order made in this direction.

2. **Tamil Nadu Public Health Act, 1939:** One of the earliest legislations in the area of Public Health in the pre -independent India comes from Tamil Nadu. The authorities faced difficulties in implementing the act which led to the constitution of 'The Tamil Nadu Public Health Act Amendment Committee' to make recommendations with regard to the amendments that need to be made to the Act. The report of the working group members has proposed the amendments following the below mentioned criteria in its report to the Director Public health & preventive medicine. Out of that, four amendments were related to adaptation of laws, one related to extension of the act to transferred territory and eight were related to principal act. The last of the amendments were made in 1990.

    - To protect the public against the new highly infectious and pathogenic diseases (e.g. emergence of HIV/AIDS)
    - Local boards have been reclassified or upgraded, downgraded or reconstituted and respective acts were promulgated and amended. Some of the acts incorporated with Tamil Nadu public health act were repealed and substituted with new acts. But they 19 were not incorporated and there is a need to incorporate them. (e.g. the district board was abolished

and instead the panchayat unions are constituted, the Tamil Nadu district boards act, 1920 repealed by Tamil Nadu Panchayat act, 1994)

- Certain new provisions have to be included to control vector borne diseases, industrial control, and implementation of total sanitation programme and definition of certain words. Existing fine is very meager and requires enhancement.
- Defining new terms (unwholesome food - s.37A), including new categories (plastic materials - s.3(11), re-designations ("surgeon general with state government" to "secretary to government health and family welfare department")

The final draft was accepted by the assembly in April, 2012 and within a year, as per modifications suggested by the assembly, the bill will come into force, as the Tamil Nadu Public Health Act, 2012.

3. **Pondicherry Public Health Act, 1973 & rules 1981:** This is a coercive based legislation. The act deals, among other areas, also with regulation of private clinical establishments. Since the Clinical Establishments (registration & regulation) Act, 2010 is in place, this portion of the Pondicherry act stands repealed. The Pondicherry Public Health rules, under the Act came into force in 1981.
4. **The Goa, Daman and Diu Public Health Act, 1985 & rules 1987:** This is a coercive based legislation. After its promulgation, the act was amended 10 times (latest 2009). The rules were also amended once (in 2010). Other than the conventional areas of public health, the act also covers areas like 'operation of ambulance', 'screening of migrant labourers for construction work, 'regulation of massage parlours' etc.
5. **Kerala Public Health Bill, 2009:** This draft is a revision to the existing Travancore Cochin Public Health Act, 1939 which covered the southern part of Kerala (and the Northern part was covered by the Madras Public Health Act of 1939). This also has followed a coercive approach but also has recognized need for providing 'essential public health services and functions'. This act also takes about creation of 'Public Health Boards' at state level.
6. **Model Public Health Act, Central Bureau of Health Intelligence - draft 1987:** This draft is expected to 'make provision for health services in the state' and has followed a coercive based approach to achieve the objective. The draft Bill mentions about creation of structures (boards / committees) of health at various levels. The Bill also regulates 'private clinical establishments', and 'food adulteration', for which specialized legislations are now available (Clinical Establishments (registration & regulation) Act, 2010 and the Food Safety and Standards Act, 2007).
7. **Gujarat Public Health Bill, 2009:** This act follows a rights based approach. This act also regulates 'healthcare establishments'. Besides the conventional areas, this act also comes forward with 'public health planning', 'public health impact assessment' and clearance of projects, 'disaster management', 'obligations of the state government', provision for 'free and universal access to healthcare services', 'public health rights', 'reasoned order' by 'designated district courts', 'public dialogues' and 'public hearings', and 'least restrictive alternative', when rights of citizens have to be infringed for public purposes. This Act was a paradigm shift in the thinking of public health legislation, in an Indian State.
8. **National Public Health Act, National Institute of Communicable Diseases - draft 2002:** In addition to the conventional areas, the act mentions about creation of a 'National Board of Public Health', with technical, administrative, planning, coordinating, monitoring, review and

supervisory roles. There is also a proposal for creation of a 'State Board of Public Health', with similar roles but functions at the state level.

9. **Karnataka Public Health Bill, 2010:** This was enacted with 4 major objectives, first one is to lay down responsibilities of individuals, corporations and the government towards promotion and protection of public health safety, two; for realizing active cooperation between the state, local governments, public and private sectors, three; monitoring of health indicators, and four; for preventing spread of disease and promoting and protecting health of people. This act also mentions about 'control of HIV and AIDS' and creation of a 'Public Health Board'.

   The act also is very peculiar in terms of some of the coercive powers, it gives to the appropriate authorities. The act mentions about the power of the health officer to 'isolate' persons who has or is suspected to be a case, carrier or contact of an infectious disease. Another coercive power is the one given to the Director of Public Health to 'vaccinate by force' (mandatorily under Sec. 104) in case of an outbreak of an infectious disease. Another peculiar feature of the act is the section dealing with 'cognizance of offence'. According to this section, no person can be tried for any offence, unless a complaint is made within 3 months of the commission of the offence by a competent 'executive authority'

10. **Karnataka Promotion of Public Health and Prevention of Diseases Bill, 2010:**This Act is intending to preserve and protect the health of the public through the Public Health System while respecting individual rights to bodily integrity, health information privacy, nondiscrimination, and other legally-protected health interests by assuring the conditions in which people can be healthy; providing essential Public Health Services and Functions and seeking adequate funding to provide them, encouraging collaboration among public and private sector partners in the Public Health System; and accomplish Public Health goals through public or private sources. This bill has lot of overlapping areas with the Public Health Bill, 2006. Both the bills continue to be in the draft stage, receiving comments.

11. **National Health Bill, MoHFW, Task Force on PH Act – 2009:** This draft argued for a National Health Act rather than a 'Public Health Act'. This followed a rights based perspective. The National Health Act was a 'framework law on health' which wanted to provide for developing and facilitating a coherent and uniform legal response to cross-sectoral convergent issues. It argued for establishment of general framework of scope, core principles, rights, obligations, and a broad structure for implementation & justice mechanism to ensure health as a right. It stopped there and did not get in to the nitty-gritty of regulating each of the areas it covers. It left room, mandate and sanction for the implementing legislations and competent governments to determine specific measures to be taken to achieve them. It makes reference to the Alma Ata declaration, which attempted to close the gap between the imperatives of health and development, in the last decade with understanding on 'health' grown beyond bio-medical determinants. It refers to the Committee on Economic, Social and Cultural Rights set up under the International Covenant on Economic, Social and Cultural Rights (ICESCR) which authoritatively interpreted health as much larger, non-medicalised, social framework, tightly linking it up with the underlying socio-economic determinants. 22 And arguing for a change in nomenclature; from Public Health Act to Health Act, the bill said; "health is today legally understood to include, but is not limited to, public health, the first option could be a more internationally consistent title, called Health Act".

12. **The** Assam **Public Health Act, 2010:** This is rights based legislation. This has been promulgated 'for the protection and fulfillment of rights in relation to health and well-being, health equity and justice, including those related to all the underlying departments of health as well as health care and for achieving the goal of health for all.

ANNEXURE 2

ACTS AND RULES RELATING TO HEALTH IN INDIA

The acts and rules relating to health in India have been classified below in to broad areas of their operation. Eighteen categories have been identified

1. Health Facilities and Services
2. Disease Control and Medical Care
3. Human Resources
4. Ethics and Patients Rights
5. Pharmaceuticals and Medical Devices
6. Radiation Protection
7. Hazardous Substances
8. Occupational Health and Accident Prevention
9. Elderly, Disabled, Rehabilitation and Mental Health
10. Family, Women and Children
11. Smoking, Alcoholism and Drug Abuse
12. Social Security and Health Insurance
13. Environmental Protection
14. Nutrition and Food Safety
15. Health Information and Statistics
16. Intellectual Property Rights
17. Custody, Civil and Human Rights

1. Health Facilities and Services

- Indian Red Cross Society Acts, 1920
- All India Institute of Medical Sciences Act, 1956
- Post-graduate Institute of Medical Education and Research, Chandigarh, Act, 1966
- Bureau of Indian Standards Act, 1986
- Bureau of Indian Standards Rules, 1987
- National Institute of Pharmaceutical Education and Research Act, 1998
- Clinical Establishment Acts
    - Bombay Nursing Homes Registration Act, 1949
    - Delhi Nursing Homes Registration Act, 1953
    - Madhya Pradesh Upcharyagriba Tatha Rujopchar Sambandi Sthapas (Registikaran Tatha Anugyapan) Adhiniyam, 1973
    - Orissa Clinical establishment (Control and Regulation) Act, 1991

- Orissa Clinical establishment (Control and Regulation) Rules, 1994
- Manipur Nursing Home and Clinics Registration Act, 1992
- Sikkim Clinical Establishments (Licensing and Registration) Act, 1995
- Nagaland Health Care Establishments Act, 1997 No.3 of 1997
- West Bengal Clincial Establishment Rules, 2003
- Clinical Establishments (registration & regulation), Act, 2010

2. Disease Control and Medical Care

- Epidemic Diseases Act, 1897
- Indian Aircraft Act, 1934
- Indian Aircraft (Public Health) Rules, 1954
- Indian Port Health Rules, 1955
- Medical Termination of Pregnancy Act, 1971
- Medical Termination of Pregnancy Rules, 1975
- Medical Termination of Pregnancy Regulations, 1975
- Transplantation of Human Organs Act, 1994
- Transplantation of Human Organs Rules, 1995
- Transplantation of Human Organs (Amendment) Rules, 2002
- Pre-natal Diagnostic Techniques (Regulation & Prevention of Misuse) Act, 1994
- Pre-natal Diagnostic Techniques (Regulation & Prevention of Misuse) Rules, 1996
- Pre-natal Diagnostic Techniques (Regulation & Prevention of Misuse) Amendment Act, 2002
- Pre-natal Diagnostic Techniques (Regulation & Prevention of Misuse) Amendment Rules, 2003

3. Human Resources

- Allopathy
  - Indian Medical Council Act, 1956
  - Indian Medical Council Rules, 1957
  - Indian Medical Council (Election of Licentiates) Rules, 1965
  - Establishment of New Medical Colleges, Higher Course Regulations 1993
  - Indian Medical Council Amendment Act, 1993
  - Medical Council of India (Norms Guidelines for Fees, Admissions Regulations) 1994
  - Medical Council of India (Amendment) 1998
  - Indian Medical CounsilAmmendment, 2001

- Eligibility Requirement for Taking Admission in an Undergraduate Medical Course in a Foreign

➢ Medical Institution Regulations, 2002

- Indian Medical Council (Professional Conduct, Etiquette and Ethics) Regulations, 2002
- Eligibility Certificate Regulations, 2002 - Screening Test Regulations, 2002
- Medical Council of India, Regulations, 2000

➢ Dentistry

- Dentist Act, 1948
- Dental Council (Election) Regulations, 1952
- Dental Council of India Regulations, 1955
- Dental Council of India Regulations, 1956
- Dental Hygienists Revised Course, 1972
- Dental Mechanics Course Regulation, 1972
- BDS Course Regulations, 1983
- MDS Course Regulation, 1983
- Dental Council of India Regulations (Pension/GPF/Gratuity), 1984
- Dentist Amendment Act, 1993
- Establishment of Dental Colleges, 1993
- Dental Council of India (Establishment of new Colleges) Regulations, 2006
- Indian Systems of Medicine & Homeopathy
- Indian Medicine Central Council Act, 1970
- Homeopathy Central Council Act, 1973 26
- Homeopathy Diploma Course DHMS 1983
- Homeopathy Minimum Standards of Education, 1983
- Homeopathy (Degree Course) BHMS Regulation, 1983
- Indian Medicine Central Council (Amendment) Act, 2002
- Central Council of Indian Medicine (General) Regulations, 1976
- Homeopathy Practitioners (Professional Conduct, Etiquette and Code of Ethics) Regulations, 1982
- Practitioners of India Medicine (Standards of Professional Conduct, Etiquette and Code of Ethics) Regulations, 1982
- Indian Medicine Central Council (Minimum Standards of Education in Indian Medicine) (Amendment) Regulations, 1989

- Indian Medicine Central Council (PG Ayurveda Education) Regulations, 2005

➢ Nursing

- Indian Nursing Council Act, 1947
- Indian Nursing Council Regulations

➢ Pharmacy

- Pharmacy Act, 1948
- Pharmacy Council of India
- Regulation Act

➢ Rehabilitation

- Rehabilitation Council of India Act, 1992
- Rehabilitation Council of India Regulation, 1997
- Rehabilitation Council of India (Condition of Service), 1998

4. Ethics and Patients Rights

➢ Consumer Protection Act, 1986

➢ Consumer Protection Rules, 1987

➢ Consumer Protection (Amendment) Act, 2002

➢ Ethical Guidelines for Biomedical Research on Human Subject 2000

5. Pharmaceuticals and Medical Devices

➢ Drugs and Cosmetics Act, 1940

➢ Drugs Control Act, 1950

➢ Drugs and Magic Remedies (Objectionable Advertisements) Act, 1954 27

➢ Medicinal and Toilet Preparation (Excise Duties) Act, 1955

➢ Drugs (Prices Control) Order, 1979

➢ Drugs (Prices Control) Order, 1995

➢ International Federation of Pharmaceutical Manufacturers Associations Code, 1994

➢ Department of Ayurveda, Yoga & Naturopathy, Unani, Siddha and Homoeopathy (AYUSH) Orders, 2005

- Drugs and Cosmetics (inclusion of Sterile Devices), 2005
- Drugs and Cosmetics (inclusion of Sterile Devices), 2005
- Guidelines for Exchange of Human Biological Material
- Part I - Drugs and Cosmetic Rules, 1945

6. Radiation Protection

➢ Atomic Energy Act, 1962

➢ Radiation Protection Rules, 1971

➢ Radiation Surveillance Procedures for Medical Application of Radiation, 1980

- Atomic Energy (Working of the Mines, Minerals and Handling of Prescribed Substance) Rules, 1984
- Atomic Energy (Safe Disposal of Radioactive Wastes) Rules, 1987
- Radiation Surveillance Procedures for Medical Application of Radiation, 1989
- Safety Code for Medical Diagnostic X-Ray Equipment and Installations
- Statutory Requirements for Safe Operation of Medical X-Ray Machines by Hospitals, Clinics and Other Medical Institutions in India

7. Hazardous Substances

- Narcotic Drugs and Psychotropic Substances Act, 1985
- Narcotic Drugs and Psychotropic Substances Rules, 1985
- Prevention of Illicit Traffic in Narcotic Drugs and Psychotropic Substances Act, 1988 • Hazardous Wastes (Management and Handling) Rules, 1989
- Rules for the manufacture, Use, Import, Export and Storage of Hazardous Micro Organisms Genetically Engineered Organisms of Cells 1989
- Manufacture, Storage and Import of Hazardous Chemical Amendment) Rules, 2000
- Hazardous Wastes (Management and Handling) Rules, 2002

8. Occupational Health and Accident Prevention

- Fatal Accidents Act, 1855
- Workmen Compensation Act, 1923
- Factories Act 1948 (Amendment), 1987
- Plantations Labour Act, 1951
- Mines Act, 1952
- Mines and Minerals (Regulation and Development) Act, 1957
- Mines Creche Rules, 1966
- Motor Transport Workers Act, 1961
- Personal Injuries (Emergency Provisions) Act, 1962
- Personal Injuries (Compensation Insurance) Act, 1963
- Beedi and Cigar Workers (Conditions of Employment) Act, 1966
- Child Labour (Prohibition and Regulation) Act, 1986
- Contract Labour (Regulation and Abolition) Central Rules, 1971
- Dock Workers (Safety, Health and Welfare) Rules, 1990
- Public Liability Insurance Act, 1991
- Public Liability Insurance Rules, 1991

- National Commission for SafaiKaramcharis Act, 1993
- Building and Other Construction Workers (Regulation of Employment and Conditions of Service) Act, 1996
- Building & Other Construction Workers (CESS) Act, 1996

9. Elderly, Disabled, Rehabilitation and Mental Health

- Mental Health Act, 1987
- Central Mental Health Auth Rules, 1990
- State Mental Health Rules, 1990
- Persons with Disabilities (Equal Opportunities, Protection of Rights and Full Participation) Act, 1995
- Persons with Disabilities (Equal Opportunities, Protection of Rights and Full Participation) Rules, 1996
- National Trust for Welfare of Persons With Autism, Cerebral Palsy, Mental Retardation and Multiple Disabilities Act 1999
- National Trust for Welfare of Persons With Autism, Cerebral Palsy, Mental Retardation and Multiple Disabilities Rules 2000 29

10. Family, Women and Children

- Supression of Traffic in Women & Girl Act, 1956
- Children Act, 1960
- Orphanages and Other Charitable Home (Supervision and Control) Act, 1960
- National Commission for Women Act, 1990
- Juvenile Justice (Care and Protection of Children) Act, 2000

11. Smoking, Alcoholism and Drug Abuse

- Cigarettes (Regulations of Production, Supply and Distribution), Act, 1975
- Cigarettes and Other Tobacco Products (Prohibition of Advertisement and regulation of Trade and Commerce, Production, supply and Distribution) Act, 2003
- Cigarettes and other Tobacco Products (Prohibition of Advt. and Regulation of Trade and Commerce Production, Supply and Distribution) Rules, 2004
- Cigarettes and other Tobacco Products (Prohibition of Sale on Cigarettes and other Tobacco Products Around Educational Institutions) Rules, 2004

12. Social Security and Health Insurance

- Payment of Wages Act, 1936
- Minimum Wages Act, 1948
- Employees State Insurance Act, 1948
- Employees State Insurance (Central) Rules, 1950
- Life Insurance Corporation Act, 1956

- Life Insurance (Emergency Provisions) Act, 1956
- Maternity Benefit Act, 1961
- Maternity Benefit (Mines and Circus) Rules, 1963
- Insurance Regulatory and Development Authority Act, 1999

13. Environmental Protection

- Insecticides Act, 1968 • Insecticides Rules, 1971
- Insecticides (Amendment) Rules, 1993
- Insecticides (Amendment) Act, 2000
- Water (Prevention and Control of Pollution) Act, 1974 30
- Water (Prevention and Control of Pollution) Rules, 1975
- Central Board for the Prevention and Control of Water Pollution (Procedure for Transaction of Business) Rules, 1975
- Water (Prevention and Control of Pollution) CESS Act, 1977
- Water (Prevention and Control of Pollution) CESS Rules, 1978
- Water (Prevention and Control of Pollution) CESS (Amendment) Act, 2003
- Air (Prevention and Control of Pollution) Act, 1981
- Air (Prevention and Control of Pollution) Rules, 1982
- Air (Prevention and Control of Pollution) (Union Territories) Rules, 1983
- Bhopal Gas Leak Disaster (Processing of Claims) Act, 1985
- Bhopal Gas leak Disaster (Processing of Claims) Amendment Act, 1992
- Environment (Protection) Act, 1986 • Environment (Protection) Rules, 1986
- National Environment Tribunal Act, 1995
- Environment (Protection) Third Amendment Rules, 2002
- Bio-Medical Waste (Management and Handling) Rules, 1998
- Recycled Plastics Manufacture and Usage Rules, 1999
- Municipal Solid Wastes (Management and Handling) Rules, 2000
- Noise Pollution (Regulation and Control) Rules, 2000
- Ozone Depleting Substances (Regulation and Control) Rules, 2000
- Biological Diversity Act, 2002 • Biological Diversity Rules, 2003
- Disaster Management Act, 2005
- Constitution of National Disaster Management Authority, 2005

14. Nutrition and Food Safety

- Prevention of Food Adulteration Act, 1954
- Prevention of Food Adulteration Rules, 1955

- Prevention of Food Adulteration (1st Amendment) Rules, 2002
- Prevention of Food Adulteration (2nd Amendment) (Infant Milk Food) Rules, 2002
- Prevention of Food Adulteration (5th Amendment), 2002
- Prevention of Food Adulteration (6th Amendment) (Mineral Water) Rules, 2000
- Prevention of Food Adulteration (7th Amendment) (Sample to be sent) Rules, 2002
- Prevention of Food Adulteration (9th Amendment) (Vegetarian Food) Rules, 2001
- Infant Milk Substitutes, Feeding Bottles and Infant Foods Act, 1992
- Infant Milk Substitutes, Feeding Bottles and Infants Food (Regulation of Production, Supply and Distribution) Rules, 1993
- Infant Milk Substitutes, Feeding Bottles and Infant Foods (Regulation of Production, Supply and Distribution) Amendment Act, 2003
- Atomic Energy (Control of Irradiation of Food) Rules, 1996
- Edible Oils Packaging (Regulation) Order, 1998
- Vegetable Oil Products (Regulation) Order, 1998
- Public Distribution System (Control) Order, 2001
- Food Safety and Standards Act, 2006

15. Health Information and Statistics

- Births, Deaths and Marriages Registration Act, I886
- Registration of Births and Deaths Act, 1969
- Collection of Statistics Act, 1953
- Collection of Statistics (Central) Rules, 1959
- Census Act, 1948
- Census (Amendment) Act, 1993

16. Intellectual Property Rights

- Patents Act, 1970
- Patent Rules, 1972
- Patents (Amendment) Act, 2005
- Trade Marks Act, 1999

17. Custody, Civil and Human Rights

- Indian Penal Code, 1860
- Societies Registration Act, 1860
- Prisoners Act, 1900
- Unlawful Activities (Prevention) Act, 1967
- Code of Criminal Procedures, 1973
- Protection of Human Rights Act, 1993

6.6 LAWS AND REGULATIONS GOVERNING TOXICANTS

In order to ensure the proper handling, usage, and disposal of hazardous substances, laws and regulations pertaining to toxicants are an essential part of protecting public health and the environment. By limiting the hazards connected to toxicants, these regulations hope to safeguard the environment and public health against hazardous exposures. An outline of the main statutes and rules pertaining to toxicants is provided below:

- **Environmental Protection Agency:** In the US, the EPA is the main regulatory body in charge of safeguarding the environment and public health from toxins. The EPA creates rules and guidelines for managing chemicals and hazardous materials, as well as for controlling air and water pollution, under the authority of statutes like the Toxic Substances Control Act (TSCA), Clean Water Act, and Clean Air Act.
- **Toxic Substances Control Act (TSCA):** The TSCA, which was passed into law in 1976, is the primary federal statute that controls the use of chemicals and other hazardous materials in the US. The TSCA gives the EPA the power to evaluate and control the production, importation, processing, distribution, use, and disposal of chemicals in order to make sure that there are no unjustified dangers to the environment or public health.
- **Occupational Safety and Health Administration (OSHA):**OSHA is in charge of establishing and implementing workplace safety standards, including laws pertaining to hazardous materials, in order to guarantee safe and healthy working conditions. Employers are required by OSHA's Hazard Communication Standard to give workers safety data sheets and training on chemical dangers and precautions, as well as information on hazardous substances that may be present in the workplace.
- **Food and Drug Administration (FDA):**To protect the efficacy and safety of food, medications, cosmetics, and other consumer goods, the FDA controls the use of toxicants in these products. Food additives, color additives, and other materials that may come into touch with food or be consumed by consumers must adhere to regulations set forth by the FDA.
- **Consumer Product Safety Commission (CPSC):** The safety of consumer goods, such as toys, home chemicals, and other goods that can contain toxicants, is governed by the CPSC. To reduce the chance that consumers will be exposed to harmful materials, the CPSC sets guidelines for product labeling, packaging, and safety warnings.
- **State and Local Regulations:** Toxicant rules and regulations may be enforced by state and municipal governments in addition to federal regulations. The use of specific chemicals may be restricted, waste management and pollution control procedures must be followed, and emergency response and hazardous spill cleanup procedures must be followed, among other things.
- **International Regulations:** International agreements and rules that safeguard the environment and public health worldwide also apply to toxicants. For instance, many highly toxic compounds that stay in the environment and bioaccumulation in the food chain are the target of the Stockholm Convention on Persistent Organic Pollutants (POPs), which seeks to ban or restrict their use and production.

In conclusion, the regulation of toxicants involves a complex framework of laws and regulations at the federal, state, and international levels. These regulations aim to minimize the risks associated with toxic substances, protect human health and the environment, and promote safer alternatives and practices for the management and use of hazardous materials. Compliance with these regulations is essential for preventing exposure to toxicants and ensuring the safety and well-being of communities

and ecosystems.

6.7 EPIDEMIOLOGICAL APPROACH TO TOXICANTS

The epidemiological approach to toxicants involves the study of the distribution and determinants of toxicant-related health outcomes in populations. Epidemiology is the science to understandingthe patterns of disease and injury within populations and identifying factors that contribute to these patterns. When applied to toxicants, epidemiological methods are used to investigate the occurrence of adverse health effects associated with exposure to hazardous substances and to identify populations at risk. The epidemiological approach is applied to toxicants are as:

Exposure Assessment: The evaluation of population exposure levels is the first step in epidemiological investigations on toxicants. This could entail figuring out how much harmful material is in the food, water, soil, air, or biological samples (such blood or urine). In addition to taking into account probable sources and pathways of exposure, exposure assessment methods also take into account variables including exposure duration, frequency, and route.

Outcome Ascertainment: Epidemiologists find noteworthy health outcomes that could be linked to exposure to toxicants. These consequences can be anything from short-term incidents like respiratory irritation or poisoning to long-term illnesses like cancer, neurodevelopment impairments, or issues with reproduction. Reviewing medical records, performing health surveys, or monitoring incidence and prevalence rates via illness registries are a few methods of determining the outcome.

Study Design: Epidemiological studies on toxicants look into the connection between health outcomes and exposure using a variety of study approaches. Depending on the study question and available data, these designs could be cross-sectional studies, case-control studies, cohort studies, or ecologic studies. Regarding proving causation and accounting for confounding variables, every research design has advantages and disadvantages.

Data Analysis: Epidemiological studies on toxicants look into the connection between health outcomes and exposure using a variety of study approaches. Depending on the study question and available data, these designs could be cross-sectional studies, case-control studies, cohort studies, or ecologic studies. Regarding proving causation and accounting for confounding variables, every research design has advantages and disadvantages.

Risk Assessment: Risk assessment, which assesses the possibility and severity of harmful health effects linked to toxicant exposure, is informed by epidemiological findings. Epidemiological data, toxicological research, exposure modeling, and other pertinent data are used with risk assessment to evaluate health hazards to humans and set acceptable exposure limits or regulatory requirements.

Public Health Action: Public health actions and policies that aim to prevent or reduce toxicant-related health hazards in communities are guided by epidemiological evidence. This could be carrying out community-based initiatives, enforcing environmental regulations, offering medical screening and surveillance, or offering guidance on risk communication and public education campaigns.

Overall, the epidemiological approach to toxicants provides a systematic framework for understanding the health effects of hazardous substances and informing evidence-based interventions to protect public health. By identifying patterns of exposure and disease, assessing risks, and guiding prevention and control measures, epidemiology plays a crucial role in addressing the complex challenges posed by toxicant exposure in communities.

6.8 BLACKLISTED TOXIC CHEMICALS

Toxic chemicals that have been blacklisted are those, that have been determined to pose a significant risk to the environment and human health, hence they are subject to tight control, prohibition, or limitation. These substances frequently have major negative health effects, such as environmental persistence, neurotoxicity, carcinogenicity, and toxicity to reproduction. To safeguard the environment and public health, governments, regulatory bodies, and international organizations keep lists of chemicals that are prohibited. Here's a summary of some of the hazardous substances that are frequently placed on blacklists:

Asbestos: The strength and heat resistance of asbestos, a naturally occurring mineral fiber, are well recognized. On the other hand, asbestos fiber exposure can result in mesothelioma, asbestosis, and lung cancer, among other major health issues. In numerous nations, asbestos is either prohibited or subject to strict regulations because of its potential health effects.

Lead: Once widely used in paint, gasoline, plumbing, and other industrial products, lead is a heavy metal. Lead exposure, especially in children, can cause brain damage, developmental delays, and other health problems. Although many nations have phased out lead-based paint and leaded gasoline, lead exposure is still a serious public health risk, particularly in low-income areas and emerging nations.

Mercury: There are several different types of mercury, including elemental mercury, inorganic mercury compounds, and organic mercury compounds like methyl mercury. Mercury is a dangerous metal. The brain system, kidneys, and cardiovascular system can all be harmed by mercury exposure, with fetal development and neurological function being especially vulnerable. There has been significant contamination of air, water, and food sources due to mercury pollution from industrial sources, mining operations, and coal-fired power plants.

Polychlorinated Biphenyls (PCBs): Synthetic organic compounds called PCBs were extensively utilized in hydraulic fluids, electrical equipment, and other industrial uses as insulating fluids. Persistent organic pollutants, or PCBs, are known to bioaccumulate in the environment and can lead to a variety of harmful health outcomes, including as immune system malfunction, cancer, and reproductive abnormalities. Although many nations have outlawed or restricted PCBs, their continued presence in the environment nevertheless endangers ecosystems and human health.

Dioxins and Furans: Dioxins and furans are extremely harmful organic pollutants that arise from industrial operations, burning, and chemical reactions involving chemicals containing chlorine. These substances can build up in the food chain and are persistent in the environment, which exposes people and wildlife to long-term exposure. Dioxins and furans are known to cause cancer and have also been connected to immune system dysfunction, abnormalities in development and reproduction, and other health issues.

Polycyclic Aromatic Hydrocarbons (PAHs): A class of organic compounds known as polycyclic aromatic hydrocarbons (PAHs) is produced when wood, other organic materials and fossil fuels burn partially. Pervasive agricultural pollutants (PAHs) can be detected in food supplies, soil, water, and the air. Long-term exposure to PAHs has been linked to lung cancer, skin cancer, and other harmful health effects. Many PAHs are carcinogenic.

Chlorofluorocarbons (CFCs): Synthetic compounds known as CFCs were previously widely utilized in a wide range of consumer and industrial products as propellants, solvents, and refrigerants. Strong greenhouse gases called CFCs cause ozone depletion in the Earth's stratosphere, which increases exposure to UV radiation and harms the environment. The manufacturing and use of CFCs and other substances that deplete the ozone layer were gradually phased out by the 1987 adoption of the Montreal

Protocol, an international agreement.

Organophosphate Pesticides: Organophosphate insecticides are a type of compounds used to control pests in residential, agricultural, and public health settings. These insecticides cause neurotoxicity in humans and animals by blocking cholinesterase enzymes. Many countries have prohibited the use and registration of organophosphate pesticides because of evidence linking them to long-term brain damage, developmental abnormalities, and acute toxicity.

Perfluorinated Compounds (PFCs): PFCs are man-made chemicals found in a variety of consumer and commercial goods, such as firefighting foams, stain-resistant textiles, and non-stick cookware. PFCs are environmental pollutants that are persistent and have been found in soil, water, air, and biota all around the world. Certain perfluorooctanoic acids (PFOA) and perfluorooctanesulfonate (PFOS) are PFCs.ThePFCshave been linked to a number of harmful health outcomes, such as cancer, immune system malfunction, and developmental abnormalities.

Bisphenol A (BPA): The chemical BPA is utilized in the manufacturing of epoxy resins and polycarbonate plastics, which are employed in food and drink containers, medical equipment, and other consumer goods. Endocrine disrupting chemicals like BPA can imitate or obstruct the body's natural hormonal processes. Certain applications of BPA have been restricted due to its association with reproductive diseases, anomalies in development, and other health concerns.

These are just a few examples of hazardous compounds that have been added on a blacklist and are exceedingly damaging to both the environment and human health. Regulatory organizations and global associations constantly monitor and evaluate chemical safety, identify new dangers, and adopt steps to protect the environment and public health from the negative effects of hazardous products. To address the issues produced by hazardous chemicals and promote safer alternatives and practices in business, agriculture, and everyday life, public awareness, advocacy, and regulatory actions are critical.

6.9 PESTICIDES

Pesticides are chemicals used to control rodents, weeds, fungi, and insects, which can harm crops, transmit disease, and cause financial losses. Pesticides are critical for agricultural, public health, and vector management in order to preserve food security, protect public health, and control vector populations. However, the widespread use of pesticides has prompted concerns about their consequences on non-target species, the environment, and human health. This page provides an overview of pesticides, such as their types, applications, benefits, risks, and regulatory difficulties.

Pesticides can be classified into several broad categories based on their target pests and chemical composition:

Insecticides: Pesticides intended to suppress insects and other arthropods are called insecticides. Based on how they work, they can be further divided into four groups: systemic insecticides, stomach poisons, contact insecticides, and insect growth regulators.

Herbicides: Herbicides are pesticides that are applied to lawns, gardens, and non-crop areas to suppress weeds and other undesirable vegetation. They may be non-selective, impacting a variety of plant species, or selective, focusing on particular plant species.

Fungicides: Fungicides are insecticides that are used to turf, ornamental plants, and crops to suppress fungal diseases. They can be used either curatively to treat fungal diseases that already exist or preventively to shield plants against infection.

Rodenticides: Pesticides known as rodenticides are used to manage rodents, including mice and rats. Usually designed as baits or traps, they can endanger pets and non-target species, if not utilized

appropriately

Nematocysts: Nematode insecticides are used to control microscopic roundworms that can injure plant roots and reduce crop productivity. In agricultural situations, they are commonly employed as soil treatments.

Molluscicides: Pesticides known as "molluscicides" are used to manage mollusks, such slugs and snails, which can harm gardens and crops. To eliminate or discourage mollusk pests, they are used as sprays or baits.

Uses of Pesticides: Pesticides are used in various sectors and applications to protect crops, human health, and the environment:

- Pesticides are widely used in agriculture to protect crops from pests and diseases, increase yields, and ensure food security. Farmers use pesticides to control insect pests, weeds, and fungal pathogens that can damage crops and reduce productivity.
- Pesticides are used in public health programs to control vector-borne diseases such as malaria, dengue fever, and Zika virus. Insecticides are applied to kill mosquitoes, flies, and other disease vectors that transmit pathogens to humans.
- Pesticides are used in household, commercial, and industrial settings to manage pests like rats, insects, and weeds. They are used both indoors and outdoors to control insect infestations and avoid property damage and health hazards.
- Pesticides are used in forestry to protect trees and forests from insect pests, diseases, and invasive species. Herbicides are used to control competing vegetation and promote tree growth in reforestation and afforestation projects.
- Pesticides are used in landscaping, turf management, and ornamental horticulture to control weeds, pests, and diseases in lawns, gardens, golf courses, parks, and other green spaces.

Benefits of Pesticides: Pesticides offer several benefits in agriculture, public health, and pest management:

- Farmers can increase yields and enhance crop quality by using pesticides to protect their crops from weeds, illnesses, and pests. Pesticides support food security and agricultural output by lowering losses brought on by pest damage.
- By eliminating or deterring insects that spread disease, such as ticks, flies, and mosquitoes, pesticides aid in the control of diseases carried by vectors. Insecticides are used by public health programs to stop the spread of dengue fever, malaria, the Zika virus, and other diseases that are carried by vectors.
- The health concerns posed by pests like ticks, mosquitoes, and rodents are lessened with the use of pesticides. People are shielded from allergens, infections, and injuries caused by pests via pest management procedures in homes, schools, hospitals, and public areas.
- By eliminating pests and invading species that endanger native ecosystems, pesticides can contribute to the preservation of natural habitats and biodiversity. In urban and agricultural settings, integrated pest management (IPM) techniques reduce the use of pesticides and support ecological balance.
- Pesticides ensure the availability of reasonably priced food and commodities while minimizing production costs and crop losses, which helps farmers, consumers, and industry economically. In

both urban and rural locations, the provision of pest management services and goods promotes economic expansion and the development of jobs.

Risks of Pesticides: Despite their benefits, pesticides pose risks to human health, the environment, and non-target organisms:

Health Hazards: Pesticides reduce production costs and crop losses, ensuring the supply of fairly priced food and commodities that benefit consumers, farmers, and the industry economically. Offering products and services for pest control encourages job growth and economic expansion in both urban and rural areas.

Environmental Contamination: Pesticides have the potential to contaminate food sources, water, soil, and air through bioaccumulation, drift, runoff, and leaching. Pollinators like bees and butterflies, as well as aquatic ecosystems, wildlife populations, and non-target creatures, can all be negatively impacted by environmental contamination.

Residue Accumulation: Pesticide residues have the potential to linger in food items, water supplies, and the environment, endangering both people and ecosystems. Pesticide exposure can result from residue buildup via food, drinking water, and ecological pathways, which could have negative effects on human health and the ecosystem.

Pesticide Resistance: Natural selection and genetic changes can cause pests to become resistant to insecticides over time. In order to manage resistant insect populations, greater pesticide doses or alternative control strategies may be necessary due to pesticide resistance, which decreases the efficacy of pest management techniques.

Non-Target Effects: Non-target creatures that are vital to ecosystems, such as beneficial insects, birds, mammals, and aquatic species, can be harmed by pesticides. Non-target impacts have the potential to interfere with ecological processes, lower biodiversity, and have an impact on ecosystem services like pest control and pollination.

Regulatory Considerations: To ensure pesticide effectiveness, safety, and environmental sustainability, governments and international organizations regulate them:

- Pesticides must undergo rigorous testing and evaluation before they can be approved for sale, distribution, and use. Regulatory agencies assess pesticide formulations for their chemical composition, toxicity, environmental fate, and efficacy in controlling target pests.

- Pesticide labels provide important information on product use, handling, storage, disposal, and safety precautions. Labels must comply with regulatory requirements and include instructions, warnings, precautionary statements, and first aid measures to protect users and the environment.

- Regulatory agencies conduct risk assessments to evaluate the potential hazards and risks associated with pesticide use. Risk assessments consider factors such as toxicity, exposure pathways, environmental fate, and ecological impacts to determine acceptable risk levels and mitigation measures.

- Pesticide use is regulated through laws, regulations, and guidelines that govern application methods.

The toxicity of pesticides can vary based on their chemical makeup, mechanism of action, and exposure pathways. Typical forms of pesticide poisoning include the following:

Acute Toxicity: The term "acute toxicity" describes the negative effects of pesticides that manifest soon

after exposure and might include symptoms like vomiting, nausea, vertigo, respiratory distress, or convulsions. Significant and even fatal acute toxicity can occur, especially in instances of accidental poisonings or high-dose exposures.

Chronic Toxicity: Chronic toxicity refers to the long-term effects of pesticides that develop over time with repeated or prolonged exposure. Chronic exposure to pesticides may lead to health problems such as cancer, reproductive disorders, neurological damage, immune system dysfunction, or developmental abnormalities.

Systemic Toxicity: When pesticides enter the bloodstream and spread throughout the body, impacting many organ systems and physiological processes, this is known as systemic toxicity. Damage to the brain system, liver, kidneys, endocrine system, or reproductive systems are examples of systemic consequences.

Neurotoxicity: The term "neurotoxicity" describes a pesticide's capacity to harm the neurological system, which includes the brain, spinal cord, and peripheral nerves. Neurotoxic pesticides can cause neurological illnesses including Parkinson's disease, Alzheimer's disease, or neuropathy by impairing motor skills, behavior, cognitive function, and sensory perception.

Carcinogenicity: The term "carcinogenicity" describes a pesticide's capacity to cause cancer in both people and animals. Regulatory bodies have designated several pesticides as carcinogens on the basis of data from epidemiological studies, animal studies, and mechanistic studies that connect pesticide exposure to an elevated risk of cancer.

Reproductive Toxicity: The term "reproductive toxicity" describes how pesticides can affect both male and female fertility and reproductive functions. Pesticides have the potential to induce infertility, miscarriages, birth malformations, disruption of hormone function, and effects on gamete production and fetal development.

Developmental Toxicity: When pesticides are introduced to offspring during crucial stages of growth and differentiation, they can disrupt both prenatal and postnatal development. This phenomenon is known as developmental toxicity. Growth retardation, cognitive deficits, behavioral issues, and congenital abnormalities are examples of developmental impacts.

6.10 AUTOMOBILE EMISSION

Automobile emissions include pollutants emitted by internal combustion engine-powered automobiles, Lorries, buses, motorbikes, and off-road vehicles. These emissions exacerbate air pollution, climate change, and public health issues, making them a major global environmental and policy concern. Car emissions are a complex mixture of gases, particles, and volatile organic compounds (VOCs) produced during engine operation and fuel combustion. Many factors influence car emissions, including engine efficiency, fuel combustion, and vehicle operating. The following are some of the primary sources of vehicle emissions: Vehicle exhaust systems emit CO, NOx, PM, VOCs, and CO2, among other gases and particles generated during fuel combustion. Vehicles emit volatile organic compounds (VOCs) and other pollutants as their fuel evaporates, particularly when refilling, parking, and in hot weather. Evaporative emissions, particularly in cities with high vehicle numbers, cause ground-level ozone and air toxics pollution. The fuel mix can influence automotive pollutant emissions, such as sulphur, benzene, aromatics, and other dangerous compounds. Toxic air pollutants, SO_2, PM, and aromatic hydrocarbon emissions, as well as low-quality fuels with high sulphur content, can be enhanced. Engine design, fuel injection systems, ignition timing, combustion efficiency, and pollution control technologies all have an impact on the amount and kind of emissions produced by automobiles. Pollutant emissions from newer, more efficient vehicles are lower than in older models that lack engine

management systems, particulate filters, and catalytic converters. Traffic congestion and stop-and-go driving can increase pollutant emissions such as CO, NOx, and VOCs due to inefficient engine performance and idle time. High levels of traffic and congestion in cities increase air pollution and pose health risks. Among the primary factors that contribute to vehicle emissions are:

- **Carbon Monoxide (CO):** A colorless and odorless gas, carbon monoxide is created when fuels containing carbon do not burn completely. Poisonous CO gas can produce symptoms like headaches, nausea, dizziness, and weariness by interfering with the body's oxygen transport system.

- **Nitrogen Oxides (NOx):** When nitrogen and oxygen react at high temperatures during combustion, a class of reactive gases known as nitrogen oxides is created. NOx, which is made up of nitrogen monoxide (NO) and nitrogen dioxide (NO_2), is linked to respiratory issues, acid rain, and the development of smog.

- **Particulate Matter (PM):** Particulate matter is made up of microscopic particles that are suspended in the atmosphere. These particles can be classified as coarse (PM10), fine (PM 2.5), or ultrafine (PM 0.1). PM emissions have the ability to deeply enter the bloodstream and lungs, where they can lead to lung cancer, cardiovascular and respiratory disorders, as well as early death.

- **Volatile Organic Compounds (VOCs):** VOCs are organic compounds that readily evaporate at room temperature. They are a contributing factor to the production of secondary organic aerosols and ground-level ozone. Vehicle emissions, exhaust gases, and gasoline evaporation all produce volatile organic compounds (VOCs), which can aggravate asthma, irritate the respiratory system, and contribute to the development of smog.

- **Carbon Dioxide (CO_2):** The majority of greenhouse gases emitted from cars come from the burning of fuel, which produces carbon dioxide. A primary cause of climate change and global warming, CO_2 raises temperatures, raises sea levels, and produces extreme weather.

- **Sulfur Dioxide (SO_2):** Burning fuels that include sulfur, such gasoline and diesel, releases sulfur dioxide into the air. In places with high levels of industrial activity and automobile traffic, in particular, SO_2 emissions are a contributing factor to respiratory issues, acid rain, and air pollution.

Impacts of Automobile Emissions: Automobile emissions have wide-ranging impacts on human health, the environment, and the economy:

- **Air Pollution:** Ground-level ozone, particulate matter, smog, and hazardous air pollutants are all caused by vehicle emissions. Poor air quality, especially in susceptible populations including children, the elderly, and those with pre-existing medical issues, can aggravate respiratory and cardiovascular disorders, increase the chance of asthma episodes, and cause premature mortality.
- **Climate Change:** One of the main sources of greenhouse gasses, such CO_2, which are linked to climate change and global warming, is automobile emissions. The effects of climate change linked to vehicle emissions include rising temperatures, altered precipitation patterns, ice caps melting, and sea level rise.
- **Environmental Degradation:** Automobile emissions have a deleterious influence on ecosystems, soil quality, water resources, and biodiversity by causing acid deposition, nutrient enrichment, habitat destruction, and soil, water, and air contamination. Automobile emissions

have a negative impact on natural ecosystems via a variety of mechanisms, including Eutrophication, acid rain, and toxic pollution.

- **Public Health:** Automobile emissions, which are linked to air pollution exposure, constitute a severe threat to public health since they can cause lung cancer, cardiovascular problems, respiratory disorders, and other issues. Young people, the elderly, pregnant women, and those with underlying medical conditions are most vulnerable to the harmful consequences of automobile emissions.
- **Economic Costs**: Property damage, premature mortality, lost productivity, absenteeism, healthcare costs, and environmental remediation are some of the economic implications of vehicular emissions. The financial cost of the health and environmental damage caused by air pollution can be enormous, affecting not just individuals but also communities, corporations, and governments.

6.11 SUMMARY

The multidisciplinary discipline of public health seeks to protect and improve population health through health equity, health promotion, and illness prevention efforts. It explores the complex interplay of biological, social, economic, and environmental factors that influence health outcomes at the local, national, and international levels. Public health encompasses the subjects of epidemiology, biostatistics, environmental health, health policy, health education, and community health. Pesticides are effective tools for controlling pests and protecting human health, but they can also be toxic to the environment, animals, and people.

It addresses how biological, social, economic, and environmental factors combine to influence local health outcomes. The epidemiological approach to toxicants provides a systematic framework for understanding the health effects of hazardous compounds and directing evidence-based responses to protect public health. Epidemiology is critical in addressing the numerous issues created by toxicant exposure in communities because it can identify patterns of exposure and disease, assess risks, and guide preventative and control actions. Toxicant regulation is managed by a complex web of federal, state, and international legislation and regulations. The goals of these laws are to limit the risks caused by dangerous substances, protect the environment and public health, and encourage the use of safer alternatives and methods for the management and disposal of hazardous materials. Adherence to these criteria is critical to avoiding toxicant exposure and ensuring the safety and welfare of communities and ecosystems. To guarantee safe and sustainable pesticide use, it is critical to understand pesticide toxicity and have procedures in place to assess, control, and reduce pesticide risks. To protect the environment and public health from the negative effects of pesticide toxicity, regulatory control, risk assessment, risk management, monitoring, and public education must be combined. Regulatory organizations and global associations constantly monitor and evaluate chemical safety, identify new dangers, and adopt steps to protect the environment and public health from the negative effects of hazardous products.

6.12 TERMINAL QUESTIONS

Q. 1. What is the role of toxicology in public health?

Answer: ----------

Q. 2. How does toxicology affect health?

Answer: ----------

Q. 3. What are the three major areas of toxicology?

Answer: ----------

Q. 4. What are the regulations on toxic chemicals?

Answer: ----------

Q. 5. What is the law of toxicity?

Answer: ----------

Q. 6. What are the steps in the epidemiological approach?

Answer: ----------

Q. 7. What is the role of epidemiology in toxicology?

Answer: ----------

6.13 FURTHER SUGGESTED READINGS

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Uttar Pradesh Rajarshi Tandon Open University

PGBCH-117N

Environmental Toxicology and Occupational Health Hazards

BLOCK

3

SYSTEMATIC TOXICITY

UNIT-7

Renal Toxicity

UNIT-8

Cutaneous Toxicology

UNIT-9

Pulmonary and Hepatic Toxicity

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BLOCK INTRODUCTION

The following three units are included in the third block of environmental toxicology & occupational health hazards are as:

Unit-7: This unit discusses renal toxicity. It also briefly touches on the structure, functioning, and sensitivity of the kidney to toxic assault, as well as chemically induced renal injury.

Unit-8: The effects of hazardous substances on dermatology were covered in this unit. A brief discussion of cutaneous carcinogenesis and allergic contact dermatitis is held.

Unit-9: This unit covers toxicity to the lungs and liver. Whereby the toxicant that causes respiratory collapse is discussed. However, the processes of toxin entry into the lungs, systemic lung toxins, liver-damaging effects of toxins, and chronic liver damage are all discussed.

UNIT-7 : RENAL TOXICITY

Structure

7.1 INTRODUCTION

The term "renal" refers to the kidney. For example, renal failure means kidney failure.Renal toxicity refers to the harmful effects on the kidneys caused by exposure to certain substances such as medications, chemicals, or poison. If not treated immediately, it can lead to impaired kidney function and other serious health problems. Nonsteroidal anti-inflammatory drugs (NSAIDs), heavy metals, some pharmaceuticals, and contrast compounds used in medical imaging methods are also common causes. Nephrotoxicity is a word used to describe the rapid deterioration in kidney function caused by medications and other chemicals. Nephrotoxicity refers to an undesirable reaction caused by medications that affect kidney function. Molds and fungi, cancer treatments, antibiotics, metals including arsenic, lead, and mercury, and illicit drugs are a few examples of these substances.The kidney regulates the toxicity of various drugs, environmental pollutants, and natural substances. Cancer treatments, recreational drugs, antibiotics, and radio contrast agents are all examples of nephrotoxic pharmaceuticals. Cadmium, mercury, arsenic, lead, trichloroethylene, bromate, brominated flame retardants, di-glycolic acid, and ethylene glycol are among the environmental toxins that have been linked to kidney damage. A drug's renal excretion can be broken down into three stages: glomerular filtration, tubular reabsorption, and tubular secretion. Tubular secretion permits medications to go from the bloodstream to the urine via tubular cells. Drug-induced nephrotoxicity causes acute and chronic renal damage, as well as chronic kidney disease, which is the most common clinical manifestation of nephrotoxicity. Despite progress in the development of biomarkers for detecting nephrotoxicity, current kidney injury biomarkers remain inadequate. A greater understanding of the metabolic pathways that cause nephrotoxicity is required to provide relevant information for diagnosing, monitoring, and treating nephrotoxicity and its clinical symptoms. Nephrotoxicant-induced renal failure mechanisms have many parallels to extrinsic causes. This common ground is primarily due to similarities in the molecular processes that regulate renal cell death. The goal of this review is to summarize the current state of nephrotoxicity. It focuses on bridging our understanding of nephrotoxicity to pathologically cause renal failure.

Objectives:

After reading this unit, the learner will able to know

- About the renal toxicity and renal system
- About renal structure and functions
- The susceptibility of kidney to toxic insult
- The chemically induced renal injury and its effects on human health

7.2 RENAL TOXICITY

Nephrotoxicity, another name for renal toxicity, is a disorder, where exposure to certain substances damages the kidneys. These compounds may consist of drugs, chemicals and poisons that found in the environment or through specific medical treatments. Renal toxicity can cause decreased kidney function, which manifests as blood chemistry alterations, electrolyte imbalances, and variations in urine production. Renal toxicity can progress to acute kidney injury (AKI) or chronic kidney disease (CKD) if not treated, all of which can have a negative impact on overall health and wellness. Renal toxicity can arise in persons suffering from renal impairment. A reduction in creatinine levels in blood and serum indicates renal impairment. Nephrotoxicity is the harmful effect of some substances, such as toxic chemicals and drugs, on the kidneys.

Drugs and metabolites can be excreted through one of two pathways: renal or extrarenal. Drugs can be eliminated through one of two mechanisms in renal excretion: glomerular filtration or tubular secretion. Each excretion pathway exposes the tubules and the surrounding interstitial fluid to potentially harmful chemicals. The (mostly proximal) tubules are exposed through apical contact with chemicals released into the tubular lumen, uptake by tubular epithelial cells, or apical efflux from the peritubular circulation into the tubular lumen.Renal toxicity can also result from exposure to specific substances and environmental pollutants, in addition to drugs. Nephrotoxins, or heavy metals, include lead, mercury, and cadmium. These metals can build up in the kidneys over time and cause tissue damage and decreased renal function. Other examples of compounds that might cause kidney toxicity through ingestion or direct exposure include insecticides, solvents, and industrial chemicals.

The use of particular medicines is one of the leading causes of kidney injury. Many medications can harm the kidneys, including antibiotics, NSAIDs (nonsteroidal anti-inflammatory drugs), chemotherapeutic treatments, and antiviral therapy. These drugs have the potential to compromise renal function by directly damaging kidney cells or interfering with normal renal activities such as reabsorption and filtration. Furthermore, some medications may produce metabolic byproducts or side effects related to their primary therapeutic action, which might contribute to renal toxicity.

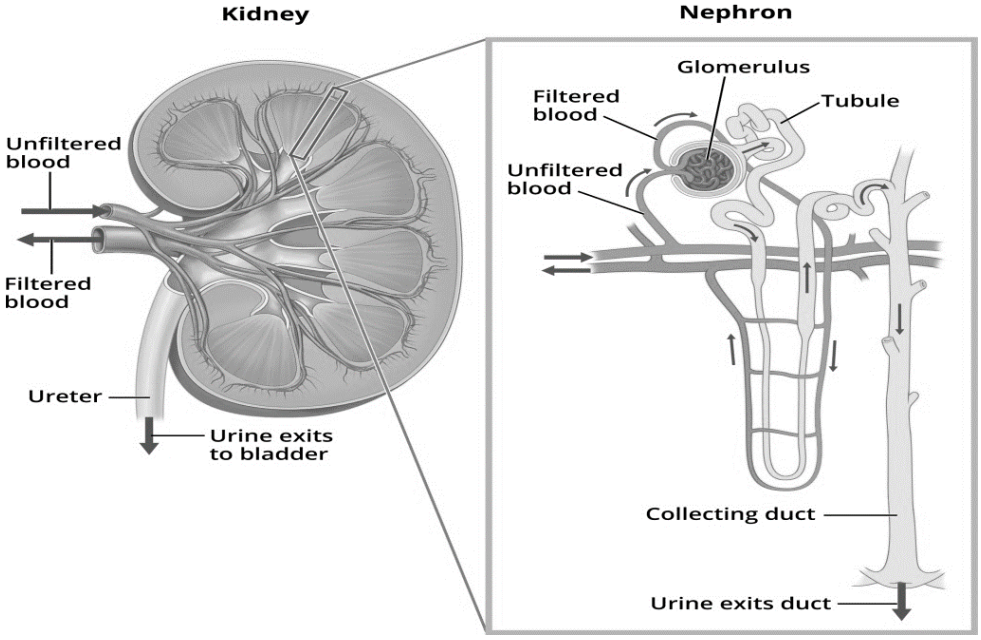
Renal toxicity can also occur from medical procedures involving the use of contrast agents for imaging examinations, especially in people with pre-existing kidney problems or other risk factors. When the contrast agent used in procedures like computed tomography (CT) scans or angiography damages the kidneys, it can lead to a temporary or permanent impairment of renal function. This condition is known as contrast-induced nephropathy, or CIN. Each medication class has a unique mechanism for reflex toxicity. Certain nephrotoxic chemicals produce oxidative stress, inflammation, or programmed cell death, which directly harms the kidneys. Others may interfere with biological functions such as protein synthesis, metabolism, or ion transport, compromising kidney function. Renal toxicity can occasionally be produced by immune-mediated reactions or harmful compounds that accumulate in kidney tissue. The clinical presentation of renal toxicity varies greatly depending on the severity of the injury and the underlying etiology. Common symptoms include changes in urine

production (such as oliguria or anuria), electrolyte imbalances, edema (swelling caused by fluid retention), hypertension (high blood pressure), and signs of systemic toxicity (such as nausea, vomiting, and weariness).

Serum creatinine, blood urea nitrogen (BUN), and urinalysis are laboratory tests used to detect renal toxicity and assess the extent of kidney damage. Renal toxicity is often treated by discontinuing the offending chemical, addressing any underlying conditions that may be causing renal dysfunction, and giving supportive care to maintain fluid and electrolyte balance. Renal replacement therapy, such as continuous renal replacement therapy (CRRT) or hemodialysis, may be necessary in severe cases to keep the kidneys functioning while they heal. Preventive approaches include avoiding nephrotoxic substances, properly monitoring medication use, and lowering risk factors such as dehydration and pre-existing kidney illness.

7.3 RENAL SYSTEM

The renal system consists of the kidneys, their vasculature, and innervation. Each kidney empties into a median urinary bladder, which drains to the outside by a single channel known as the urethra. The kidney is made up of three basic sections. The brain, medulla, and papilla are three anatomical regions. The renal cortex is the kidney's outermost layer, which houses glomeruli, tubules (proximal and distal), and peritubular capillaries. Cortical blood flow is robust, accounting for about 90% of total renal blood flow. Toxicants administered in the bloodstream are more likely to affect the cortex than the medulla or papilla. The renal medulla, located in the center of the kidney, is mostly made up of Henle loops, vasa recta, and collecting ducts. Despite receiving only 6% of total renal blood flow, the medulla can be exposed to high quantities of toxicants within tubular structures. The papilla is the smallest portion of the kidney, receiving only 1% of renal blood flow. Toxicants in the papilla may cause damage to papillary tubular and interstitial cells due to the high concentration of tubular fluid and low concentration of luminal fluid.



The kidneys remove water-soluble compounds from the blood as part of the reverse filtering process. Size and water solubility are the two most important elements in determining whether a chemical will be eliminated by the kidneys.

- **Size.** The reverse filtration process requires that chemicals to be removed from the blood are able to pass through 70 to 100A° pores. As a rule, chemicals having a molecular mass of less than 65,000 are sufficiently small to be subject to reverse filtration.

- **Water Solubility**: Non-water-soluble chemicals will be transported to the kidneys in association with transport proteins. Thus, in association with these proteins, the chemicals will not be able to pass through the pores during reverse filtration.

Renal arteries transport blood to the kidneys in humans. A mature human's kidneys get blood at a rate of approximately 1 L/min. The adult human kidney is made up of approximately a million nephrons, which are functional units that receive blood in order to eliminate solutes. The body excretes accumulated things in its pee.

The renal system excretes waste from both endogenous and xenobiotic metabolism. The kidney maintains bodily homeostasis, extracellular fluid volume, and electrolytes. Other kidney functions include hormone synthesis, which influences metabolism. For example, 25-hydroxyvitamin D3 is transformed to its active form, 1,25-dihydroxyvitamin D3. The kidney generates renin, a hormone that aids in the manufacture of angiotensin, aldosterone, and numerous prostaglandins. Kidney poisoning can impair any of these functions, but only the clinically recognized symptoms are utilized to diagnose. Kidney disease can alter excretory function, resulting in changes in urine volume, osmolality, and the pH. Changes in BUN, creatinine, and serum enzymes could suggest kidney disease.The kidney's sensitivity to toxicants is influenced by several circumstances, including high blood flow and elevated excretory product concentrations from tubular fluid reabsorption. The kidneys account for less than 1% of the body's bulk yet receive approximately 25% of cardiac output. The kidney receives considerable amounts of external substances and/or metabolites.The kidney's sensitivity to chemicals is further influenced by its ability to concentrate tubular fluid, which removes water and salts and concentrates any compounds present. Thus, a harmless quantity in the plasma. In the tubular fluid, it may be transformed into a hazardous compound. The renal tubules' transports characteristics help deliver potentially hazardous compounds to cells. Chemicals produced from the blood into the tubular fluid can collect within the proximal tubule cells or be reabsorbed and pass into the cells in high concentrations. Nephrotoxicity is defined as the biotransformation of chemicals into reactive, potentially hazardous metabolites. The kidney and liver have similar activation pathways, and toxicants can be released in both. Acetaminophen, bromobenzene, chloroform, and carbon tetrachloride can be toxic to the liver or kidneys. The kidney has a large number of xenobiotic metabolizing enzymes, notably cytochrome P450 in the pars recta of the proximal tubule, which is susceptible to chemical damage. Reactive metabolites, which are unstable and transient, are more likely to interact with cellular macromolecules near their source.

7.4 RENAL STRUCTURE AND FUNCTIONS

The kidneys are essential organs that filter waste materials and excess chemicals from the blood to generate urine, maintain fluid and electrolyte balance, regulate blood pressure, and release hormones that aid in red blood cell development and bone health. Renal structure is extremely specialized to carry out these activities efficiently. All blood components with a molecular mass of less than 50,000 (depending on structure and charge) pass through the kidney's filtering process before entering the tubular system, where important nutrients and the majority of the filtered water are extracted. Only a little amount of the primary filtrate is eliminated in urine (one to two liters per day).The human kidney has around two million nephrons, which are functional units responsible for filtering blood and retrieving important nutrients. Let's look at the anatomy and structure of the kidneys in depth.

A. Anatomy: The kidneys are bean-shaped organs that are situated in the retroperitoneal area, beneath the rib cage, on either side of the spine. The renal capsule, a strong fibrous capsule, encloses each kidney, which is about the size of a fist. Blood arteries, nerves, and the ureter enter and exit the kidney through a region known as the renal hilum, which is formed by the convex outer surface and concave inner surface of the kidney.

B. Renal Cortex: Renal cortex is the outer layer of the kidney. Nephrons, or functional units of the kidney, are millions of microscopic structures that produce urine and filter blood. A nephron is made up of renal tubules and renal corpuscles. The renal corpuscle is made up of the glomerulus, a tuft of capillaries, and Bowman's capsule, which surrounds it.

C. Renal Medulla: Renal pyramids are found in the renal medulla, which is located beneath the renal cortex. The renal tubules, which are parallel bundles of tubules that collect urine, give these pyramids their striped appearance. Every renal pyramid has a base that faces the cortex and an apex called the renal papilla that develops into a structure called the minor calyx that resembles a cup. The renal pelvis is formed when several minor calyces combine to generate big calyces. Urine is stored in the renal pelvis prior to being transferred via the ureter to the bladder.

A. Structure of Nephron: The nephron is the functional unit of the kidney that is responsible for the removal of water-soluble wastes and foreign compounds from the blood. Nephrons, as previously stated, are the kidney's functional units in charge of producing urine. Renal tubules and renal corpuscles make up each nephron. The glomerulus, a tuft of capillaries encircled by Bowman's capsule, makes up the renal corpuscle. An afferent arteriole delivers blood into the glomerulus, while an efferent arteriole transports it out. The high pressure inside the glomerulus allows small molecules such as water, ions, and waste elements to filter out of the blood and into the Bowman's capsule. This fluid is known as the glomerular filtrate.

There are two different types of nephrons: juxtamedullary nephrons make up the remaining 20%, while superficial cortical nephrons make up 70% to 80%. When we examine the components that make up a nephron, we find that the renal tubule and the renal corpuscle are its two main sections.

i. Renal Corpuscle: The renal corpuscle is a vital component of the nephron and is where blood filtration begins. The glomerulus, a network of microscopic blood vessels, and the Bowman's capsule, which encloses the glomerulus, power the nephron's basic tasks. The glomerulus functions as a sieve, blocking the passage of bigger molecules like proteins and blood cells while permitting the passage of smaller molecules like water, electrolytes, and waste materials. The Bowman's capsule is divided into three layers:

- **Outer Parietal layer:**The outer parietal layer is composed of epithelial cells that have minute pores of diameter 12nm.
- **Middle Basement membrane:**There is selective permeability in this layer.
- **Inner Visceral Layer:**The inner visceral layer is made up of big, nucleated cells called podocytes that have projections that resemble fingers and are referred to as podocel.

ii. Renal tubule: The renal tubule, a long, convoluted structure that extends from the Bowman's capsule, is the next major component of the nephron. It is separated into several divisions, each serving a particular purpose. Some of these segments are the collecting duct, proximal convoluted tubule, Henle's loop, and proximal convoluted tubule.

a) Proximal Convoluted Tubule (PCT): After being filtered by the glomerulus, blood from the renal artery is sent to the PCT. The nephron's PCT is where the most reabsorption happens. Renal tubule PCT is where essential molecules including glucose, proteins, amino acids, and a large number of electrolytes and water are reabsorbed. Their fundamental cuboidal epithelial lining broadens the surface area available for reabsorption. Reabsorption happens actively, which

means that energy is utilized in the process.PCT selectively releases ions into the filtrate, such as potassium, ammonia, and hydrogen, after which it absorbs HCO_3^-. PCT preserves the electrolyte and acid-base balance of body fluids.In the proximal tubule, 75% of all solids are reabsorbed. The first segment of the tubule absorbs amino acids, glucose, lactate, and phosphate, while the entire convolution absorbs sodium, potassium, calcium, and chloride, as well as mildly acidifying the fluid by removing bicarbonate.

b) **Henle's Loop:** The second section is known as the loop of Henle or nephritic loop because it forms a loop (with descending and ascending limbs) that passes through the renal medulla. Henle's loop contains both ascending and descending limbs. Because they are both part of the same loop, the permeability of the ascending and descending limbs varies. The ascending limb is permeable to electrolytes but impermeable to water, whereas the descending limb is permeable to water but impervious to electrolytes. The filtrate becomes diluted as it approaches the ascending limb due to electrolyte resorption at the ascending loop of Henle. The descending limb of the Henle loop receives approximately one-third of the volume of glomerular filtrate. This fluid, like plasma, is isosmotic. The bend of the loop and the descending thin limb have very different resorption properties than the ascending thick limb. The thin epithelium that lines the thin limb cannot actively transport chemicals and is permeable to water. Given this, the fluid entering the limb and the loop's bend absorbs the concentration of the interstitial peritubular fluid surrounding it. The thick ascending limb, which is flanked by taller cells, actively transfers sodium and chloride into the peritubularfluid that surrounds both limbs, but has little permeability to urea and water.

c) **Distal Convoluted Tubule (DCT):** The DCT, the final segment of the nephron, joins and empties into the collecting ducts that run the length of the medullary pyramids. As the collecting ducts approach the renal medulla's papillae, they gather material from several nephrons and merge. DCT reabsorbs the HCO_3^- from the filtrate while secreting ions such hydrogen, potassium, and NH_3. This procedure is comparable to that of PCT. In DCT, water and sodium ions are reabsorbed under certain conditions. As a result, the pH of the blood cells and the sodium-potassium balance remain steady. The fluid entering the distal convoluted tubule is less concentrated than plasma because sodium is actively transferred out of the ascending limb. The early portion of the collecting duct is part of the distal tubule's continuous zone of active sodium reabsorption. A large concentration gradient of sodium and chloride exists between the luminal fluid and the plasma, with the concentration of sodium in the tubule remaining significantly lower than that of the plasma due to the nephron's relative impermeable to water. Furthermore, the luminal fluid in this location has a noticeable electronegative effect on the tissues around it.The secretion of potassium and hydrogen ions into the tubule from the blood and tissues appears to be closely related to the sodium reabsorption mechanism.

d) **Collecting** Duct**:** The collecting duct is a long, straight tube that secretes K^+ and H^+ ions to keep the blood's electrolyte balance stable. This is also the area where the most water reabsorption occurs, resulting in concentrated urine.

7.5 RENAL EXCRETION

The only organs primarily intended for excretion are the kidneys. The majority of the waste products of regular metabolism are eliminated due to the activity of this organ. The majority of polar xenobiotics and lipophilic xenobiotic metabolites that are introduced to experimental animals and humans.All components of blood with a molecular mass of less than 50,000 (depending on structure and charge) pass through the kidney's filter and reach the tubular system. From there, the majority of the

filtered water and essential nutrients are restored. Urine makes up one to two liters of the primary filtrate, which is expelled in little amounts each day. The two million or so nephrons that make up the human kidney are the functional units responsible for filtering blood and recovering vital nutrients.

Table: 7.1: The role of the tubules may be assessed by comparing the amounts of various substances in the filtrate and in the urine.

Effect of tubular reabsorption on urine (illustrative 24-hour figures			
	glomerular filtrate	**urine**	**tubular reabsorption (percent**
water	170 L	1.5	99.1
glucose	170 g	-	100
sodium	560 g	5 g	99.1
chloride	620 g	9 g	98.5
phosphate	5.1 g	1.2 g	76.5
calcium	17 g	0.2 g	98.8
urea	51 g	30 g	41.4
Sulfate	3.4 g	2.7 g	20.6

The proximal convoluted tubule (PCT), the distal convoluted tubule (DCT), the loop of Henle (descending and ascending limbs), and the collecting duct are the segments that make up the renal tubule, which receives the glomerular filtrate after that. Though excreting waste and surplus compounds into the urine, each segment of the renal tubule has a distinct function in the process of reabsorbing vital substances from the filtrate, including water, ions, and glucose. Multiple nephrons send urine to the renal pelvis for excretion, where it is transported via the collecting ducts.

Glomerular Filtration: Renal excretion is the result of three interdependent processes: tubular reabsorption, tubular secretion, and glomerular filtration. Plasma passively filters as it travels through glomerular pores (7-10 nm in diameter) created by the heart's hydrostatic pressure. The procedure is known as glomerular filtration. Adults have a glomerular filtration rate of about 200 litres per day, or 125 mL/minute. The filtrate will contain all free solutes in the plasma that pass through the glomerular pores; glomerular filtration is solely selective for molecular size. Only low molecular mass xenobiotics bound to proteins escape the filtrate and remain in the bloodstream. The integrity of the membrane and hydrostatic pressure both has an effect on globular filtration.

Tubular Reabsorption: Since the amount of glomerular filtrate produced each day is four times greater than the amount of water in the entire body and includes numerous essential nutrients including salt, glucose, and amino acids, the majority of the filtrate needs to be recovered. Thus, tubular reabsorption is the second main process that takes place in the kidney. Tubular reabsorption involves a variety of separate mechanisms, both active and passive, with differing levels of specificity. Numerous re-absorptive mechanisms can be found in the cells of the tubules' proximal segments. 65–90% of the glomerular filtrate is reabsorption due to these cells. Active reabsorption occurs for glucose, certain cations, amino acids, organic acids, and low molecular mass proteins. Because of the osmotic and electrochemical gradients produced by the active transport of sodium and potassium, water and chloride

are passively reabsorbed. The majority of the leftover water and ions are reabsorbed in the distal tubules and collecting ducts; the osmolarity of the fluid in the collecting duct is regulated in the loops of Henle. To maintain the blood's osmolar concentration, the rate of reabsorption in these proximal tubule segments is controlled. After glomerular filtration, the majority of xenobiotics are also passively diffused back into the body as they pass through the nephron. Thus, lipophilic xenobiotic' passive tubular reabsorption is higher than that of polar xenobiotics or endogenous wastes.

Tubular Secretion: The kidney can also eliminate foreign substances from the blood by tubular secretion. Xenobiotics are transported by this secretion from the blood-like peritubular fluid to the tubule's lumen, or urine. Active transport pathways are responsible for the secretion of several organic acids, such as glucuronides and sulfates, as well as potent organic bases. Tubular secretion is frequently selective. There is also a passive system that uses the pH variations between urine and peritubular fluid to secrete weak bases and some weak acids. These substances ionize at the pH of the tubular lumen and stop diffusing back through the cell wall.

7.6 SUSCEPTIBILITY OF THE KIDNEY

Multiple parameters influence the kidney's sensitivity to various toxicants. However, it is clear that enhanced renal blood flow and excretory product concentrations following water reabsorption from the tubular fluid are considerable. The kidneys receive around 25% of cardiac output despite accounting for less than 1% of total body mass. As a result, the kidney gets high levels of exogenous chemicals and/or metabolites. The kidneys' capacity to concentrate tubular fluid and, subsequently, concentrate whatever chemicals it contains after water and salts are removed is a second key factor determining the kidneys' sensitivity to chemicals. As a result, a safe amount in plasma may become poisonous in the tubular fluid. The transport properties of the renal tubules contribute to the delivery of potentially dangerous chemical concentrations to cells. Chemicals actively secreted from the blood into the tubular fluid either accumulate in the proximal tubule cells or enter the cells at very high quantities if they are reabsorbed from the fluid. The biotransformation of substances into reactive, possibly harmful metabolites is an important characteristic of nephrotoxicity. several of the same activation events found in the liver are also found in the kidney, and several toxicants, including acetaminophen, bromobenzene, chloroform, and carbon tetrachloride, have the potential for either hepatotoxicity or nephrotoxicity

Some areas of the kidney have high quantities of xenobiotic metabolizing enzymes, particularly cytochrome P450 in the pars recta of the proximal tubule, which is particularly vulnerable to chemical damage. Because reactive metabolites are often unstable and hence more or less ephemeral, they are likely to interact with cellular macromolecules around the site of generation. Because they are closer to the site of action, activation enzymes such as cytochrome P450, which is less active in the kidney than in the liver, have a greater impact on nephrotoxicity. The final appearance of a toxic end point, like toxicity in other organs, results from a balance between reactive metabolite production and detoxification. Clearly, the kidney's high glutathione levels are critical to the detoxication process. Clearly, the kidney's high glutathione levels are critical to the detoxication process. Factors Affecting Kidney Susceptibility to Toxicants

- High renal blood flow
- Concentration of chemicals in tubular fluid
- Reabsorption and/or secretion of chemicals through tubular cells
- Activation of protoxicants to reactive, and potentially toxic, metabolite

7.7 CHEMICALLY INDUCED RENAL INJURY

Chemical-induced renal injury refers to damage to the kidneys caused by exposure to various chemicals, toxins, or drugs. The kidneys play a crucial role in filtering blood, removing waste products, regulating electrolyte balance, and maintaining fluid balance in the body. When exposed to certain chemicals, the kidneys can sustain damage, leading to impaired function and potentially serious health consequences. Some chemicals have inherent toxic properties that can directly damage the cells and tissues of the kidneys. These chemicals may disrupt cellular function, cause inflammation, or induce oxidative stress, leading to injury. Chemicals with direct nephrotoxic effects include heavy metals such as lead, mercury, and cadmium, as well as certain solvents and industrial chemicals. Certain substances are hazardous to the kidneys only after they have been metabolically activated by the liver or other organs. During metabolism, these substances may form reactive intermediates or metabolites that can harm renal cells. Certain medications, such as acetaminophen and non-steroidal anti-inflammatory drugs (NSAIDs), can be metabolically activated and cause kidney impairment in sensitive people. Certain chemicals or metabolites can crystallize and create obstructive deposits in the renal tubules or urinary system, causing blockage and subsequent kidney disease. Cidofovir, an antiviral medicine, can crystallize in the renal tubules, resulting in tubular blockage and acute kidney damage.

The clinical manifestations of chemical-induced renal injury can vary depending on the specific chemical involved, the duration and intensity of exposure, and individual susceptibility factors. Common signs and symptoms may include:

- Decreased urine output
- Fluid retention and swelling (edema)
- Hypertension
- Proteinuria (protein in the urine)
- Hematuria (blood in the urine)
- Elevated serum creatinine and blood urea nitrogen levels
- Acute kidney injury or chronic kidney disease

Diagnosis of chemical-induced renal injury typically involves a combination of medical history, physical examination, laboratory tests (including urine analysis, blood tests, and imaging studies), and sometimes kidney biopsy to evaluate the extent of tissue damage.

The kidneys are especially vulnerable to toxic injury because they remove water from the filtrate and allow high amounts of harmful substances to accumulate. Renal damage occurs when endogenous or exogenous toxicants impair renal function by preventing adequate kidney-specific excretion and detoxification. The kidneys, one of the body's primary regulatory mechanisms for maintaining homeostasis, are commonly poisoned by drug exposure. A variety of mechanisms, including changes in tubular cell toxicity, inflammation, rhabdomyolysis, crystal nephropathy, and thrombotic microangiopathy, might contribute to drug-induced nephrotoxicity. Despite being less than 1% of total body mass, they get 20-25% of cardiac output.

Immunologically induced glomerular disease: Immune-induced glomerular disease immunologically mediated glomerulonephritis can be caused by the deposition of free circulating antibodies that interact with a structural glomerular antigen or a "planted" non-glomerular antigen. On the other hand, circulating immune complex deposition may cause glomerular injury. Membranous glomerulonephritis (also known as immune complex-type mediated glomerulonephritis) and anti-GBM-mediated disease are the two main kinds of antibody-mediated glomerulonephritis.The longitudinal IgG deposits found

along the glomerular basement membrane are diagnostic of the former illness. Many medications, dangerous chemicals, and potential environmental variables have been connected to this kind of glomerulonephritis. Medicines and dangerous chemicals such as gold and mercury, d-penicillamine, nonsteroidal anti-inflammatory medicines, and heroin can all induce glomerulonephritis in humans. Other drugs and chemicals include hydrocarbon exposure, interferon, silica exposure, and toxic-oil syndrome, for which a link is suspected but not confirmed. When combined with a lupus-like disease, other drugs can cause immunological complicated glomerulonephritis.

Direct glomerular toxicity: A drug's or chemicals direct toxicity may result in glomerular lesions. Aside from immunologically induced harm, direct toxicity to glomerular apparatus components is relatively unusual. Nevertheless, it has been reported after exposure to puromycin or tosubstances that could end up in the basement membrane. Particulate matter, including silica and gold, can accumulate in mesangial cells. It's unknown if the substance inside meningeal cells gets phagocytized, however glomerular cell growth and an inflammatory cell response could be the response to such deposits. Mesangium injury may affect glomerular permeability. Water and solutes go through the glomerular capillary walls via an extracellular channel composed of pores, the glomerular basement membrane, and endothelial fenestrae, in that sequence.

Tubulointerstitral disease: Tubulointerstitial illness can be caused by hypersensitivity to specific medications or chemicals, as well as direct toxicity to tubular epithelial cells. The majority of tubular injuries also include the interstitial, hence these types of renal injury are treated together. However, based on their pathological aspects, they can be classified into three types of illnesses.

Acute interstitial nephritis (AIN): Acute interstitial nephritis (AIN) is caused by an immunoallergic or cell-mediated immunological response to a variety of medicines, particularly penicillin and its derivatives (including methicillin). However, thiazdes, nonsteroidal anti-inflammatory medications, gold salts, and occupational mercury exposure have all been related to AIN. Both humoral and cellular immunity are activated. Anti-tubular basement membrane antibodies are most likely involved in some cases of methicillin- or diphenylhydantoin-induced immunological nephritis. The majority of instances of acute interstitial nephritis show no immune reactants. AIN is often milder in adults, with a high prevalence of renal failure; nevertheless, AIN is more severe in people under the age of 15. It has also been observed that the risk of AIN remains unchanged in the absence of a previous allergic reaction to a medicine (penicillin, for example). The kidneys enlarge as a result of oedema fluid and cellular infiltration, which is primarily composed of lymphocytes and plasma cells, as well as eosinophilic and polymorphonuclear neutrophils.

Acute tubular toxicity: Drug and chemical-induced acute tubular effects are caused by direct cellular toxicity. These could range from tubular cell necrosis, which results in acute renal failure, to small subcellular damage and functional effects. Antibiotics, particularly amino glycosides, contrast agents, nonsteroidal anti-inflammatory drugs, and chemotherapeutic treatments such as cis-platinum and cyclosporine A are the most common causes of acute tubular toxicity. Increased excretion of substances normally reabsorbed by these cells, such as glucose, amino acids, phosphate, and sodium, indicates injury to the proximal tubular lining cells. When the lesion spreads to the distal parts of the tubule, the ability to maintain the balance of water and electrolytes in the urine and acidify it is compromised.

Chronic interstitial nephritis (CIN): Chronic interstitial nephritis (CIN) has fewer differentiating morphological markers than other types of acute renal illness. It is characterized morphologically by mononuclear cell infiltration, significant interstitial fibrosis, and tubular atrophy. Analgesic nephropathy is the well-documented cause of CIN, and it is frequently associated with acute papillary necrosis. Acute interstitial nephritis or severe acute tubular sickness can also produce CIN, as can persistent low-dose exposure to certain nephrotoxins, such as lead or cadmium nephropathy. The term "tubulointerstitial

disease" is selected since it better appropriately reflects the pathogenic process's primary regions. As the number of functional nephrons decreases due to increasing interstitial tissue fibrosis, azotaemia develops and the glomerular filtration rate falls. Before renal failure, there may be few symptoms.

7.8 SUMMARY

Renal toxicity is a hazardous condition in which several substances injure the kidneys. Renal toxicity can be induced by medications, chemicals, environmental pollutants, or certain medical procedures. This can lead to impaired kidney function and potentially serious health problems. Early detection and treatment of renal toxicity are critical for maintaining overall renal function and wellbeing and preventing renal toxicity from progressing to more significant kidney injury. The kidneys are vital organs that offer a range of functions necessary for maintaining homeostasis and overall health. Maintaining renal health is critical because kidney malfunction can cause a variety of health problems, including fluid and electrolyte imbalances, hypertension, acid-base disorders, anaemia, and inadequate waste removal.

The renal cortex contains nephrons, the kidney's functional components, whereas the renal medulla contains renal pyramids, which are made up of tubules used to collect urine. Understanding renal health and disease causes, as well as organ function, requires an understanding of the kidneys' complex anatomy and structure. Chemical-induced kidney injury can result from exposure to a wide range of hazardous drugs, pharmaceuticals, and industrial chemicals. To limit the risk of kidney damage and maintain renal function, it is critical to understand the processes of toxicity and implement preventive treatments. Early detection and appropriate intervention are critical for treating chemically induced kidney impairment and avoiding long-term effects.

7.9 TERMINAL QUESTIONS

Q. 1. What are the symptoms of a toxic kidney?

Answer:----------

Q. 2. What chemicals cause nephrotoxicity?

Answer:----------

Q. 3. What are the indicators of nephrotoxicity?

Answer:----------

Q. 4. What are nephrotoxic substances?

Answer:----------

Q. 5. Write about renal system structure and functions.

Answer:----------

Q. 6. Define the susceptibility of kidney to toxic insult.

Answer:----------

Q. 7. Briefly explain chemically induced renal injury in humans.

Answer:----------

7.10 FURTHER SUGGESTED READINGS

1. Principles of toxicology: environmental and industrial applications / edited by Phillip L. Williams, Robert C. James, Stephen M. Roberts.—2nd ed., Awiley-Interscience Publication, Johnwiley& Sons, Inc.

2. Environmental Toxicology, third edition, Sigmund F. Zakrzewski, Published by Oxford University Press, Inc. New York, New York 10016.

3. Environmental Toxicants, Human Exposures and Their Health Effects, Third Edition, Morton Lippmann, Published By John Wiley & Sons, Inc., Hoboken, New Jersey.

4. Toxicology in Occupational and Environmental Setting, Wolfgang Dekant, Institute of Toxicology, University of Wurzburg, Germany.

5. A Textbook of Modern Toxicology, Ernest Hodgson, Published By John Wiley & Sons, Inc., Hoboken, New Jersey.

6. A Textbook of Modern Toxicology: Ernest Hodgson, A John Wiley & Sons, Inc., Publication

UNIT-8 : CUTANEOUS TOXICOLOGY

Structure

8.1 INTRODUCTION

Cutaneous toxicology studies the impact of dangerous substances on the skin, which includes a wide range of chemicals, drugs, pollutants, and environmental factors. It investigates how these substances interact with the skin, causing undesirable effects ranging from minor discomfort to serious dermatological diseases. This discipline investigates harmful pathways such as direct skin contact,

bloodstream absorption, and immune-mediated reactions. Furthermore, cutaneous toxicity contributes to the development of dermatological treatments, including therapy for skin diseases induced by hazardous exposures. Understanding the mechanisms underlying skin toxicity enables the creation of targeted medicines that alleviate symptoms and enhance skin health. Overall, cutaneous toxicology is crucial for protecting human health and promoting the safe use of chemicals in everyday products and environments. Dermatological toxicology research is essential for determining the safety of consumer goods such as cosmetics, personal care products, and household chemicals. It also influences regulatory decisions about occupational exposure and environmental contaminants. Researchers want to discover possible risks, determine safe exposure limits, and create risk-mitigation measures by studying the effects of numerous substances on the skin. The skin is the body's primary line of defence against external toxins. Normal skin is an efficient barrier to many substances, but its enormous surface area (1.5-2.0 m2) may allow toxins to enter, resulting in both local and systemic consequences. The skin has two layers: the outer epidermis and the inner dermis. The two layers form a barrier with a thickness of 0.5-4 mm or more in various parts of the body. The epidermis and dermis are separated by a foundation membrane that seems to undulate. The uneven interface results in skin ridges that are unique to each person and serve as the foundation for fingerprint identification. The epidermis has hair follicles, sebaceous glands, and sweat glands that are implanted in the dermis. Adipocytes make up the majority of the third subcutaneous layer, which lies beneath the dermis. The epidermis is composed of numerous layers of cells, some living and some dead. Keratinocytes move from the epidermis's lower layers to accumulate keratin, and they comprise the majority of the epidermis. Chemicals travel through the skin by passive diffusion, with minimal evidence of active transport. The outer stratum corneum is the primary layer that regulates the rate of diffusion, which is exceedingly slow for most substances. This layer also minimizes water loss from the body by diffusion and evaporation, except, of course, when the sweat glands help regulate body temperature. Toxicants can easily penetrate the epidermis and dermis because hydrophilic agents disperse into intercellular fluids whereas hydrophobic chemicals embed in cell membranes, eventually reaching the dermis' blood supply. Human skin can come into contact with potentially dangerous chemicals. Skin is relatively resistant to aqueous solutions, and most xenobiotic exist as ions. As a result, it serves as a somewhat effective barrier between the human body and the environment. Skin is permeable to many xenobiotic, and some compounds can be absorbed at high enough concentrations to cause toxicity. Many agricultural workers have been poisoned by parathion (dermal LD50 $\approx$ 20 mg/kg) during application or from previously treated plants, emphasizing the significance of skin absorption.

Objectives

After reading this unit, the learner will able to know

- The dermatology and dermatological system
- the effects of toxic agents in dermatological system
- The allergic contact dermatitis and its mechanism
- The cutaneous carcinogenesis and its mechanism

8.2 DERMATOLOGICAL EFFECTS OF TOXIC AGENTS

The skin, the body's biggest organ, is constantly exposed to external stimuli such as chemicals and natural factors. Contact dermatitis, photosensitivity, contact urticaria, chemical-induced acne, pigmentary disturbance, medication rash, and hair disturbance are the several types of cutaneous toxicity.

Skin reactions ranging from mild irritation to severe dermatitis, as well as systemic poisoning in specific situations, are among the harmful consequences of hazardous substances on humans. The skin can experience unwanted reactions from a variety of substances, drugs, pollutants, and environmental factors that can impact the skin's overall health and structure. Skin irritation or allergy contact resulting in contact dermatitis is a common dermatological reaction brought on by harmful substances. Itchy, red, and often blistering skin at the site of exposure are the hallmarks of irritant contact dermatitis. Examples of irritants include acids, alkalis, solvents, and detergents. However, an immune-mediated response to particular allergens, such metals, fragrances, preservatives, or plant extracts, results in allergic contact dermatitis. This type of dermatitis frequently presents as a delayed hypersensitivity reaction with pruritus, vesicles, and erythema as symptoms. Phototoxic reactions happen when a medication that sensitizes to UV light interacts with it directly. This can lead to erythema, edema, and sometimes blistering, especially in areas that are exposed to the sun. When subjected to a photosensitizing drug again, photoallergic reactions are an immune-mediated reaction that results in a delayed hypersensitivity reaction. Moreover, dermatological symptoms may accompany a more serious clinical condition caused by systemic poisoning from dangerous drugs. Drug eruptions, for instance, are cutaneous adverse reactions that vary in severity from mild rashes to severe blistering and exfoliative dermatitis, and can be brought on by specific drugs or substances. Immune-mediated reactions, metabolic alterations, or direct skin toxicity can all result in these reactions.

8.3 CUTANEOUS TOXICITY AND ITS TYPES

Cutaneous toxicology studies the effects of hazardous substances on the skin, including chemicals, medications, pollutants, and environmental factors. It looks into how these compounds interact with the skin, causing unpleasant reactions ranging from slight irritation to serious dermatological illnesses. The discipline looks on toxicity mechanisms consist of skin contact, bloodstream absorption, and immune-mediated reactions. Dermatological toxicology research is essential for establishing the safety of consumer goods such as cosmetics, personal care products, and household chemicals. It also influences regulatory decisions about occupational exposures and environmental toxins. Through researching the effects of various substances on the skin, researchers hope to identify possible risks, establish safe exposure limits, and create measures. Cutaneous toxicity can be divided according to its mode of onset into the following:

- contact dermatitis
- photosensitivity
- contact urticaria
- chemical-induced acne
- pigmentary disturbance
- drug rash
- hair disturbance
- nail disturbance
- tumor-induced

Cutaneous toxicity can also be characterized based on the route of exposure, such as systemic effects or local skin irritation (local toxicity

8.3.1 Contact Dermatitis

The contact dermatitis is skin inflammation caused by direct touch with a medication and can be categorized into three kinds based on the mechanism of onset.

8.3.1.1 Irritant Dermatitis

Skin irritation caused by direct contact with a chemical, without the involvement of an immunological system. Irritan's dermatitis is an inflammatory condition caused by direct skin irritation that can be temporary or chronic. The activation of mast cells, complement, or prostaglandin synthesis results in reversible skin damage, which manifests as irritation within 4 hours of topical application. Irritant dermatitis is distinguished by inflammatory cell infiltration, acanthosis, epidermal hyperkeratosis, and hyperplasia, as well as other epidermal changes such erosion, ulceration, necrosis, or vesicle formation. Irritant dermatitis is determined by the degree of the irritants and their duration of exposure.

Table.8.1: The following plants and pesticides may cause primary irritant dermatitis.

Pesticides				
Sulfur	Omite	Methomyl	Maneb	Weed Oil
Captafol	Folpet	Kelthane	DinitroBenomyl	Dacthal
Endosulfan	Lindane	Zineb	Captan	Chlorothalonil
Toxaphene	Ziram	Dinoseb	TOK	Organophosphates
Chloropicin	Thiram	Triazine	Glyphosate	
Plants Flowers Trees				
Tomatoes	Dieffenbachia	Carrot	Castor Bean	Fig tree Sap
Mushroom	Rubber Tree	Daffodil	Cucumber	Buttercup
Parsnip	Foxglove	Turnip	Tulip bulb	Narcissus bulb
Parsley	Cowslip	Celery	Milkweed	

8.3.1.2 Allergic Dermatitis

Allergic contact dermatitis is caused by a delayed (type IV) allergic reaction. A low molecular weight medicine binds as a hapten to a protein in the body, acting as a complete antigen. Inflammation often develops approximately 12 hours after a sensitized animal comes into contact with the medicine again. Known sensitizers include preservatives in topical application agents, nickel sulfate, potassium dichromate, neomycin, aroma chemicals, formaldehyde, rubber/latex medical equipment, and plants. On the first encounter with the allergenic chemical, there is little or no reaction. Following the initial encounter, the individual becomes sensitive to the chemical, and subsequent exposures cause the normal delayed type IV hypersensitivity reaction. The allergenic substances (haptens) are frequently low in molecular weight.

Chemicals that is hydrophilic or electrophilic. These agents are rarely allergenic alone and require a carrier protein to generate a full allergy. Allergens are formed when certain chemicals are activated by the skin's metabolic activity during phase I and II. Sensitization occurs when an antigen-presenting cell, such as macrophages or Langerhans cells, engulfs the hapten/carrier protein and presents the processed antigen to a helper T cell (CD_4^+). The T cell produces cytokines, which activate and promote the growth of more T cells that identify the antigen. Cytokines trigger inflammation in the

contact area and activate monocytes into macrophages. Active macrophages are the major effector cells in the response. They eliminate foreign antigens and cause inflammation at the contact site by secreting more chemical mediators. Keratinocytes are also involved in the hypersensitivity reaction. They can generate a variety of cytokines and, in some situations; act as antigen-presenting cells. Following sensitization, subsequent exposure to the allergenic chemical triggers the same sequence of events as described above. Prior sensitization reactions generate a reservoir of antigen-specific T cells, which accelerates the chain of events. Individual sensitivity to allergens, like irritating contact dermatitis, varies greatly and is determined by a variety of factors.

Table. 8.2 : These plants and pesticides may cause allergic contact dermatitis (ACD).

Pesticides							
Captan	Captafol	Benomyl	Dichlorovos	PCNB	Zineb	Maneb	Formaldehyde
Naled	Thiram	Triazine	Parathion	Malathion	TOK	Cresol	Some natural pyrethroides
Plants Flowers Trees							
Poison Ivy	Primrose	Cedar	Poison Sumac	Cashew	Chrysanthemum	Onions	Garlic
Poison Oak	English Ivy	Pine	Tulip bulbs	Liverwort	Narcissus Bulbs	Lichens	Celery

The individual's genetic makeup is likely the most crucial determinant in determining whether a response occurs. Individuals' susceptibility to IgE-mediated allergens, including hay fever, may differ, with some responding and others not. Patch testing is done to discover which agents a person with suspected allergic contact dermatitis is sensitive to. When a contact allergen is eaten or enters the bloodstream, it creates a unique condition. The most serious adverse effects are generalized skin eruption, headache, malaise, and arthralgia. Flare-ups of previous contact dermatitis, vesicular hand eruptions, and eczema in other areas of the body may be less severe.

Systemic exposure can trigger a delayed type IV hypersensitivity reaction, leading in the deposition of immunoglobulins and complement in the skin. These proteins are potent triggers of secondary inflammation.

8.3.1.3 Chemical Burns

Chemical burns are injuries caused by a highly caustic or irritating chemical agent (such as a strong acid or alkali), which are typically accompanied with itching and/or ulceration due to local coagulative necrosis. This type of harm is not caused by any of the currently known medications. Accidental skin exposure or oral consumption of these chemicals is a paediatric emergency, and they have previously been employed as suicide agents. Cement burn is widely known throughout the developed world. The majority of patients are construction workers, who often kneel or stand on cement. The injury is caused by a combination of cement alkalinity and mechanical abrasion.

8.4 PHOTOSENSITIVE DERMATITIS

8.4.1 Photosensitivity

Photosensitive dermatitis (photosensitivity) is a general term for skin irritation produced by the

combination of medicine and light. It is divided into two types: those with an immunological mechanism and those without. Numerous systemic and topical drugs, fragrance chemicals, plants, and cosmetics have been associated to this condition. Photosensitive drugs include phenothiazine, tetracyclines, sulfonamides, chlorpromazine, nalidixic acid, and fluorocoumarins.

Table 8. 3: Plants and situations that can cause photosensitization when consumed.

Plants					
Tetradymiasp (Horsebrushes)	Lecheguilla	Lantana	Kochia	Tribulusterrestris (Goatshead)	Hypericium sp. (St Johnswort)
Conditions / Other drugs					
Phenothiazines	Sulfonamides	Tetracyclines	Copper Toxicosis in Sheep	Blue-green algae poisoning	Any condition that seriously damages the liver (pyrrolizidine alkaloid poisoning).

Excessive sunlight induces erythema (redness or sunburn) due to vasodilation in the affected areas. Inflammatory mediators may be generated in these locations, and they have been linked to systemic symptoms of sunburn such as fever, chills, and malaise. UVB is the most significant radiation band that causes erythema. Sunlight contains up to 100 times more UVA (320-400 nm), yet UVA is 1000 times less powerful than UVB in inducing erythema. UVB exposure darkens the skin via increasing melanin synthesis or by oxidizing melanin. Melanin oxidation happens immediately, but it provides no further UV protection. Within 3 days of exposure, melanin production increases significantly. UV exposure thickens the skin, especially in the stratum corneum, reducing UV absorption. UV light exposure over time can cause skin changes, including freckling, wrinkling, and precancerous and malignant tumors. UV light isn't the only form of radiation that can cause skin abnormalities. Ionizing radiation can induce acute symptoms such redness, blistering, swelling, ulceration, and discomfort, depending on the dosage. Chronic exposure can lead to epidermal thickness, freckling, ulcers that don't heal, and cancer.

Table 8.4. Plants which cause contact photo-sensitization.

Figs	Parsley	Carrots
Dill	Lime	Buttercup
Mustard	Klamath weed	Celery (with pink rot)

8.4.2 Phototoxic Dermatitis

Phototoxic dermatitis is a skin irritation caused by a light-sensitive pharmaceutical (ultraviolet light), rather than the drug itself, due to photon energy absorption in the absence of an immune system. According to accounts, this response includes free radicals and per-oxidative damage. To investigate pharmaceutical photo-toxicity, preclinical investigations of topical application medicines use guinea pigs. Phototoxic chemicals absorb UV light and achieve a greater energy level. When an excited chemical returns to its ground state, it loses energy, causing the formation of reactive oxygen species

and other products that damage cellular components and macromolecules, eventually leading to cell death. The resulting damage is akin to that caused by irritant chemicals, which kill cells. Phototoxicant-induced cell death induces inflammation, which manifests clinically as phototoxicity. Phototoxic drugs and chemicals include dyes (eosin, acridine orange), polycyclic aromatic hydrocarbons (anthracene, fluoranthene), tetracyclines, sulfonamides, and furocoumarins (trimethoxypsoralen, 8-methoxypsoralen).

8.4.3 Photoallergic Contact Dermatitis

Photoallergic contact dermatitis is caused by a delayed (type IV) allergic reaction. A light-sensitive medicine (ultraviolet light) captures photon energy and turns it into a chemical (hapten) that binds to a protein in the body to form a complete antigen. Inflammation is often induced about 12 hours after a sensitized animal comes into touch with the medicine again. Photoallergy, like contact allergic dermatitis, is a delayed type IV hypersensitivity reaction. Photoallergenic compounds, unlike allergenic chemicals, require light, usually UVA, to activate. When activated, photoallergens mix with cellular proteins to create a complete allergen, resulting in a delayed type IV hypersensitivity reaction. This hypersensitive reaction requires prior exposure to the phototoxic chemical to elicit a response. Subsequent exposure to a photoallergen might result in a hypersensitive reaction, similar to allergic contact dermatitis. Photoallergy testing is comparable to patch testing for traditional allergies, except it includes possible all

8.4.4 Contact Urticaria

Contact urticaria is an acute redness or rash that appears between a few minutes to one hour of being exposed to a medication. It can be induced by the drug's direct effect on vascular walls, an indirect influence on vascular walls via histamine release from mast cells (without the involvement of an immunological mechanism), or an IgE-mediated acute (type I) allergic reaction that involves an immune mechanism. Systemic reactions to penicillin or food, as well as urticaria caused by natural rubber products (latex allergy), are established causes of immunological contact urticaria; however, reproducing such conditions in preclinical research using experimental animals is difficult. Most chemicals that cause urticaria must enter the systemic circulation. Urticaria can be triggered by specific allergies or idiopathic causes. Some putative no immune inducers of urticaria (direct Curare, aspirin, azo dyes, and plant and animal poisons all operate as mast cell activators. Some substances may elicit contact urticaria exclusively on the epidermis. This type of urticaria may be caused by cobalt chloride, benzoic acid, butylhydroxyanisol (BHA), or methanol. Latex rubber goods, including gloves, are a leading cause of contact urticaria in the medical community. Natural latex rubber contains a protein that can cause an instant type I hypersensitivity reaction. Contact with latex rubber items, such as gloves, can produce hypersensitivity reactions, including hives, asthma, anaphylaxis, and even death.

8.4.5 Chemical Induced Acne

Chemical-induced acne is a hair follicle condition caused by a chemical substance that is characterized by keratin plugs in hair follicles due to increased keratinocyte proliferation in hair follicles (comedo), sebum retention, and inflammation. Chemical-induced acne is known to include occupational skin problems such as oil acne, which is produced by repeated skin exposure to cutting oils, and chloracne, which is caused by dioxins such as TCDD and PCB. Clinically, the lesions are localized around the eyes, ears, back, and genitalia. Other symptoms include hyperpigmentation, conjunctivitis, and ocular discharge.

8.4.6 Pigmentary Disturbance

Pigmentary disturbance is only visible in animals with short hair or who have been shaved, making it difficult to detect in preclinical testing. Altered pigmentation is a histopathological illness that

can develop during skin inflammation and is characterized by an increase or decrease in the number of melanocytes and melanin generation. Hyperpigmentation can occur in conjunction with increased melanin production due to medication-induced melanocyte stimulation, hemosiderin deposition caused by bleeding, or the deposition of a heavy metal or substance. Busulfan, cyclophosphamide, long-term high-dose ACTH, and inorganic arsenic all enhance melanin production.

8.4.7 Drug Rash (Cutaneous Response)

The most common antibiotic-related adverse drug reaction is a rash (cutaneous response). The most serious types of drug rash are toxic epidermal necrolysis (TEN) and Stevens-Johnson syndrome, which have been linked to the use of a variety of medications, including penicillin derivative or cephem derivative antibiotics, antipyretic analgesics (especially NSAIDs), allopurinol, amine antiepileptic drugs (phenytoin and carbamazepine), and sulfa drugs. Many novel anticancer drugs with specific molecular targets have been approved in recent years (known as "targeted therapies"), and their skin side effects are highly specific.

8.4.8 Hair Disturbance

Many medications induce hair irregularities, including hair loss, increased hair growth, and, more infrequently, changes in hair structure and color. Hair loss (hypotrichosis or alopecia) is a common problem, affecting around 60 million men, women, and children. The onset of alopecia (toxic alopecia) is typically defined by the hair cycle during medication administration. Androgenic medicines can cause alopecia by shortening the hair cycle during the resting phase. Antimitotic medications (e.g., anticancer treatments) and irradiation can cause alopecia by triggering death of hair follicles during the anagenphase, resulting in hair follicle shrinkage and prolonging of the resting phase of the hair cycle (chemotherapy or radiation-induced follicular dystrophy).

8.4.9 Nail Disturbance

Nail alterations that reflect a previous general state are a health indication that can be used to predict the presence or absence of an abnormality several weeks before it occurs. The use of metoprolol, retinoids, anticancer drugs, or irradiation has been linked to transverse ridges (Beau's line), washboard nail plates, and onycholysis. Adverse effects of targeted molecular medications, like as EGFR inhibitors, are also quite specific to nails in human patients.

Table: 8.5

Classification	**Type**	**Definition and characteristics**
A. Classification based on drug exposure route.	Cutaneous toxicity from systemic effects. Skin irritation (local toxicity)	
B. Classification by method of onset		
1. Contact dermatitis	Irritant dermatitis	Skin inflammation caused by direct contact of the skin with a medication, without the involvement of an immune system.
	Allergic dermatitis	Skin inflammation upon re-exposure

		to a substance that was previously delivered and bound as a hapten to a protein in the skin to become immunogenic (type IV allergic reaction).
2. Photosensitivity	Phototoxic dermatitis	A situation caused by a medication with covalent binding as a result of a photochemical reaction with UV light.
	Photoallergic dermatitis	Skin inflammation following re-exposure to a previously administered medicine that absorbed ultraviolet light and was changed to behave as a hapten to interact with a protein in the skin to become immunogenic (type IV allergic reaction).
3. Contact urticaria		Acute erythema with histamine release from mast cells (increased vascular permeability), occurs shortly after contact with the medication
4. Chemical acne		Inflammation of hair follicles caused by increased keratin and sebum.
5. Pigmentary disturbance	Hyperpigmentation	A condition that is associated with enhanced melanin production due to melanocyte activation, hemosiderin deposition due to bleeding, or medication deposition.
	Hypopigmentation	A disease characterized by the loss of melanin or selective injury to melanocytes
6. Drug rash (cutaneous reaction)	Toxic epidermal necrolysis, oculomucocutaneous syndrome.	The cause is unknown, however an allergic reaction has been hypothesized. Reported for more than 1100 medications, including sulfa medicines.
7. Hair disturbance	Alopecia	A condition caused by medications with an androgenic action working on hair follicles to shorten the hair cycle, or pharmaceuticals with an antimitotic effect producing follicle atrophy and prolonging the resting period of the hair cycle.
	Hypertrichosis	A disorder caused by prolonging the anagen phase of hair follicles induced

		by some immunosuppressants, antihypertensives (minoxidil), or medications for benign prostatic hyperplasia (finasteride).
8. Nail disturbance	Nail transverse ridges, onycholysis, discoloration	A condition resulting from damage to the nail matrix cells due to medications with an antimitotic effect or the deposition of the drugs themselves.

(Sources: Drug-Induced Cutaneous Toxicity, Katsuhiko Yoshizawa, Michiko Yuki And AiroTsubura, Open Access Peer-Reviewed Chapter, Doi: 10.5772/64473)

8.5 CUTANEOUS CARCINOGENESIS

Skin carcinogenesis can be operationally and mechanistically classified into at least three major stages: start, promotion, and progression. Chemicals cause cutaneous cancer in a wide range of experimental animals and people. Skin carcinogenesis starts with initiation, which is a reversible process involving genetic changes, gene activation, or inactivation. Mutations in the v-Haras oncogene or inactivation of the p53 tumor suppressor gene can both be considered initiation. The following phase of carcinogenesis is tumor promotion, which is characterized by a reversible phase of clonal expansion of initiated cells containing mutations/inactivated genes, with a dysregulation of apoptosis of the initiated cells, as well as accumulation of epigenetic changes such as DNA methylation, inflammation characterized by infiltration of activated leukocytes, production of growth factors, cytokines and reactive intermediates.

Carcinogenesis is the process through which cancer develops. Chemical carcinogenesis is the study of how chemicals cause cancer and the application of experimental systems to identify potential human carcinogens. Detecting probable human carcinogens is an important aspect of toxicology. Cancer is a collection of disorders defined by uncontrolled cell development, resulting in a population of cells that can infect surrounding tissues. This invasive trait is what causes the host to die. According to epidemiology research, the prevalence of most malignancies rises exponentially as people age. Cancer is defined as the uncontrolled reproduction and expansion of the body's own cells (somatic cells). Carcinogenic agents can be categorized as follows:

- Chemical agents, such as nitrosamines and polycyclic aromatic hydrocarbons
- Biological agents, such as hepadna viruses or retroviruses
- Ionizing radiation, such as x-rays
- Genetic factors, such as selective breeding

Chemical carcinogenesis has a long history. In 1775, Sir PercivallPott, surgeon general under King George III of England, identified a significant incidence of scrotal cancer among London chimney sweeps, which he attributed to their exposure to soot and tar from bituminous coal combustion. Recent research has enhanced our understanding of the molecular pathways that drive chemical carcinogenesis. Cancer induction can be a complex process with numerous steps. Carcinogenesis consists of two stages: initiation and promotion.

Carcinogenesis can be initiated by the reaction of a DNA-reactive species with DNA or by the

activity of an epigenetic carcinogen that does not react with DNA but causes cancer through another mechanism. The majority of DNA-reactive species are genotoxicity carcinogens and mutagens. These chemicals react permanently with DNA. They are either electrophilic or, more commonly, metabolically activated to produce electrophilic species, such as the electrophilic $+CH_3$ produced by dimethylnitrosamine, as described in the mutagenesis section above. Precarcinogens and procarcinogens are substances that cause cancer and require metabolic activation. The metabolic species that causes cancer is referred to as an ultimate carcinogen.

Proximate carcinogens are organisms that serve as intermediate metabolites between precarcinogens and ultimate carcinogens. **Figure 7.3** illustrates these classifications, with benzo(a)pyrene as the procarcinogen, benzo(a)pyrene 7,8-epoxide as the proximate carcinogen, and benzo(a)pyrene 7,8-diol-9,10-epoxide as the ultimate carcinogen.

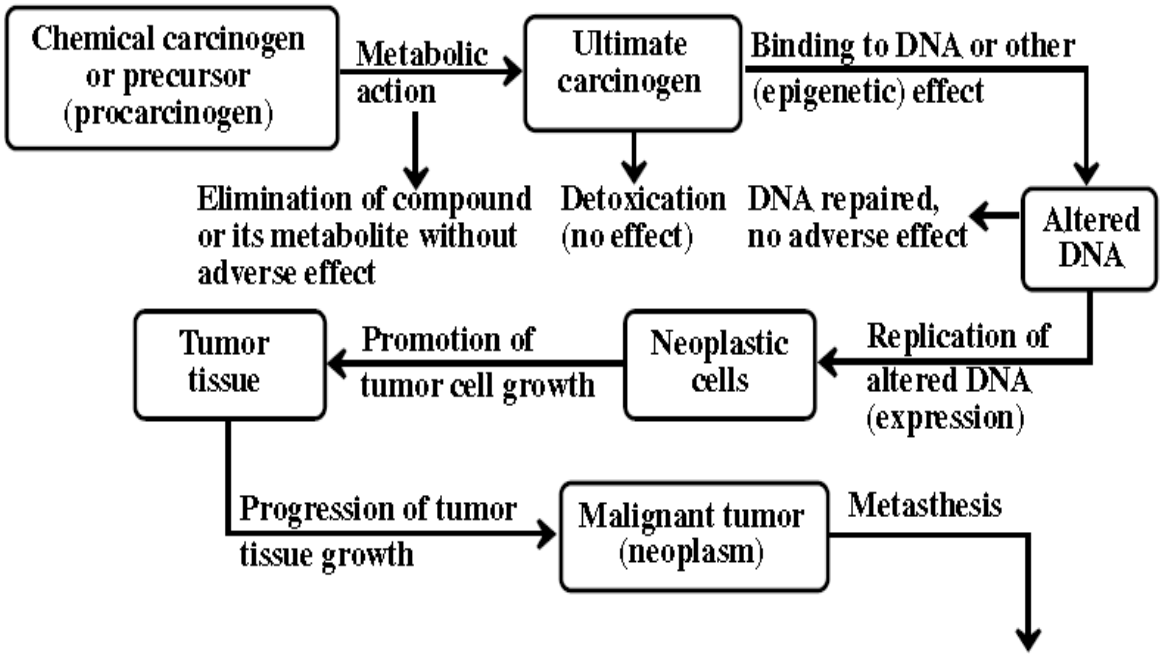


Fig. 8.1: Outline of the carcinogenic process

The majority of chemicals identified as epigenetic carcinogens are post-initiation promoters. Promotion manifests as an increase in the number of tumour cells and a shorter latency period for tumour development. Promoters do not cause cancer, are not electrophilic, and do not attach to DNA. A classic example of a promoter is decanoylphorbol acetate, also known as phorbolmyristate acetate, which is derived from croton oil.

Initiation-Promotion Model: Experiments have revealed that the initiation-promotion process takes place in a variety of organs and tissues, including the skin, liver, lung, colon, mammary gland, prostate, and bladder, as well as cultured cells. Tumour promoters share fundamental functioning principles, despite their distinct methodologies and organ specificity. These features include the following:

a) following a sub threshold dose of initiating carcinogen, chronic treatment with a tumor promoter will produce many tumors;

b) initiation at a sub threshold dose alone will produce very few if any tumors;

c) chronic treatment with a tumor promoter in the absence of initiation will produce very few if any tumors;

d) the order of treatment is critical; that is, you must first initiate and then promote;

e) initiation produces an irreversible change; and

f) promotion is reversible in the early stages;

For example, if an equal number of stimulating doses are given but they are spaced out over time, tumors will not develop or will be considerably reduced in quantity. Many tumorpromoters are organ specific. For example, 12 - O - tetradecanoylphorbol - 13 - acetate (TPA), also known as phorbol 12 - myristate 13 - acetate (PMA), is a member of the phorbol ester family of chemicals. Phorbol esters are generated from croton oil (seeds of the croton plant) and are nearly entirely active in the skin. Phenobarbital, DDT, chlordane, TCDD, and peroxisome proliferators Wy 24,643, clofibrate, and nafenopin all induce liver tumors. TCDD also acts as a promoter in the lung and skin. Some bile acids cause colonic tumors, whereas estrogens stimulate tumors in the mammary gland and liver. Tumor promotion has various pathways, which may explain why the many promoters are organ-specific. It is widely known that many tumor promoters allow for the clonal expansion of started cells by interfering with signal transduction pathways and/or modifying gene expression that regulates cell proliferation, differentiation, and/or apoptosis. While the precise processes of many tumor promoters are not fully understood at the molecular/biochemical level, recent research is revealing new and intriguing mechanistic insights into how tumor promoters enable the selective development of started cells.

Alkylating Agents in Carcinogenesis: Chemical carcinogens typically have the potential to create covalent connections with macromolecular living molecules. Covalent bonding can develop between proteins, peptides, RNA, and DNA. Although the majority of binding occurs with more numerous chemicals, DNA adducts play a key role in cancer development. Alkylating agents, which attach alkyl groups such as methyl (CH_3) or ethyl (C_2H_5) to DNA, are among the most common species that link to DNA during carcinogenesis. A similar type of molecule, arylating agents, attaches aryl moieties, such as the phenyl group to DNA.

Testing for Carcinogens: Some substances are recognized to be carcinogenic based on epidemiological studies of exposed persons. Carcinogenicity tests are conducted on animals, and the results can be extrapolated to humans with some uncertainty. The Bruce Ames technique is the most widely applied test for suspected carcinogens, as it displays mutagenicity. This approach works by reverting mutant histidine-requiring Salmonella bacteria to a type capable of synthesizing their own histamine.

8.6 SUMMARY

Cutaneous toxicology is the study of hazardous chemicals and how they affect the skin. Chemicals, pollutants, drugs, and other environmental factors can produce a wide range of skin reactions, from slight irritation to severe allergic reactions, inflammation, and cancer. Chemicals can enter the skin through a variety of pathways, including absorption through hair follicles, sweat glands, and the epidermis. These substances, once consumed, can interact with skin cells, causing damage to DNA, proteins, and other biological components. One of the major issues in cutaneous toxicity is the development of skin cancer, often known as carcinogenesis. Chronic exposure to some chemicals, such as polycyclic aromatic hydrocarbons (PAHs), arsenic, and pesticides, has been linked to an increased risk of skin cancer. These substances can change skin cells, leading to uncontrolled growth and multiplication of malignant cells. Sunlight emits ultraviolet (UV) radiation, a well-known environmental factor associated with skin cancer development. UV rays can directly damage the DNA in skin cells, resulting in mutations that can lead to cancer. Furthermore, UV radiation impairs the immune system's ability to identify and remove malignant cells, promoting tumour growth. Carcinogenesis happens in three stages: initiating, promoting, and progressing. During initiation, DNA damage occurs, leading in

the formation of mutant cells. Promotion is the clonal expansion of mutant cells induced by factors such as inflammation and oxidative stress. Finally, progression describes the transformation of pre-malignant cells into invasive cancer.

Skin cancer is divided into several types, including basal cell carcinoma, squamous cell carcinoma, and melanoma. Basal cell carcinoma and squamous cell carcinoma are more common and frequently associated with excessive sun exposure and environmental pollutants. Melanoma, while less common, is more aggressive and can spread to other parts of the body if not detected and treated early. To prevent cutaneous toxicological effects and carcinogenesis, a variety of strategies are required, including limiting exposure to known carcinogens, wearing protective clothing and sunscreen to reduce UV radiation exposure, and increasing skin cancer awareness and early detection through regular skin examinations.

8.7 TERMINAL QUESTIONS

Q. 1. What is cutaneous toxicity? Discuss briefly.

Answer:----------

Q. 2. Define the dermatological effects of toxic agents.

Answer:----------

Q. 3. Discuss the allergic contact dermatitis.

Answer:----------

Q. 4. What do you know about photosensitivity?

Answer:----------

Q. 5. Discuss about the contact urticaria toxicity.

Answer:----------

Q. 6. Write about cutaneous carcinogenesis and mechanism of carcinogenesis.

Answer:----------

8.8 FURTHER SUGGESTED READINGS

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2. Environmental Toxicology, third edition, Sigmund F. Zakrzewski, Published by Oxford University Press, Inc. New York, New York 10016.

3. Environmental Toxicants, Human Exposures and Their Health Effects, Third Edition, Morton Lippmann, Published By John Wiley & Sons, Inc., Hoboken, New Jersey.

4. Toxicology in Occupational and Environmental Setting, Wolfgang Dekant, Institute of Toxicology, University of Wuerzburg, Germany.

5. A Textbook of Modern Toxicology, Ernest Hodgson, Published By John Wiley & Sons, Inc., Hoboken, New Jersey.

6. A Textbook of Modern Toxicology: Ernest Hodgson, A John Wiley & Sons, Inc., Publication.

7. Principles of Environmental Toxicology, I. Shaw, J. Chadwick, CRC Press.

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UNIT-9 : PULMONARY AND HEPATIC TOXICITY

Structure

9.1 INTRODUCTION

Pulmonary and hepatic toxicity are severe medical disorders affecting the lungs and liver, respectively. Both organs perform critical functions in the overall function of body, and any damage to either can have serious implications. Pulmonary toxicity is defined as lung damage induced by exposure to hazardous substances such as chemicals, pollutants, medications, or radiation. This damage can cause a variety of respiratory symptoms and illnesses, such as inflammation, fibrosis, pneumonia, and pulmonary edema. Chemotherapy treatments, environmental pollutants such as asbestos or silica, and

specific medications such as amiodarone or methotrexate are all common causes of pulmonary toxicity. Symptoms of pulmonary toxicity can vary depending on the cause and severity of the damage but may include shortness of breath, coughing, wheezing, chest pain, fatigue, and difficulty breathing. In severe cases, pulmonary toxicity can progress to respiratory failure, which can be life-threatening if not treated promptly. Diagnosis typically involves a combination of medical history, physical examination, imaging tests (such as X-rays or CT scans), pulmonary function tests, and sometimes lung biopsy. Treatment of pulmonary toxicity often involves discontinuing the offending agent and providing supportive care to alleviate symptoms. Depending on the severity, patients may require oxygen therapy, corticosteroids to reduce inflammation, or other medications to manage specific symptoms. In some cases, lung transplantation may be necessary for patients with end-stage lung disease due to irreversible pulmonary toxicity. On the other hand, hepatic toxicity refers to damage to the liver, the largest internal organ responsible for crucial functions like detoxification, metabolism, and nutrient storage. Hepatic toxicity can result from various factors, including excessive alcohol consumption, viral infections (such as hepatitis B or C), autoimmune diseases, certain medications (like acetaminophen, statins, or isoniazid), and exposure to toxins or environmental pollutants. Symptoms of hepatic toxicity can be nonspecific and may include fatigue, jaundice (yellowing of the skin and eyes), abdominal pain, nausea, vomiting, and loss of appetite, dark urine, and pale stools. Severe cases can lead to liver failure, a life-threatening condition characterized by hepatic encephalopathy, coagulopathy, and multi-organ dysfunction. Diagnosis typically involves blood tests to assess liver function, imaging studies (such as ultrasound or MRI), and sometimes liver biopsy. Treatment of hepatic toxicity depends on the underlying cause and severity of liver damage. It may involve discontinuing the offending agent, lifestyle modifications (such as avoiding alcohol or certain medications), supportive care to manage symptoms, and medications to improve liver function or treat underlying conditions. In severe cases, liver transplantation may be necessary for patients with irreversible liver failure.

Objectives:

After reading this unit, learner will able to know

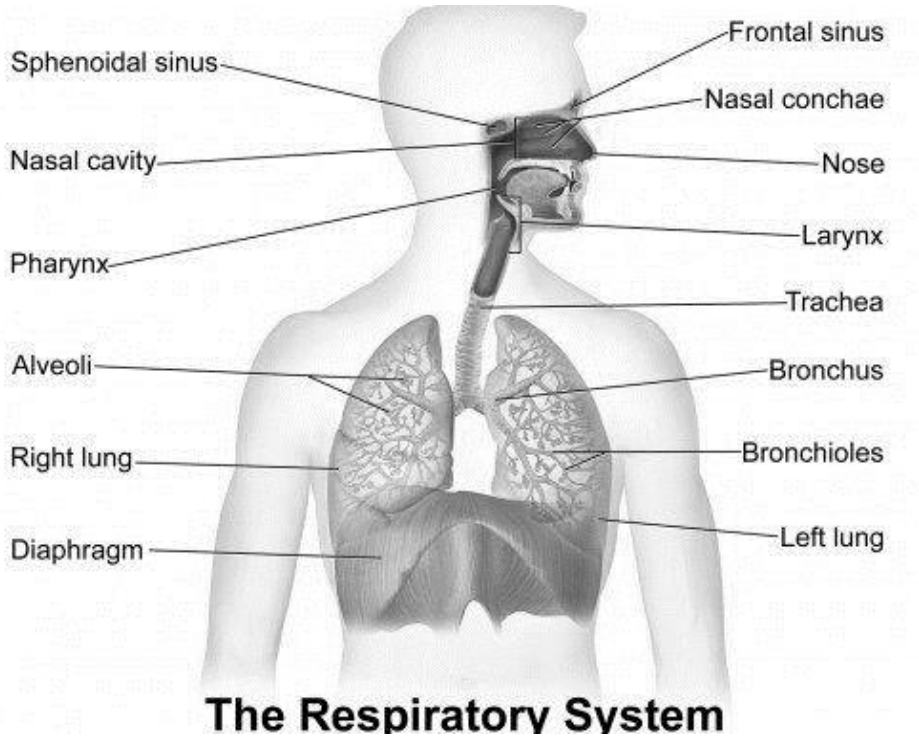
- Pulmonary and hepatic toxicity and its effects on human
- The Respiratory System and respiratory toxicity
- The mechanism of entry of toxicant into the lungs
- Systematic lung toxins and Actions of toxins on the liver
- Chemical-induced liver injury and its mechanism
- Types of liver damage and chronic liver injury

9.2 RESPIRATORY SYSTEM

Toxicants can be particularly harmful to the respiratory system, as the lungs are the primary entry point for inhaled gases and particles. Furthermore, the lungs receive the full cardiac output; thus, Toxicants that reach the bloodstream have the potential to induce lung damage. The respiratory system transports oxygen to the bloodstream, making the alveolar portion of the lung the principal entry point for exposure to many toxins. Mammalian lungs have advanced cellular defense mechanisms to remove inhaled toxins and finely tuned repair processes to restore their delicate architecture after harm.

The upper respiratory tract includes the mouth, nose, and pharyngeal region. Mammals breathe through their noses or mouths, although certain species, like rodents, rely solely on their nasal passages. The upper respiratory tract serves several tasks, including olfaction, temperature and humidity regulation, and inhalation of particles and irritants. The lower airway system consists of the larynx,

the trachea, the stem bronchi, and all the airways ramifying intensively within the lungs, such as the intrapulmonary bronchi, the bronchioles, and the alveolar ducts. The lower respiratory tract starts from the pharyngeal region and includes the tracheobronchial and pulmonary parenchyma/alveolar regions. The lower respiratory tract's principal job is to extract oxygen from the ambient and transfer CO_2 from the blood to exhaled air. The lower respiratory tract also plays a significant role in against inhaled toxicants.



Four different pulmonary lung volumes are defined as follows:

1) The **tidal volume** is the amount of air inspired or expired with each normal breath.;

2) The **inspiratory reserve volume** refers to the maximum amount of air that can be inspired above the typical tidal volume;

3) The **expiratory reserve volume** is the maximum excess volume of air that can be exhausted by strong expiration after the end of a regular tidal expiration.

4) The **residual volume** refers to the amount of air remaining in the lungs following the most powerful expiration.

Pulmonary capacities refer to the sum of two or more volumes, and are defined as follows:

1) Inspiratory capacity = tidal volume + reserve volume;

2) The functional residual capacity is equal to the expiratory reserve volume plus the residual volume.

3) The vital capacity is equal to the sum of the inspiratory, tidal, and expiratory reserve volumes.

4) Total lung capacity refers to the greatest volume that the lungs can expand, which is equal to the vital capacity plus residual volume.

Lung mechanics refers to how the lung expands and fills with air during inspiration and deflates

during exhale. The lung's elasticity and airway diameter determine these features.

Toxicity in the respiratory tract can disrupt gas exchange by affecting airway tone and disrupting the alveolar/capillary barrier in the deep lung. Impaired gas exchange can cause tissue damage, resulting in persistent structural alterations and diminished lung volumes or mechanics. Fibrotic lung disease reduces both total and vital lung capacity, causing the lung to shrink and stiffen. Restrictive lung disease is characterized by decreased lung capacity and little airflow. In emphysematous, the breakdown of alveolar walls and loss of elastin fibers can increase overall lung capacity and allow for deflation. On exhale, however, vital capacity is diminished due to airway collapse. Obstructive lung disease is characterized by decreased airflow.

9.3 RESPIRATORY TOXICITY

Respiration, the exchange of O_2 and CO_2 with blood, is only one of several functions of the lungs, albeit the most important of them. Other roles include gaseous metabolite excretion and metabolism, as well as control of vasoactive hormones like angiotensin, biogenic, amines, and prostaglandins. Damage to the lung tissue responsible for regulatory activities can impact blood pressure and blood flow to the lungs. Proper blood oxygenation requires a match between alveolar ventilation (5250 mL of air per min) and the volume of blood flowing through the lungs (5000 mL/min). Changing blood flow disrupts the ventilation-perfusion balance, leading to organ failure. Toxins (gases, vapors, or aerosols) can harm respiratory tissue or induce systemic toxicity by permeating and entering the circulation. Respiratory system injuries can range in severity from irritation to edema, fibrosis, or neoplasia, depending on the substance and degree of toxicity. The location of toxicity is determined by the water solubility of a gas or the size of aerosol particles or droplets.

Water-soluble gases like ammonia, chlorine, sulfur dioxide, and hydrogen fluoride can cause damage to the upper respiratory system. Before a gas can contact the tissue, it must first penetrate the mucous lining. This barrier provides some protection against very small amounts of hazardous gasses, but it does not shield the tissue from larger concentrations. Toxicity to respiratory tissue in this location is most commonly manifested as irritation. However, edema may develop in more severe situations. Edema is caused by damage to the cell membrane, which alters membrane permeability and causes cellular fluid to leak. Edema symptoms include tissue swelling, airway constriction, trouble breathing, and increased susceptibility to infection.

Aerosols containing particles greater than 2 mm can harm the upper respiratory system. Arsenic oxides, sulfides, and chlorides are utilized in a wide range of industries, including the production of colored glass, ceramics, semiconductors, and fireworks, as well as hide processing. Upper respiratory exposure to these chemicals is particularly common in ore-smelting and pesticide manufacture. Arsenic particles are typically too big to enter the lung alveoli, resulting in deposits in the nasopharynx and upper bronchi. Their toxicity is manifested as irritation. Chronic coughing, laryngitis, and bronchitis-like symptoms are caused by airway inflammation. Arsenic trioxide (As_2O_3) is a probable human carcinogen, hence exposure should be limited.

Chromium and its derivatives are employed in various industries, including stainless steel, chrome plating, pigment manufacture, and hide processing. Hexavalent chromium compounds, including chromate (CrO^{2-}_4) and bichromate ($Cr_2O^{2-}_7$). Long-term contact can lead to nose irritation, bronchitis-like symptoms, lung tumors, and cancer. Nickel exposure, including monoxide (NiO) and subsulfide (Ni_2S_3), may occur during ore processing. Because ore dust particles are big, their toxicity is limited to the nasal mucosa and large bronchi. Nickel subsulfide, whether in dust or fumes, is a known human carcinogen of the nasal cavity.

Gases such as ozone (O_3), nitrogen dioxide (NO_2), and phosgene ($COCl_2$) can damage alveolar tissue due to their low water solubility. The mechanism of action for ozone and nitrogen dioxide is connected to their oxidizing potential. The peroxidation of cellular membranes induces edema. Furthermore, NO_2 interacts with alveolar fluid to produce corrosive acids like HNO_2 and HNO_3, which can harm cells.

Certain metals and their compounds, including cadmium oxide (CdO), nickel carbonyl [$Ni(CO)_4$], and beryllium, can cause pulmonary edema. Cadmium oxide is utilized in the production of semiconductors, silver alloys, and glasses. CdO fumes contain tiny particles that penetrate alveoli. Inhaling such fumes causes edema, pneumonitis, and growth of type I pneumocytes in the alveolar lining. Nickel carbonyl is a very volatile liquid used for nickel refining and plating. Inhaled fumes can cause pulmonary edema. In the event of exposure, 48 hours of surveillance is required. Metallic mercury is very volatile and can quickly enter the body through the respiratory system, making it a particularly deadly substance. Despite inhaling mercury vapor, although, largely a toxin of the central nervous system, it can also cause corrosive bronchitis and interstitial pneumonitis. Phosgene, used in the preparation of many organic chemicals, is also manufactured as a war gas. It is highly toxic as it undergoes hydrolysis to CO_2 and HCl in the lungs.

Paraquat is an extremely hazardous pesticide that affects the respiratory system. No matter how it enters the body, it causes pulmonary edema. Paraquat penetrates the alveolar area and concentrates in type II pneumocytes after being inhaled or swallowed. Its toxicity is most likely caused by the formation of superoxide radicals (O_2), which can induce cellular membrane peroxidation.
Pulmonary fibrosis: Pulmonary fibrosis, commonly known as pneumoconiosis, is another type of lung reaction to respiratory pollutants. The first harm to the cells is induced by the physical rather than chemical action of minute solid particles or fibers. In the early stages of the disease, tiny collagen islets (1-10 mm in diameter) are deposited in the lungs. As the islets expand, they form a network of fibers that cover the entire lung, causing loss of elasticity. Additionally, damaged areas experience blood vessel narrowing and alveolar wall destruction, leading to decompartmentalization and emphysema. The harm is considered to be connected to the action of macrophages that engulf the damaging particles and destroy lysosomal membranes and release lysozymes.

Silicosis: Silicosis is caused by long-term exposure to irrespirable crystalline silica particles, not amorphous ones. Animal studies show that inhaling amorphous silica induces minimal fibrosis. However, under these settings, only a trace of silica was preserved in the lungs. When injected into the peritoneum or lungs, amorphous silica was more fibrogenic than crystalline quartz. Tuberculosis often complicates silicosis.

Black Lung Disease: Black lung disease, a prevalent condition among coal miners, was previously assumed to be caused by continuous exposure to coal dust since the deceased victims' lungs had been blackened by coal. It currently appears that the condition, which exhibits all of the features of lung fibrosis, is most likely caused by silica dust created during coal mining.

Asbestosis: Asbestos consists of two types of hydrated fibrous silicates: serpentine (curly) and amphibole (rod-like). The amphibole family is the most pathogenic, with toxicity varying based on fiber size and physical features. The most damaging fibers are 5 mm long and 0.3 mm in diameter. Asbestosis symptoms include fibrosis, lung calcification, and the production of mesothelial tumors. The latency period for mesothelial tumor growth is extremely prolonged. Up to 30 years can pass between exposure and the clinical development of neoplasia.

Pulmonary Neoplasia: Polycyclic aromatic hydrocarbons (PAHs) are a common cause of lung neoplasia in the workplace. PAHs enter the lungs through tiny particles of soot and fly ash, as explained in subsequent chapters. Workers in coke ovens and coal tar pits are at highest risk of developing lung

cancer from this source. Tobacco smoke, the leading cause of lung cancer, raises the risk of pulmonary neoplasia among those exposed to PAHs at work.

9.4 TOXICANT CAUSING RESPIRATORY DYSFUNCTION

Several toxicants can adversely affect the respiratory system, leading to various forms of dysfunction ranging from acute irritation to chronic diseases. These toxicants can be found in occupational settings, environmental pollutants, or even in everyday products. Understanding their effects is crucial for prevention and management. Here is a review of several frequent toxicants producing respiratory dysfunction, with examples:

- **Particulate Matter (PM):** Fine particles present in the air, such as dust, smoke, and soot, can travel deep into the respiratory tract, causing irritation and inflammation. Long-term exposure to PM can cause chronic respiratory diseases like bronchitis and asthma. For example, industrial activity, car emissions, and wildfires are major causes of PM pollution.

- **Volatile Organic Compounds (VOCs):** Chemicals like benzene, formaldehyde, and toluene, which are often present in paints, solvents, and household cleansers, can produce fumes that irritate the respiratory system. Prolonged exposure to VOCs may raise the risk of respiratory illnesses such asthma and chronic obstructive pulmonary disease (COPD).

- **Ozone (O_3):** Ground-level ozone, a main component of smog, is produced by the interaction of VOCs and nitrogen oxides in the presence of sunlight. Ozone exposure can cause airway irritation, coughing, and the worsening of respiratory diseases such as asthma. Urban locations with high traffic density frequently have excessive ozone levels.

- **Heavy Metals:** Metals such as lead, mercury, and cadmium, which are commonly found in industrial pollutants, can build in the lungs and interfere with respiratory function. Lead exposure, for example, can cause impaired lung function and an increased susceptibility to respiratory infections.

- **Asbestos:** Asbestos fibers, which are widely found in construction materials, can cause serious respiratory illnesses such asbestosis, lung cancer, and mesothelioma. Inhaling asbestos fibers causes lung tissue scarring and inflammation, which impairs respiratory function over time.

- **Tobacco Smoke:** Cigarette smoke contains thousands of harmful compounds, such as nicotine, carbon monoxide, and tar that can harm the respiratory system. Smoking is a major cause of respiratory illnesses such lung cancer, COPD, and emphysema. Secondhand smoke is equally harmful, especially to youngsters and nonsmoking adults.

- **Biological Agents:** Mold, pollen, and some bacteria and viruses can cause allergic reactions and respiratory problems in sensitive people. Indoor mold development, for example, can exacerbate asthma symptoms and lead to respiratory infections.

- **Airborne Pollutants from Industrial Processes:** Industrial emissions, including sulfur dioxide (SO_2), nitrogen oxides (NOx), and ammonia (NH_3), can contribute to air pollution and respiratory health issues. These pollutants can irritate the airways, worsen asthma, and raise the risk of respiratory infections.

Exposure to numerous toxicants can cause respiratory dysfunction, ranging from acute irritation to chronic disorders like asthma, COPD, and lung cancer. Efforts to prevent exposure to these hazardous

compounds by regulatory measures, environmental controls, and public health interventions are critical to protecting respiratory health and well-being.

9.5 DYSFUNCTIONS OF THE IMMUNE SYSTEM

Immunological system dysfunctions can lead to allergies, immunological suppression, uncontrolled growth, and autoimmune. Allergic reactions arise when the immune system reacts negatively to environmental substances. Certain drugs can cause the immune system to react improperly, despite its purpose of eliminating foreign bodies. Allergies include asthma and contact dermatitis. Examples of uncontrolled growth include leukemia and lymphoma.

Defense Mechanisms: The respiratory system contains complex defense systems to protect itself from harmful particles and gasses. Particles of 1-2 micrometers are ideal for reaching the alveoli. Large particles are either retained in nasal hairs or eliminated through coughing or sneezing, preventing them from entering the lower respiratory tract. Particles as small as 2 micrometers enter the trachea and adhere to the airway surfaces and mucus. Finer particles settle less efficiently and are typically expelled. Some materials may disintegrate in the alveoli and be absorbed into the circulation or interstitial fluid. Macrophages can phagocytize non-dissolving particles, which are then swept up the tracheobronchial tree on the mucous blanket or move to the interstitial fluid. Some insoluble particles may linger in the lungs.

The immune system helps protect the lungs. While this background piece does not provide a thorough explanation, OTA has previously examined immune system responses to hazardous chemicals. Exposure to compounds containing animal or vegetable proteins can sensitize immune cells. The cells react in a sophisticated manner to eliminate or immobilize the inhaled chemical. Inflammation of surrounding tissues is a natural element of the repair process that restores normal function. Repeated exposure and inflammation may cause lasting tissue damage.

9.6 MECHANISM OF ENTRY OF TOXICANT INTO THE LUNGS

The lung is exposed to toxicants and medications through the systemic circulation, as well as direct contact with airborne toxins. As a result, both inhaled and circulating toxins have the potential to cause significant damage. The lungs absorb gases and vapors, including carbon monoxide, sulfur dioxide, and volatile hydrocarbons, as well as liquid or particulate aerosols like sulfuric acid or silica dust with solid and liquid particles. The lungs, like the liver and kidney, also have high quantities of xenobiotic metabolizing enzymes, which can help activate and detoxicate foreign substances. The location of deposition is important in determining the degree of absorption of a chemical.

Solid and Liquid Particulates absorption- The lung is divided into three regions: nasopharyngeal, tracheobronchiolar, and distal or alveolar.

Nasopharyngeal: Particles larger than 5 μm are typically deposited in the nasopharyngeal area. When deposited at the surface, they can be easily removed through sneezing, blowing, or wiping. If deposited further back, the mucus-blanked cilia lining the lung (the mucociliary "escalator") can pick them up and move them back up into the nasopharyngeal region. They can then be swallowed and absorbed in the GI tract based on their solubility and absorption characteristics.

Tracheobronchiolar: Particles with a size of 2-5 μm typically enter the tracheobronchial area before reaching the lung surface. Most of these particles are likewise cleaned by the mucocilliary escalator and returned to the nasopharyngeal region, where they are eliminated immediately, ingested and absorbed, or excreted in the GI tract.

Alveolar or alveolar: Particles smaller than 1 μm may enter the alveolar areas of the lung. Absorption occurs mostly in the alveolar portion of the lung, but may also occur in the tracheobronchial region if the material is soluble in mucus.

Size is arguably the most important single factor influencing particle absorption efficiency in the lung. Size dictates where the aerosol is likely to be deposited in the lung. Even in the case of very small particles that reach the alveolar region and may be absorbed there, size is inversely proportional to particle deposition.

Particulates accumulated in the alveolar region might disintegrate and absorbed the bloodstream, thus affecting the circulatory system. Alveolar macrophages can phagocytize non-soluble particles and transmit them to the lymphatic system for further processing. They can remain for a long time or be transferred to the mucocilliary escalator for clearing with macrophages. Sometimes they can stay in the alveolus for a long time. Water-soluble compounds can be easily absorbed in the lungs and nasal cavities. Aspirin is 100% bioavailable in the rat nasal cavity, but only 59% when taken orally. Nicotine was completely absorbed from the intratracheal and bronchial and distal regions in the dog lung, albeit absorption was not equally fast from all three locations.

Gases and Vapors abortion: The lung absorbs gases and vapors based on their solubility in the blood that circulates there. In a single respiration, very soluble chemicals are virtually entirely removed from the breathed air and transported to the pulmonary bloodstream. For such substances, increasing pulmonary blood flow makes minimal change in absorption rate. To improve absorption, raise the rate of breathing, often known as ventilation. These chemicals have low absorption due to ventilation. If they are fat-soluble, they will quickly accumulate in the body's lipid depots.

Chloroform is an excellent example of such a chemical. It is very lipid-soluble and easily removed from the air. Chloroform is transferred to fat as it circulates through the body, allowing it to be eliminated and picked up by the lungs during the following pass.

9.7 SYSTEMATIC LUNG TOXINS

A growing variety of drugs and toxicants have been identified to be hazardous to the lungs after systemic administration. These agents cause damage to lung tissue, either alone or in combination with other tissues. The lung is a diverse organ with more than 40 cell types. Each of these cell types has the potential to cause toxic harm, but only a few have been shown in practice to be significant targets for systemic lung toxins. Toxins primarily target lung cells such as capillary endothelial cells, nonciliated bronchiolar epithelial cells (Clara cells), ciliated bronchiolar epithelial cells, and type I and II alveolar epithelial cells. The lung is a common target organ due to its cellular heterogeneity and dependence on the heart's output.The agents covered are paraquat, thioureas, butylatedhydroxytoluene, trialkylphosphorothioates, lung-toxic furans and antineoplastic agents, pyrrolizidine alkaloids, metals and organometallic compounds, amphiphilic agents, hydrocarbons, oleic acid, 3-methylindole, and diabetogenic agents.

Paraquat: Paraquat (1,1'-dimethyl-4,4'-bipyridylium dichloride), also known as methyl viologen, was originally manufactured in 1882 and the first report of lung damage in humans. Since then, over 600 cases of paraquat poisoning have been reported, prompting extensive research into the toxin's causes and potential remedies. Paraquat is a very water-soluble di¢ation. This chemical's aqueous solutions cause irritation in most biological systems. Oral consumption typically causes mucosal sores in the mouth and throat, as well as nausea and vomiting.Toxic indicators, such as diarrhea and impaired kidney function, can occur quickly. However, unless a large amount is consumed, these symptoms typically subside within a day and the patient returns to normal health. This is deceiving, however, as severe lung damage

is gradually developing. Animal experiments with single or multiple doses of paraquat showed severe lung damage, including both destructive and proliferative phases. The first morphological change noticed during the destructive phase is damage to type I and II alveolar epithelial cells. The pulmonary capillaries can be damaged within 48 hours, but the extent is limited. Some terminal bronchiolar cells exhibit early necrosis. During the destructive stage, lung parenchyma collapses and there is alveolar and interstitial edema.Paraquat easily accepts electrons from NADPH in pulmonary microsomal preparations and promptly reoxidizes under aerobic circumstances, producing superoxide and other oxygen radicals. This chemical cascade may cause cell damage through NADPH depletion, free radical production, lipid peroxidation, or a combination of these causes. Lipid peroxidation has long been regarded as a potential mechanism of paraquat poisoning. Paraquat is very harmful to lung tissue in mammals. The mechanisms underlying lung injury appear to be related to paraquat's unique absorption into this tissue and its redox capacity, which may result in NADPH depletion and/or the formation of oxygen free radicals.

THIOUREAS: Phenylthiourea and alpha-naphthylthiourea (ANTU) are known to cause severe pulmonary edema and pleural effusion in rats. Damage to type I alveolar epithelial cells has also been described. Light and electron microscopy show gaps in the endothelium and blebs projecting into the capillaries. These pores can leak fibrin-rich fluid, causing pulmonary edema and pleural effusions. Rarely, animals experience hemorrhage, and edema typically resolves within 48 hours. Surprisingly, no inflammatory response was observed as a result of ANTU-induced lung damage. When fluid leakage stopped, gaps at endothelial cell connections disappeared, and no permanent damage to lung cells was seen.

The presence of particular binding sites is one theory postulated to explain the toxicity of several lung toxins, including thioureas. Thioureas may cause lung damage by metabolic activation. The pulmonary toxicity and binding of ANTU to lung proteins were significantly increased in mice treated with diethyl maleate.A drug that depletes reduced glutathione (GSH) in both the lung and liver. ANTU and related thioureas appear to be metabolically activated, producing molecular species that specifically harm pulmonary endothelial cells. This injury causes pulmonary edema and pleural effusion in rats, resulting in death within 8-10 hours. Survivors recover quickly, regaining normal lung shape within 2 days.

Butylatedhydroxytoluene: Butylatedhydroxytoluene (3,5-di-t-butyl-4 hydroxytoluene, BHT) is a synthetic antioxidant that is commonly used as a food, medicinal, and cosmetic ingredient. At low dosages, it is relatively non-toxic to all mammalian species, but at high levels, it causes a diffuse lung lesion that appears to occur only in mice. BHT-induced lung injury leads to increased lung weight, DNA, RNA, and protein synthesis, cyclic GMP, and protein phosphorylation. BHT treatment in mice causes widespread and consistent lung damage. This model has been widely utilized to study acute lung damage and fibrosis because to its accurate cell damage and healing sequence. Numerous biochemical changes have been studied, including collagen metabolism, which is intimately involved in the development of the fibrotic lesion. While it is unclear if humans may develop a lung lesion after consuming a big dosage of BHT, the chemical's species specificity and the high doses needed to cause lung injury in mice imply this is not a significant worry.

Trialkylphosphorothioates: Trialkylphosphorothioates, a category of compounds, have been linked to acute lung injury when administered systemically. The sequence and type of alveolar cells destroyed by trialkylphosphorothioates in rat lung is comparable to that of a BHT-induced lung lesion in mice. At the alveolar level, type I epithelial cells are selectively destroyed within 24-48 hours, exposing the basement membrane. This is sequentially followed by hypertrophy and hyperplasia of type II alveolar epithelial cells and massive interstitial thickening. Trialkylphosphorothioates are primarily eliminated by the liver. Lung toxicity occurs in rats and mice and appears to be induced by a metabolite produced in the lung. It is unclear what this chemical is, what cells in the lung produce it, and how it causes lung injury in other species.

Furans: At least 13 furan derivatives have caused acute lung injury in laboratory animals when inhaled or administered systemically. Some of these chemicals occur naturally in the environment, others are used in industry and research, while some are found in food and drugs. Systemic exposure to lung-toxic furans causes pulmonary bronchiolar necrosis as the major pathological pathology. Pathological results with 4-ipomeanol in mammals are mostly limited to the lungs. The "lung edema factor" found in sweet potatoes infected with Fusariumsolani causes significant edema, pleural effusion, congestion, and bleeding in animals within 6-24 hours of systemic treatment. Furan derivatives cause lung damage that mostly affects Clara cells. This is due to the ability of these cells to convert furans into a highly reactive species. The resulting damage causes edema, which can be fatal or resolve without leaving any lingering damage. Nitrofurantoin, which has a furan moiety, causes a distinct lung lesion due to its propensity to undergo cyclic oxidation and reduction, rather than bioactivation to an electrophilic species.

Antineoplastic Agents: The most significant lung toxicity is seen with 1,3bis-(2-chloroethyl)-I - nitrosourea (BCNU or carmustine), bleomycin, cyclophosphamide, busulfan, mitomycin c and methotrexate. Bleomycin causes lung damage, including protein buildup, edema, epithelial metaplasia, and fibroblast growth without inflammation. Cytotoxic drug-induced lung illness might be extremely rare or occur at a rate of up to 30%. While there is evidence for ideas surrounding bleomycin, cyclophosphamide, and BCNU, the mechanism underlying this impact has yet to be proven. It is clear that there is an increased risk of lung injury when treating patients.

Pyrrolizidine Alkaloids: Pyrolizidine alkaloids (PA) are chemical compounds found in various plant species worldwide. Examining certain lung functions can help determine the type of cells affected by PA. PA therapy inhibits pulmonary endothelial cells' usual active uptake of biogenic amines like serotonin. The PA-induced lung lesion appears to occur only in species that develop persistent liver lesions. This overview cannot fully address the complicated metabolism and toxicity of PA. What is obvious, however, is that this group of compounds is a classic example of lung toxicity caused by the bioactivation of a toxin in the liver, which is then transported to the lung via the bloodstream. The ensuing tissue damage manifests largely in pulmonary endothelial cells, which are intimately in contact with the toxin.

Metals and Organometals: There are numerous studies on the effects of heavy metal exposure through inhalation or intratracheal routes on histopathology and metabolism. There are fewer reports on their lung damage following systemic dosing. Systemic cadmium injections are a useful way to study the progression of lung harm caused by this environmental toxin. One day after cadmium treatment, there was no significant difference in thymidine incorporation into lung DNA, indicating cell proliferation in response to acute lung injury, compared to controls. Nickel carbonyl, a colorless liquid, causes severe lung damage in many species, including humans. Following systemic treatment, the alveolar region is most impacted, with maximum damage appearing 4–6 days later. MMT, along with other organometallic chemicals, has been linked to lung toxicity.This drug has been shown to cause lung damage in mice, rats, and hamsters within one day after systemic injection. When injected parenterally, vanadium accumulates in the lung, causing histological alterations such as intraalveolar bleeding and regional septal necrosis. Heavy metal exposure, whether inhalation or systemic, alters pulmonary tissue metabolism and morphology (see Table III). With the exception of organometallic compounds, the lung does not appear to be a key target tissue for metals administered parenterally in animals. This analysis highlights the need for additional research on the pulmonary effects of metal ingestion. Furthermore, research suggests that age has a significant impact on metals' effects on lung structure and function.

9.8 LIVER AND ITS PHYSIOLOGY

The liver is the biggest organ in all vertebrates, although not in invertebrates.

The liver has a simple structure; it is made up of a continuum of hepatic cells (known as hepatocytes or parenchymal cells) that are punctured by a network of cylindrical tubes. These tunnels are connected by a network of blood capillaries known as sinusoids. Kupffer cells are phagocytic cells that line sinusoid walls. Their function is to eliminate undesirable particles, germs, and worn-out blood cells in incoming blood. The liver is a very important organ for chemical-induced toxicity as it is rather vulnerable to attack by chemicals. The portahepatis is a huge depression that allows venous and arterial blood to enter the liver. The liver receives its main blood supply from intestinal capillaries. These capillaries connect to larger veins called mesenteric. Blood enters the liver and departs through the hepatic veins. It then returns to the heart via the inferior vena cava. The hepatic artery, which branches from the aorta, delivers oxygenated blood to the liver. A steady supply is required for the myriad of metabolic energy-consuming activities. Bile-carrying canaliculi accumulate waste and eventually form bigger ducts. These ducts follow the portal vein branches, with bile flowing in the opposite direction as blood. In the portahepatis, the bile ducts finally unite with the hepatic duct. Bile then drains into the duodenum, the upper section of the small intestine.

Understanding the structure of the liver is critical since a widely used classification of hepatotoxic responses is based on histological location and appearance. Necrosis around the central vein is known as centrilobular (occasionally pericentral), whereas necrosis in the portal space is known as periportal (or periacinar). Midzonal refers to liver cell injury that occurs in between.

At the cellular level, the liver consists of four systems:

- the hepatocyte (liver cell) system
- the biliary tract system, involved in the production of bile from the breakdown of
- haemoglobin from blood cells
- In blood circulation system. The liver receives blood from two circulatory systems: systemic circulation (one-quarter of cardiac output via the hepatic artery) and portal vein, which draws blood from the intestine system. The liver's small pathways allow blood from both systems to flow together. The hepatic vein and vena cava carry blood from the liver back to the heart.
- The reticuloendothelial system contains various cell types, including Kupffer cells (highly mobile macrophages), fat-storing lipocytes, natural killer lymphocytes, and endothelial cells.

Physiology of the liver: The liver performs a wide range of tasks, including biotransformation, homeostasis, and blood sugar management.

Biotransformation of chemicals: The liver biotransforms chemicals taken from various sources, including food, drink, environment, and employment. These include endogenous chemicals that circulate in the body (such as hormones and waste products) as well as foreign chemicals that are absorbed. The main process involves converting fat-soluble molecules into water-soluble ones. This allows for easier elimination of absorbed toxins through urine. Other materials may be excreted in the bile.

- **Regulation of blood sugar:** The blood sugar level remains around 0.1%, with any excess from the gastrointestinal tract stored as glycogen. Insulin, a hormone released by the pancreas, converts excess glucose into glycogen.
- **Regulation of lipids:** Lipids are removed from the circulation and, depending on the body's needs, transformed to carbs or comparable compounds, or stored as fat if not needed right away.

- **Regulation of amino acids:** Amino acid levels in the blood are maintained within physiological limits. Because necessary amino acids cannot be stored in the body, the amine groups of spare circulating amino acids are transformed to urea. The reallocated acid molecule is then turned into a carbohydrate structure for reuse.

- **Formation of bile:** Bile is composed of bile salts and excretory bile pigments. These aid digestion of fats.

- **Metabolism of cholesterol:** This fatty material is used by the cells. Excess blood can cause blood vessel blockages, leading to heart attacks and other illnesses.

- **Formation of plasma proteins:** Plasma proteins play important roles in blood coagulation and plasma stability. Blood proteins consist primarily of fibrinogen, prothrombin, albumin, and globulins.

- **Making heparin:** This chemical acts as an anticoagulant, preventing blood clotting throughout the body.

- **Storage of blood:** The liver may store a large amount of blood and release it when needed, such as after injury or illness.

- **Removal of haemoglobin molecules:** When red blood cells become frail, they are broken down to convert haemoglobin into bile pigments and preserve iron atoms for later use.

- **Storage of vitamins:** The liver converts carotene, an orange-red pigment found in plants, into vitamin A. Vitamin B12 is also found in the liver.

- **Production of heat:** The liver generates significant heat as one of the body's most active organs. This circulates throughout the body in the blood, warming less active parts.

9.9 ACTIONS OF TOXINS ON THE LIVER

Toxins can have a number of negative effects on the liver, affecting normal function and potentially causing major health problems. The liver is an important organ that regulates several metabolic processes, including detoxification, protein synthesis, and bile generation. When exposed to toxins, numerous pathways are activated, resulting in liver damage.

Firstly, toxins can directly damage liver cells, known as hepatocytes via oxidative stress and inflammation. Toxin-generated free radicals can damage cell membranes, proteins, and DNA, resulting in cell death and reduced liver function. Toxin exposure causes inflammatory responses that aggravate tissue damage and hinder regeneration.

Second, certain poisons can inhibit the liver's detoxification functions. Toxins are metabolized and neutralized by the liver via phase I and phase II processes, turning them into less toxic compounds that may be eliminated. However, some toxins can overload these pathways or interfere with specific enzymes involved in detoxification, resulting in the buildup of hazardous intermediates and increased oxidative stress.

Toxins can also affect bile flow within the liver, impairing bile secretion, which is required for fat breakdown and absorption. This can lead to cholestasis, a condition in which bile acids and toxic metabolites are retained inside the liver, exacerbating liver injury and functioning. Chronic exposure to

toxins, such as alcohol, certain drugs, industrial chemicals, or environmental pollutants, can also encourage the development of liver illnesses such as fatty liver disease, hepatitis, fibrosis, and cirrhosis. If not addressed, these disorders can lead to liver failure or hepatocellular cancer. Furthermore, some chemicals have a direct carcinogenic effect on liver cells, raising the possibility of developing liver cancer.

For example, aflatoxins produced by some molds typically found in contaminated foods can cause genetic abnormalities and tumor growth in the liver. Toxins can cause considerable liver damage through a variety of methods, including direct cellular destruction, interference with detoxification pathways, disruption of bile flow, and increased inflammation and oxidative stress. Understanding how toxins affect the liver is critical for creating measures to avoid and reduce liver damage and related health consequences.

Several metals, organic compounds, and medications can cause fatty liver and necrosis. Several compounds, including chloroform, carbon tetrachloride, bromotrichloromethane, dimethylaminoazabenzene, and dimethylnitrosamine, can cause both states. Certain chemicals have a specific activity. Acetaminophen, allyl alcohol, bromobenzene, and beryllium causes necrosis but not fatty liver. However, allylformate, ethanol, cycloheximide, and cesium cause fatty liver but no necrosis. Exposure to fumes of volatile halogenated hydrocarbons (e.g., chloroform, carbon tetrachloride, and bromobenzene) through the lungs is a leading cause of occupational liver injury. Hepatotoxins can reach the liver as tiny particles from the gastrointestinal system. Inhaled particles are ejected from the bronchi or trachea, entering the oral cavity and swallowed with saliva.

While both natural and manufactured substances can induce liver cancer in animals, the incidence of primary liver cancer in people is minimal in the United States. Naturally occurring liver carcinogens include aflatoxin, cycasin (a glycoside from cycad nuts), and safrole (found in sassafras and black pepper). Animals can get liver cancer from synthetic substances such as dialkylnitrosamines, organochlorine insecticides, PCBs, and dimethylbenzanthracene. Workers exposed to vinyl chloride in polyvinyl plastic manufacturing factories developed angiosarcoma, a rare blood vessel malignancy, which is the most well-known case of occupational liver cancer. Industrial toxins can have serious effects on the hematological and neurological systems.

Hematopoietic Toxins: Benzene, a hematological toxin, is commonly found in motor fuel, industrial solvents, and chemical synthesis. Chronic exposure to benzene fumes causes pancytopenia, or decreased formation of all types of blood cells (erythrocytes, leukocytes, and platelets). The long-term consequence of benzene exposure is acute leukemia. Lead is a hematopoietic toxin. It inhibits the manufacture of porphyrin, a crucial component of hemoglobin. Lead poisoning can cause severe anemia, among other symptoms.

Neurotoxins: Toxic metals include lead, thallium, tellurium, mercury (particularly organic compounds), and manganese, which can harm the nervous system. This article discusses the nephrotoxicity of lead and its main sources of exposure. Lead and its derivatives are harmful to both the central and peripheral neurological systems. Chronic lead exposure affects adults differently than children. In adults, occupational exposure to lead fumes and dust induces a peripheral nervous system condition known as peripheral neuropathy. The majority of lead exposure in children comes from paint, water, and soil. The condition alters brain structure and is known as encephalopathy. Neurotoxic metals can enter the body through inhalation of vapors or dust (e.g., mercury, tellurium, manganese), or skin absorption (thallium).

9.10 TYPES OF LIVER DAMAGE

Chemical injuries to the liver vary depending on the toxic chemical, intensity of the poisoning and duration of exposure (acute or chronic). There are six types of liver damage: fatty liver, necrosis,

hepatobiliary dysfunctions, virallike hepatitis, and (with chronic exposure) cirrhosis and neoplasia. This section covers all sorts of harm except neoplasia (liver cancer), which is addressed in the Hepatotoxins section below.

Fatty liver: Fatty liver is the abnormal buildup of fat in hepatocytes. This syndrome is characterized by a simultaneous reduction in plasma lipids and lipoproteins. Disruptions in lipoprotein production or secretion can contribute to fat storage. As lipids accumulate in the liver, blood biochemistry changes. Serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), 3 alkaline phosphatase, and 50-nucleotidase levels rise, while blood-clotting factors and cholesterol decrease. Blood chemistry analysis is thus an effective diagnostic tool.

Liver Necrosis: Liver necrosis is a degenerative process resulting in cell death. Necrosis can occur in isolated hepatocyte foci or over an entire lobe or both lobes. Massive necrosis is defined as the involvement of whole lobes. The mechanism of necrosis remains uncertain. Blood chemistry alterations are similar to those seen in fatty liver, but more significant.

Hepatobiliary Dysfunctions: Hepatobiliary Dysfunctions Cholestasis, a reduction or full halt of bile flow, is a sign of hepatobiliary dysfunction. Bile salts and bilirubin are retained as a result, with bilirubin retention causing jaundice. The cause of cholestasis is unclear, but alterations in membrane permeability of hepatocytes or biliary canaliculi, as well as canalicular plug development, have been linked. SGOT and SGPT are elevated only slightly or not at all, but alkaline phosphatase, 50-nucleotidase, and cholesterol are greatly elevated. These hepatobiliary dysfunctions are usually induced by drugs (such as anabolic and contraceptive steroids) but are not likely to be induced by occupational exposure.

Cirrhosis: Cirrhosis is defined by the accumulation of collagen throughout the liver. Cirrhosis can be induced by chronic chemical injury or a single incidence of severe liver cell loss. Fibrous substance deposition distorts blood arteries and restricts blood flow. Poor blood flow disrupts the liver's regular metabolic and detoxifying activities. Toxin buildup occurs when the detoxification mechanism is disrupted, resulting in additional damage and potential liver failure.

9.11 CHEMICAL-INDUCED LIVER INJURY

Hepatotoxicity is classified based on the pattern of incidence and histological morphology. Intrinsic hepatotoxicants have a broad incidence, a dose-dependent relationship, and typically exhibit similar toxicities in humans and animal models. Idiosyncratic hepatotoxicants have restricted toxicity in susceptible individuals due to hypersensitivity or atypical metabolic conversions caused by drug metabolizing gene polymorphisms. Liver injury varies depending on the toxic substance, level of intoxication, and duration of exposure (acute or chronic). This section provides a brief overview of the primary types of liver injury. Hepatotoxicity is characterized by reduced hepatocyte function and viability, which can be shown histological as steatosis (fatty liver), cholestasis, fibrosis, necrosis, or apoptosis. Some types of damage, such as cholestasis, are specific to the liver, whereas others, including necrosis and carcinogenesis, are more widespread. Damaged liver cells produce certain enzymes, including ALT, AST, and alkaline phosphatase, into the blood. Biomarkers for hepatocyte injury include ALT and AST, while alkaline phosphatase shows damage to the bile duct epithelial cells. Enzymes are frequently examined in clinical and animal research to identify hepatotoxicity.

Histological change: The liver is vulnerable to toxicity from medicines, xenobiotics, and oxidative stress due to its unique metabolism and connection to the gastrointestinal tract. Drug metabolism, lipid peroxidation, and thiol oxidation are common causes of liver damage. Chemicals can be classed based on the region of the lobule that is affected. Carbon tetrachloride, beryllium, and phosphorus are examples of hepatotoxicants that can cause centrilobular, midzonal, or periportal effects.

Table 9.1: Appearance of alterations in the liver under microscopic examination

Lesion type	Cause	Examples
Necrosis	cell death, acute exposure to a hepatotoxic agent	Carbon tetrachloride, beryllium
Steatosis	intracellular fat accumulation	Carbon tetrachloride, ethanol
Cholestasis	slowing of bile flow, describe any interference with biliary function	Organic arsenicals
Apoptosis	chronic active hepatitis, associated with immune cell-induced cytotoxicity, sole cause of chemical-induced damage	Uncertain
Immune cell infiltrate	conjunction with chemical-induced cell injury, debris removal function	-
Fibrosis/cirrhosis	ongoing liver injury, long-term exposure	Carbon tetrachloride, trinitrotoluene
Neoplasia	hepatic carcinoma being the most common type of cancer	Carbon tetrachloride, vinyl chloride
Mixed	ore than one type of histological alteration	Carbon tetrachloride

Many chemicals cause liver injury in a manner that is normally expected, that is, in a predictable way with clear evidence of a dose-effect relationship. This unpredictable hepatotoxicity has also been referred to as an 'idiosyncratic response', which may have an immunological basis resulting in a hypersensitivity type reaction, or it may be related to a metabolic imbalance. Hepatotoxicants can be classified by the organelle they primarily impact, which is a less prevalent strategy. Chemicals have been identified as primarily harmful to mitochondria, endoplasmic reticulum, plasma membrane, lysosomes, and cytoskeleton. If serious injury does occur to one or other of these organelles then death of the cell may result.

Liver damage can be identified through various procedures, including external palpation, enlargement and soreness, blood enzyme testing, and needle biopsy.

Acute hepatotoxicity can be identified with basic noninvasive tests; however, subacute and chronic liver damage are more difficult to detect. Table 6.3 lists the procedures for testing for liver damage due to chemical exposure.

- Physical examination
- Clinical chemistry
- Enzymes
- Bilirubin

- Bile salts
- Proteins
- Histopathology
- Light microscopy
- Electron microscopy
- Organ function tests
- Dye excretion
- Drug biotransformation

Fatty Liver: Fatty liver, also known as steatosis, is the abnormal buildup of lipids in hepatocytes, primarily as triglycerides, caused by an imbalance between extrahepatic triglyceride uptake and hepatic production of triglyceride-containing lipoproteins and fatty acid catabolism. Toxicants can cause lipid buildup in the liver (Table 13.1), however the processes may vary. Lipid buildup is caused by abnormal lipoprotein production or secretion. Excess lipid can be caused by excess free fatty acids from adipose tissues or poor triglyceride release from the liver into the bloodstream. Triglycerides are secreted by the liver as lipoproteins, including very low density lipoprotein (VLDL). As hypothesized, there are several places at which this process can be disturbed.

Cholestasis: Cholestasis is the suppression or blockage of bile flow caused by either intrahepatic or extrahepatic sources. When the bile ducts become obstructed or blocked, bile salts and bilirubin accumulate, causing jaundice. Other causes of cholestasis include membrane permeability alterations in hepatocytes or biliary canaliculi. Bile is formed and transported into the canalicular lumen by ATP-dependent mechanisms. Chemicals that affect cellular Na+ and K+ gradients can impair the ATP-dependent flow of bile, leading to cholestasis. Cholestasis is typically induced by drugs (Table 9.2) and is challenging to replicate in experimental animals. Again, variations in blood chemistry can be used as a diagnostic technique.

Table. 9.2: Cholestasis (Drug Induced)

Cholestasis (Drug Induced)		
Chlorpromazine	Imipramine	Carbarsone
Promazine	Diazepam	Chlorthiazide
Thioridazine	Methandrolone	Methimazole
Mepazine	Mestranol	Sulfanilamide
Amitriptyline	Estradiol	Phenindione

Necrosis: Necrosis is the permanent loss of cell viability caused by a loss of normal function. Necrosis, which is typically an acute damage, might be localized and impact only a few hepatocytes (focal necrosis) or affect the entire lobe. Cell death occurs when the plasma membrane ruptures and is preceded by morphologic changes such as cellular swelling, endoplasmic reticulum dilation, triglyceride accumulation, mitochondrial swelling with cristae disruption, organelle dissolution, and a shrunken nucleus. Necrosis causes eosinophilic staining in the cytoplasm and an immunological response, with neutrophils infiltrating the affected area. Reactive metabolites can bind to proteins and unsaturated

lipids, causing membrane destruction, disrupting Ca^{2+} homeostasis, interfering with metabolic pathways, altering Na^{+} and K^{+} balance, and inhibiting protein synthesis.

Apoptosis: Apoptosis, a controlled form of cell death, regulates biological processes and serves as a counterweight to mitosis. This "ordered" mode of cell death, unlike necrosis, is most active during development and senescence. Exogenous stimuli, such xenobiotic substances, oxidative stress, anoxia, and radiation, can promote apoptosis, which is a natural physiological process. Morphologic criteria, such as light or electron microscopy, can distinguish apoptosis from necrosis. The absence of inflammatory infiltration is a hallmark of apoptosis. Toxicants, on the other hand, do not always behave in a straightforward manner, and some toxicants can cause both apoptosis and necrosis at the same time or in sequence.

Hepatitis: Hepatitis is often caused by a viral infection of the liver. However, certain substances, such as medications, can also cause hepatitis similar to viral infections. This form of liver injury causes an increase in immune cells and may be linked to certain hepatotoxicants like diclofenac. This distinctive response is typically not shown in laboratory animals and may only affect vulnerable individuals. Fortunately, the occurrence of this condition is extremely low.

Carcinogenesis: Hepatocellular carcinoma is the most frequent type of primary liver cancer, with other types including cholangiocarcinoma, biliary cystadenocarcinoma, and undifferentiated liver cell carcinoma. Naturally occurring liver carcinogens include aflatoxin, cycasin, and safrole. Animal studies have linked several synthetic compounds to liver cancer, including dialkylnitrosamines, dimethylbenzanthracene, aromatic amines like 2-naphthylamine and acetylaminofluorene, and vinyl chloride. Workers exposed to high amounts of vinyl chloride in manufacturing plants are more likely to develop angiosarcoma, a rare blood vessel malignancy, which is the most common cause of occupational liver cancer in humans.

9.12 MECHANISM OF HEPATIC INJURY

Understanding how chemicals induce liver injury is crucial for preventing and treating the condition. The liver has gotten greater attention than other organs in this regard, most likely due to the high number of compounds that target the liver. This could be attributed to the abundance of biotransformation enzymes in the endoplasmic reticulum. The availability of in vitro liver preparations with in vivo properties may also contribute to investigations on the hazardous agent's mechanism of action. Despite thousands of publications published over the last 40 years, there is still no clear knowledge of the pathways involved in cell death caused by hazardous agents. The role of each mechanism in cell death is supported by evidence, however conflicting evidence makes causality difficult to establish. The notion that lipid peroxidation causes liver harm from certain substances is appealing due to its autocatalytic nature once launched. However, some experimental evidence suggests that lipid peroxidation can be controlled without preventing cell death. This obviously indicates that peroxidation is not directly responsible for the death of cells caused by the chemical. Similarly, covalent binding of reactive metabolites to cellular macromolecules and disturbances in calcium ion homeostasis have strong experimental support. Some critical data also contradicts unequivocal adoption of them as the primary event in cell death. The notion of inhibiting protein synthesis has lost favor due to inconsistent timing with other observations in cell death. The timing of the occurrence led to a decline in the importance of mitochondria as a crucial cause. Recently, there has been a renewed focus on how mitochondrial damage contributes to cell death. Mechanisms of liver injury are such as:

- Lipid peroxidation
- Covalent binding
- Alteration of calcium homeostasis

- Alteration of protein synthesis
- Depletion of protein thiols
- Mitochondrial dysfunction
- Immune-mediated
- Endonuclease and apoptosis
- Interference with triglyceride secretion
- DNA damage

The immunological component refers to the hypersensitive reactions mentioned before. Some substances may behave as haptens, binding to tissue components and triggering an immune response. This may result in cell destruction. Apoptosis may play a role in this process, as multiple studies have linked it to lymphocytotoxicity. Certain substances may activate apoptosis-related enzymes, leading to cell destruction. The suppression of triglyceride secretion is indicated as the last mechanism.

The suppression of triglyceride secretion is listed last because, while it contributes to steatosis, fat accumulation does not always lead to hepatocyte mortality. Many substances can induce liver harm in workers. Previously, exposure to chemicals like carbon tetrachloride has been linked to acute and chronic liver harm in workers. Improvements in workplace environment and knowledge have reduced the frequency of such examples. Case reports of workers having liver injury after handling chemicals like dimethyl formamide and methylene dianiline show that these incidents still happen. Chemical groups (e.g. organic solvents) may be listed if multiple compounds have been linked to a specific response.

Table: Examples of workplace exposures thathave resulted in hepatic toxicity

Exposure	Agent	Type of lesion
Acute	Organic solvents	Mixed
Short-term repeated dose	Tetrachloroethane, trinitrotoluene	Acute or ongoing necrosis, may progressto cirrhosis
Chronic	Arsenicals, vinyl chloride, organicsolvents	Fibrosis, cirrhosis, cancer

9.13 CHRONIC LIVER INJURY

The liver is an organ located on the right side of the abdomen, just below the rib cage. It can weigh up to 4 pounds (1.8 kg). The liver is required to assist digest food, cleanse the body of waste items, and produce compounds known as clotting factors that keep the blood flowing properly, among other duties. A liver injury, often known as a laceration, is a type of damage to the liver. This can be caused by either a blunt force, such as a vehicle collision, or a piercing foreign instrument, such as a knife. Liver injuries account for 5% of all traumas, making it the most prevalent abdominal injury. In most cases, nonoperative care and observation are sufficient for complete recovery. Chronic liver injury is characterized by the slow breakdown of liver tissue over time.

Because of its front position in the abdominal cavity and large size, the liver is vulnerable to gunshot and stab wounds. Its solid placement beneath the diaphragm also makes it susceptible to shearing forces. This sort of injury is commonly caused by blunt force mechanisms such as car

accidents, falls, and sports injuries. Typically, these blunt forces disperse through and around the liver structure, causing irreversible damage to the tissue's interior microstructure.

Imaging, such as using ultrasound or a computed tomography scan, is the recommended method of diagnosis since it is more accurate and sensitive to bleeding; but, due to logistical constraints, this is not always available. If a person is hemodynamically unstable, a focused assessment with sonography for trauma (FAST) scan may be performed to detect free floating fluid in the right upper quadrant and left lower quadrant of the abdomen. The FAST scan, however, may not be recommended for obese people or those with subcutaneous emphysema.

Liver injuries are classified on a Roman numeral scale with I being the least severe, to V being the most severe, according to the AAST (American Association for the Surgery of Trauma) liver injury scale. In the case of multiple liver injuries with different grades, the overall grade should be classified by the higher grade of injury. One grade should also be added in case of multiple injuries, up to grade III shown in table

Table : The Liver Injury Scale classification (2018 revision)

Grade	Subcapsular hematoma	Laceration	Vascular injury
I	<10% surface area	<1 cm in depth	-
II	10–50% surface area	1–3 cm	-
III	>50% or >10 cm	>3 cm	Any injury in the presence of a liver vascular injury or active bleeding contained within liver parenchyma
IV	--	25–75% of a hepatic lobe	Active bleeding extending beyond the liver parenchyma into the peritoneum
V	--	>75% of a hepatic lobe	Juxtahepatic venous injury to include retrohepatic vena cava and central major hepatic veins

The first therapy of liver trauma is largely the same as for other traumas, with an emphasis on maintaining airway, breathing, and circulation. A physical examination is a cornerstone of the assessment, and several non-invasive diagnostic instruments can be used. Surgery is typically required for serious liver damage (class ≥III) or hemodynamic instability. Hemorrhage can be controlled using surgical procedures such as perihepatic packing or the Pringle manoeuvre. Direct manual pressure applied to the wound site can provide temporary bleeding control. The common cause of death while operating is exsanguination caused by profuse loss of blood volume.

9.14 SUMMARY

Pulmonary toxicity is the damage or harm done to the lungs by a range of substances, including chemicals, drugs, pollutants, and radiation. It addresses a wide range of conditions, such as acute respiratory distress syndrome (ARDS), chronic obstructive pulmonary disease (COPD), and lung cancer. Acute pulmonary poisoning frequently produces inflammation, edema, and reduced gas exchange, leading to symptoms such as coughing, shortness of breath, and chest pain. Severe cases could result in

respiratory collapse and death. Chronic pulmonary toxicity is a common result of persistent exposure to harmful substances. It can result in irreversible lung damage, fibrosis, and impaired lung function. Occupational exposure to asbestos, silica, or coal dust is a typical source of chronic lung damage. Certain medications, such as chemotherapeutic agents and antibiotics, can produce lung toxicity as an adverse reaction. Radiation therapy for chest cancers can harm lung tissue, resulting in radiation pneumonitis or fibrosis. To minimize pulmonary toxicity, limit exposure to dangerous substances, use protective equipment in occupational situations, and closely monitor patients receiving potentially toxic medications or radiation therapy. Early detection and treatment are crucial for minimizing the impact of pulmonary toxicity on lung function and overall health. Treatment may involve discontinuing the offending substance, providing supportive care, administering oxygen therapy, and, in severe situations, doing lung transplantation. Hepatic toxicity is the damage or injury to the liver produced by a variety of reasons, including drugs, poisons, infections, and metabolic abnormalities. The liver is essential for metabolism, cleansing, and nutrient storage, therefore any damage can be severe. Acute hepatic toxicity is characterized by symptoms such as jaundice, stomach discomfort, nausea, vomiting, and exhaustion. In severe situations, it can lead to fulminant liver failure, a life-threatening illness that necessitates prompt medical intervention. Chronic liver damage develops gradually and may initially be asymptomatic. However, if liver damage worsens, symptoms like weight loss, abdominal edema, itching, and easy bruising may develop. Chronic liver injury can progress to cirrhosis, which is defined by irreversible scarring of the liver tissue and reduced liver function. Hepatic toxicity can be caused by a variety of reasons, including alcohol addiction, viral hepatitis (such as hepatitis B and C), autoimmune illnesses, certain medications (such as acetaminophen, statins, and chemotherapy treatments), and environmental pollutants.

9.15 TERMINAL QUESTION

Q. 1. What do you understand about respiratory system, discuss about respiratory disease.

Answer:----------

Q. 2. What do you understand about pulmonary toxicity?

Answer:----------

Q. 3. Discuss about liver and its physiology.

Answer:----------

Q. 4. What are the lungs toxins? Discuss about systematic lung toxins.

Answer:----------

Q. 5. Discuss about actions of toxins on the liver.

Answer:----------

Q. 6. What do you know about liver injury? Discuss about chronic liver injury.

Answer:----------

Q. 7. Discuss about chemical-induced liver injury and its toxicants.

Answer:----------

9.16 FURTHER SUGGESTED READINGS

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Environmental Toxicology and Occupational Health Hazards

BLOCK

4

CARCINOGENESIS AND TESTING METHODS

UNIT-10

Carcinogenesis and Mutagenic

UNIT-11

Transformation of Toxicants

UNIT-12

Occupational Toxicology

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BLOCK INTRODUCTION

The following three units are included in the fourth block of Environmental toxicology & occupational health hazards are as:

Unit 10 : This unit discusses carcinogenesis and the toxicity of carcinogens. This unit discusses the many kinds of carcinogens and the process of carcinogenesis. The succinct explanation of mutagenesis, kinds of mutation, and mutagenicity

Unit-11 : The topics of bioaccumulation, biomagnifications, and biotransformation are covered in this section. This section also briefly discusses the many forms of biotransformation, the biotransformation of DDT, and hazardous materials in the environment.

Unit-12 : This unit addresses exposure limits, risks related to hazardous compounds, and occupational toxicants. This topic covers occupational/industrial hygiene, hazard control, and risk assessment and management principles.

UNIT-10 : CARCINOGENESIS AND MUTAGENICITY

10.1 INTRODUCTION

The complex processes of mutagenesis and carcinogenesis are what lead to the development of cancer. Mutagenesis is the process of causing genetic mutations, whereas carcinogenesis is the process of cancer creation. Although these processes that can occur on their own, they are typically triggered by mutations, which play a significant role in cancer formation. Mutations are DNA sequence variations that occur spontaneously during DNA replication or are caused by outside factors known as mutagens. Mutagens include viruses, chemicals, and radiation (e.g., ionizing radiation or UV light). These compounds have the ability to directly damage DNA or hinder its replication, which can lead to genetic code errors. Mutations can disrupt genes that regulate cell division, growth, and death, interfering with normal cellular functioning and eventually leading to cancer. These genes include tumor suppressor genes, which inhibit tumor growth, and oncogenes. Mutations in these genes can result in the loss of control over apoptosis, DNA repair pathways, and cell cycle progression. According to the multistep model of carcinogenesis, cancer is caused by a series of genetic alterations that occur over time. According to this paradigm, normal cells move through premalignant stages before acquiring additional mutations that lead to increasingly malignant traits. This process includes three critical phases: initiation, promotion, and advancement. The first genetic mutation caused by a mutagen that offers the affected cell a growth advantage is known as initiation. Promotion is the process by which the initial cell population expands due to new mutations and changes in the surrounding tissue. Ultimately, progression implies that the disease becomes more capable of spreading and becoming invasive, resulting in the establishment of clinically visible malignancy. Understanding the causes of mutagenesis and carcinogenesis is critical to cancer prevention, diagnosis, and treatment. Researchers and clinicians work to improve cancer patients' prognoses by identifying and lowering mutagen exposure, developing

customized treatments against specific mutations, and using the body's immune system to recognize and eliminate malignant cells.

Objectives :

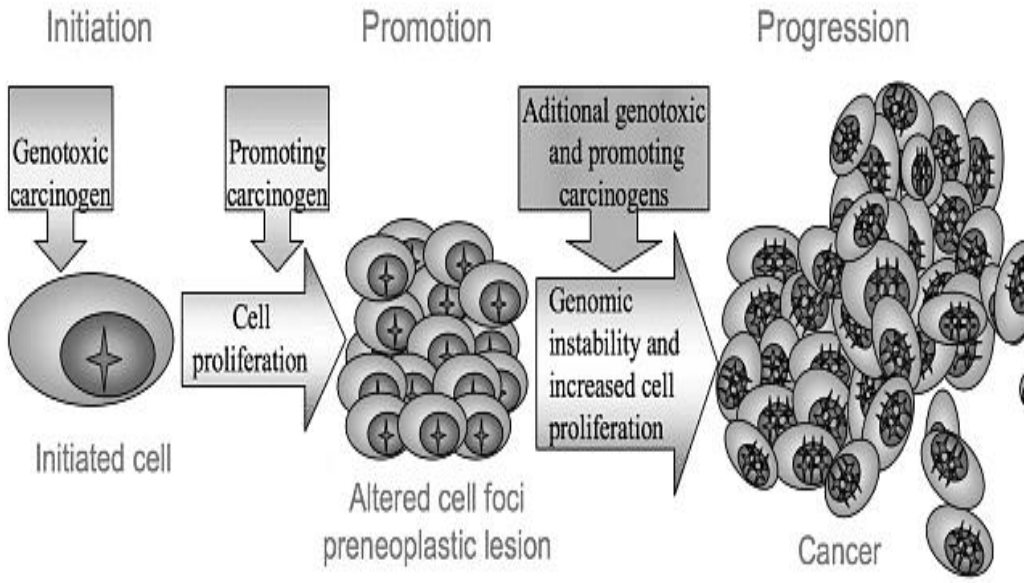
After reading this unit, the learner will be able to know

- Carcinogens and carcinogenesis and its types and effects on living beings
- Mutation and mutagenesis effects on living beings
- Mechanism to mutagenesis and factor effecting of mutagenesis.

10.2 CARCINOGENS

Substances or agents with the potential to cause cancer are known as carcinogens. They exist in a variety of forms, such as biological agents, chemicals, and radiation. Carcinogens work by either directly or indirectly causing damage to DNA, which can result in mutations and the growth of malignant cells. Among the most well-known types of carcinogens include those found in tobacco smoke, some industrial chemicals, pesticides, and pollution. By interacting with cellular DNA and altering its structure and function, these substances can enter the body by ingestion, inhalation, or skin contact. The process of carcinogenesis is commonly understood to consist of multiple phases, including initiation, promotion, and progression. The first genetic change that gives a single cell a growth advantage and increases its susceptibility to subsequent mutations is known as initiation. Exposure to carcinogens like chemicals, radiation, or viruses can cause this first mutation. Tobacco smoke, for instance, has a variety of carcinogens that can damage lung cells' DNA and cause lung cancer to develop. The normal regulation of cell growth, division, and death is disrupted by the accumulation of genetic abnormalities leading to cancer. These mutations can impact a variety of genes, including tumor suppressor genes and oncogenes, and they can be inherited or acquired throughout life. Tumor suppressor genes prevent these processes and, when required, encourage cell death, whereas oncogenes encourage cell division and survival. Mutations in these genes can cause cells to become less able to control their growth, which can result in unchecked growth and the development of tumors. After initiation, which is aided by carcinogens, the initiated cells expand clonally to form a population of pre-malignant cells. Additional genetic and epigenetic changes that improve cell survival and proliferation take place at this stage, which is referred to as promotion. These modifications could involve new mutations in tumor suppressor or oncogene genes, as well as adjustments to the cellular milieu that fosters tumor development. For example, environmental pollutants or infections can cause persistent inflammation, which might encourage the growth of started cells and raise the risk of tumor development. Further genetic changes that facilitate invasion and metastasis, which allow cancer cells to migrate from their site of origin to distant organs, are acquired by the tumor as it advances. Alterations in genes related to cell adhesion, motility, and angiogenesis occur during this stage, which is referred to as progression. These alterations facilitate the invasion of nearby tissues and the development of secondary tumors at distant locations. Because it frequently makes tumors resistant to traditional medications and complicates treatment plans, metastasis is a significant factor in determining cancer mortality. Despite the fact that carcinogenesis is a complicated and varied process, certain similar pathways and mechanisms have been linked to several cancer forms. A possible strategy for treating cancer is to target these pathways with particular medicines, such as immunotherapies or medications with specific targets on their molecules. Cancer incidence can also be decreased by initiatives to detect and lessen exposure to recognized carcinogens through regulatory actions and public health campaigns. In the end, a better comprehension of the molecular processes behind carcinogenesis will aid in the

creation of methods for cancer diagnosis, prevention, and therapy that are more successful. Chemical compounds contain chemicals known as chemical carcinogens that can lead to cancer. These carcinogens, which might be manmade or naturally occurring, are frequently found in consumer goods, industrial settings, and environmental pollution. It is essential to comprehend how chemical carcinogens contribute to the development of cancer in order to evaluate and reduce cancer risk.



What is the Cancer

Cancer is the uncontrolled proliferation of cells of the body. Tumor cells typically develop in rapidly dividing cells such as those of the skin and often spread to other parts of the body. Hundreds of different types of cancer exist and many behave differently, a fact that has complicated efforts to find a cure for the disease. Cancer is one of the most dangerous outcomes of cell mutations (defined shortly). According to recent data, one in three women and one in two men in the United States will experience some kind of cancer. An estimated 560,000 Americans lose their lives to cancer each year in the US. The World Health Organization estimates that there are roughly six million fatalities globally each year. Two experts from Oxford University claim that environmental variables including air pollution cause 8,000 cancer deaths in the United States annually. Another 8,000 cancer deaths are linked to industrial items like insecticides used around the house and food additives: Each year, occupational exposure to hazardous substances causes 16,000 deaths.

Cancer is a disease that occurs when a single cell or a group of cells "escape" from the systems that regulate their growth. Unchecked division of these cells causes the creation of a tumor or neoplasm. In some cases, the tumor is limited to a single growing mass of cells. This is known as benign tumor. Benign tumors can cause complications, such as squeezing nerves or other important structures. A malignant tumor is one that continues to develop and spread into the surrounding tissues and organs. Cells can break off from the main tumor and migrate through the blood and other body fluids to other locations. The spread of malignant cells is called metastasis (meh-TASS-tahsiss). Secondary tumors can arise in remote locations where malignant cells have spread. Certain forms of cancers spread (metastasize) in unique ways. Breast cancer, for example, can extend to the bones. Lung cancer usually spreads to the brain. Malignant tumors are harmful because they continue to grow and require vast amounts of nutrients. They frequently infiltrate nearby locations, destroying essential tissues and organs. Cancers most typically develop in the body's rapidly dividing cells, such as the skin, bone marrow, lungs, and gut lining. Nondividing cells, such as nerve and muscle cells, seldom develop cancer.

Nonetheless, tumors can be formed by a variety of cell types, and there are hundreds of distinct cancers. Not only are there many varieties, but many of them behave differently, complicating efforts to find a cure for the condition. The most likely scenario is that we will discover several therapies, many of which are specific to one type of cancer.

What Causes Cancer?

Cancer can be induced by a multitude of sources, including toxins in our food, physical agents such as X-rays, and biological agents like viruses. Toxic chemicals are the most common carcinogenic (cancer-causing) agents. Carcinogens are chemicals that raise one's risk of developing cancer. Carcinogens typically require several exposures over many years to trigger tumor formation.

10.3 TYPES OF CARCINOGENS

Carcinogenesis appears as a multistage process at molecular level, being triggered either by the action of retrovirus oncogenes, which all induce RNA synthesis and cell division, or by the disturbed, abnormal activity of protooncogenes, one cellular oncogenes. Researchers divide carcinogens into three main categories. These include:

10.3.1 Chemical Carcinogens

Chemical carcinogens induce cancer by a variety of mechanisms, including mutagenesis, DNA damage, and interference with cellular signaling networks. A typical procedure involves the formation of reactive intermediates that can react with DNA to cause genetic mutations and DNA adducts. For example, grilled meals and tobacco smoke contain polycyclic aromatic hydrocarbons (PAHs), which can be metabolically activated to produce reactive intermediates that bind to DNA and cause mutations, particularly in genes involved in tumour suppression and cell cycle regulation. Chemical carcinogens can also cause cancer by inhibiting DNA repair pathways. Certain chemicals can disrupt DNA repair processes, allowing DNA damage to accumulate and increasing the risk of mutations and cancer. These molecules include aromatic and heterocyclic amines, which can be found in industrial chemicals and charred meats. Chemical carcinogens can also disrupt cellular signaling pathways, which are required for cell division, growth, and apoptosis. Certain carcinogens, for example, mimic the effects of growth factors or hormones, resulting in uncontrolled cell proliferation and tumor formation. Others may promote cancer growth by directly activating oncogenes or inhibiting tumor suppressor genes. Chemical structure and mode of action enable the classification of chemical carcinogens into numerous classes. Cancer prevention includes detecting and regulating chemical carcinogens. To reduce risks to public health, regulatory bodies such as the International Agency for Research on Cancer (IARC) and the Environmental Protection Agency (EPA) identify and control cancer-causing substances. Chemical carcinogen exposure in the workplace and environment can be reduced by implementing consumer product labeling, environmental laws, and occupational safety standards. Furthermore, public health measures such as food standards and smoking cessation programs can help reduce the risk of cancer associated with chemical carcinogen exposure through lifestyle choices.

Typical chemical carcinogen classes include the following:

1. **Polycyclic aromatic hydrocarbons or PAHs:** These are compounds that are commonly found in burnt food, automobile exhaust, and tobacco smoke. They are composed of numerous fused aromatic rings. Reactive intermediates produced when PAHs are metabolically activated can bind to DNA and cause mutations, increasing the risk of bladder, lung, and other cancers.

2. **Aromatic amines:** These substances, which are present in industrial chemicals, dyes, and medications, are composed of an aromatic ring and an amino group. When reactive intermediates from the metabolism of aromatic amines attach to DNA and cause mutations, bladder, liver, and other malignancies can result.

3. **Nitrosamines:** These are substances that include a nitroso group (–NO) and are present in processed foods, tobacco smoke, and some makeup products. Nitrosamines have the ability to cause mutagenesis and damage to DNA, especially in the gastrointestinal system and liver, which raises the risk of stomach and liver cancer.

4. **Alkylating agents:** These are substances that have the ability to add alkyl groups to DNA, resulting in the creation of genetic alterations and DNA adducts. Alkylating agents raise the incidence of leukemia, lymphoma, and other malignancies. They are present in several industrial chemicals, chemotherapy medications, and environmental pollutants.

5. **Metals and metalloids:** Because they can harm DNA and interfere with biological functions, several metals and metalloids, including nickel, chromium, and arsenic, has been labeled as carcinogens. These carcinogens increase the risk of lung, skin, and other cancers. They are frequently found in mining operations, industrial processes, and contaminated drinking water.

10.3.2 Physical Carcinogens

Physical carcinogens are agents that have the potential to cause cancer due to their physical properties or interactions with biological systems. These agents include many types of radiation and environmental factors that predominantly damage cellular DNA or interfere with normal cellular activities, hence causing cancer. Understanding how physical carcinogens contribute to the development of cancer is critical for assessing and reducing cancer risk.

1. **Ionizing Radiation:** Ionizing radiation refers to high-energy particles or electromagnetic waves capable of ionizing atoms and molecules. This process produces reactive species, such as free radicals, which have the potential to damage DNA. Sources of ionizing radiation include radioactive isotopes, gamma rays, and X-rays. Ionizing radiation can cause a wide range of malignancies depending on the dose, duration, and kind of radiation exposure.

2. **X-rays and Gamma Rays:** Patients are exposed to ionizing radiation during medical imaging techniques such as computed tomography (CT) scans and X-rays, increasing their risk of developing cancer, particularly leukemia and solid tumors. Workers in the healthcare industry may be at risk due to work exposure to gamma and X-rays.

3. **Radioactive Isotopes:** Exposure to radioactive isotopes, such as radon gas and radionuclides from industrial activity or nuclear accidents, increases the risk of developing lung cancer. Lung cancer is mostly caused by radon gas, a naturally occurring radioactive gas produced when uranium in rocks and soil decays. This is especially true in areas where indoor radon levels are elevated.

4. **Ultraviolet (UV) Radiation:** Ultraviolet radiation is a form of electromagnetic radiation produced by artificial sources such as tanning beds and sunlight. UV rays can permeate through skin and damage DNA, primarily in the form of thymine dimers. These damages can cause mutations and skin cancer. There are three basic categories of UV radiation: UVA radiation, which enter the skin deeper, can cause skin cancer, including melanoma, as well as premature aging. UVB light primarily damages the epidermis and is the leading cause of skin cancers other than melanoma, such as squamous and basal cell carcinoma. Although UVC radiation cannot reach the Earth's surface because it is absorbed by the atmosphere, some man-made sources, such as germicidal lamps, are employed for disinfection.

5. **Visible and Infrared Radiation:** Long-term exposure to strong sources of visible and infrared radiation, such as direct sunlight or heat sources, can damage skin and raise the risk of skin cancer, even though these radiations are typically thought to be less dangerous than ionizing and UV radiation.
6. **Electromagnetic Fields (EMFs):** Electrical appliances, power lines, and wireless communication equipment all generate electromagnetic fields. Some studies have found a correlation between long-term exposure to high levels of EMFs and an increased risk of leukemia, brain tumors, and other cancers, despite ongoing debate and research into the possibly carcinogenic effects of EMFs. However, further research is needed to establish the link between EMFs and cancer, as the evidence remains inconclusive.
7. **Temperature:** Extreme heat or cold can stress and harm cells, indirectly increasing oxidative stress, DNA damage, and inflammation, all of which can contribute to cancer formation. Long-term exposure to high temperatures, such as in hot climates or in some industrial settings, may increase the risk of getting skin cancer and other cancers.
8. **Mechanical Forces**Physical forces such as shear stress, tension, and compression can have an impact on cellular function and contribute to cancer formation. Persistent mechanical stress and tissue injury can generate an environment that promotes cancer growth and metastasis, as well as inflammation, tissue remodeling, and DNA damage.
9. Physical carcinogens can induce cancer through several mechanisms, including DNA damage, cellular disruption, and oxidative stress and inflammation. Reducing physical carcinogen exposure by occupational safety rules, lifestyle adjustments, and other ways can reduce the risk of cancer while improving public health outcomes. Developing effective cancer prevention and treatment strategies also requires ongoing study into the mechanisms of action and health effects of physical carcinogens.

10.3.3 Biological Carcinogens

Biological carcinogens are compounds produced through biochemistry that interact with biological systems to cause cancer. Viruses, bacteria, parasites, and certain types of fungi all play a role in the development of cancer in humans and other animals, either indirectly or directly. Recognizing and minimizing the cancer risk posed by infectious pathogens necessitates an understanding of biological carcinogens' function in cancer development.

1. **Viruses:** Viruses are infectious pathogens that can introduce their genetic material into host cells, altering how they function and perhaps hastening the genesis of cancer. Numerous viruses, including the following, have been linked to biological carcinogens: Papillomavirus in humans The sexually transmitted virus known as HPV mostly affects the skin and mucous membranes by infecting epithelial cells. Cervical, anal, vaginal, and oropharyngeal cancers can arise from persistent infection with high-risk HPV strains, such as HPV-16 and HPV-18. These modifications in the cells can lead to these malignancies. Cervical cancer is assumed to be caused predominantly by HPV infection, and HPV vaccination has been shown to reduce the incidence of HPV-related malignancies. The herpesvirusEpstein-Barr Virus (EBV) infects B and epithelial cells, causing infectious mononucleosis (mono) and associated diseases. Several malignancies, including Burkitt lymphoma, Hodgkin lymphoma, nasopharyngeal carcinoma, and gastric carcinoma, have been linked to EBV infection. EBV may contribute to the development of cancer due to its ability to stimulate cellular proliferation, inhibit apoptosis, and modify immune responses. Hepatitis B and C viruses infect liver cells, resulting in cirrhosis, hepatocellular carcinoma (liver cancer), and chronic hepatitis. Prolonged HBV or HCV infection

can lead to fibrosis and inflammation in the liver, which raises the possibility of genetic abnormalities and the emergence of cancer. The incidence of HBV-related liver cancer has been successfully decreased by HBV immunization and antiviral medications. Adult T-cell leukemia/lymphoma (ATLL) and other hematological malignancies are linked to the infection of T cells by the retrovirus known as Human T-cell leukemia virus-1 (HTLV-1). HTLV-1 infection may contribute to cancer formation by causing immune response dysregulation and clonal expansion of infected T cells.

2. **Bacteria:** Several bacterial infections, particularly in the gastrointestinal tract and other mucosal surfaces, have been linked to an increased risk of cancer. By causing genotoxic chemicals, altering host immunological responses, and causing chronic inflammation, bacterial carcinogens can accelerate the development of cancer. The main culprit behind gastric cancer and peptic ulcers is the stomach lining bacterium Helicobacter pylori. The risk of stomach cancer can be raised by a persistent H. pylori infection that causes inflammation, epithelium damage, and genetic instability. In high-risk populations, the incidence of stomach cancer has been demonstrated to decrease with the eradication of H. pylori infection with antibiotic therapy. Certain Escherichia coli (E. coli) strains, including enteropathogenic (EPEC) and enterohemorrhagic (EHEC), have been linked to the emergence of colorectal cancer. These microorganisms have the ability to create genotoxic compounds, like Shiga toxin and Colibactin, which can harm DNA and encourage the development of colon cancer. An increased risk of cancer, mostly in the liver, bladder, and gastrointestinal tract, has been related to parasite infections, particularly those caused by helminths (worms) and protozoa. Parasitic carcinogens can promote cancer formation by suppressing the immune system, causing tissue damage, and increasing chronic inflammation. Hepatocellular carcinoma (liver cancer) and bladder cancer are associated with the schistosoma parasites that cause schistosomiasis. Chronic Schistosoma species infections can induce fibrosis, inflammation, and genetic changes in the bladder and liver, hastening the onset of cancer. In locations where liver flukes such as Opisthorchisviverrini and Clonorchissinensis are common, the risk of developing cholangiocarcinoma, or bile duct cancer, is increased. Persistent liver fluke infections can cause DNA damage, fibrosis and inflammation of the bile ducts, and an increased risk of cancer.

3. **Fungi:** Some fungal species have been linked to a possible risk of biological carcinogenesis, especially in those with weakened immune systems. Through the generation of carcinogenic chemicals, immunosuppression, and persistent inflammation, fungal infections can accelerate the development of cancer. Compared to bacteria, viruses, and parasites, the involvement of fungal carcinogens in the development of cancer is less clear-cut; however, further research is required to clarify their possible contribution to cancer risk.

Overall, biological carcinogens are a diverse group of infectious agents that can induce cancer through a variety of pathways, including immunosuppression, genetic instability, and chronic inflammation. Vaccination, antibiotic treatments, public health programs to restrict infectious agent exposure, and early detection and treatment of infection-related malignancies are all options for lowering the risk of cancer caused by biological carcinogens. Furthermore, in order to develop targeted preventive and therapeutic methods and reduce the global burden of infection-related cancers, ongoing research into the molecular pathways of cancer development associated to infectious agents is critical.

10.3.4 Lifestyle-Related Carcinogens

Lifestyle-related carcinogens, such as environmental, behavioral, and nutritional factors, can increase the risk of cancer when they are present in excess or when they are combined with inherited sensitivity. Numerous factors that can be changed in daily life and are associated with these carcinogens include exposure to pollutants in the environment, poor dietary habits, alcohol and tobacco use, and

physical inactivity. Understanding the role that lifestyle-related carcinogens play in cancer formation is essential to implementing effective prevention strategies and reducing the worldwide cancer burden. Thousands of chemical components, including carcinogens like nitrosamines, heavy metals, and polycyclic aromatic hydrocarbons (PAHs), are found in tobacco smoke.

Smoking is highly linked to an increased risk of lung cancer as well as cancers of the mouth, throat, esophagus, bladder, pancreas, kidney, and cervix. Smoking is the greatest preventable cause of cancer worldwide. Additionally, there is a considerable cancer risk associated with secondhand smoke exposure, especially for nonsmokers who cohabitate with smokers or work in smoke-filled surroundings. A number of malignancies, including those of the mouth, throat, esophagus, liver, colon, rectum, and breast, are linked to excessive alcohol drinking. Alcohol can cause cancer via changing hormone levels, causing damage to DNA, and interfering with DNA repair processes. Higher levels of alcohol use are linked to a higher risk of alcohol-related malignancies, with the risk of cancer being dose-dependent.

A significant risk of cancer has been linked to diets high in processed foods, red and processed meats, saturated fats, and sugary beverages. On the other side, diets rich in fruits, vegetables, whole grains, and lean meats have been associated to a lower risk of cancer. Red and processed meats are two dietary components that have either good or malignant effects: Consuming red and processed meats such as sausage, bacon, pig, and cow is associated with an increased risk of colon cancer. Nitrates and nitrites, which are common additives in processed meats, can cause the body to create cancer-causing chemicals.

Grilling and frying are two examples of high-temperature cooking processes that can emit polycyclic aromatic hydrocarbons (PAHs) and heterocyclic amines (HCAs), which have been linked to an increased risk of cancer. Produce and Fruit: Fruit and vegetable-rich diets provide essential vitamins, minerals, antioxidants, and fiber, all of which have been shown to reduce the risk of cancer. Fruits and vegetables include phytochemicals such as flavonoids, carotenoids, and polyphenols, which have been shown to have anti-inflammatory, antioxidant, and anticancer properties. Eating a range of vibrant fruits and vegetables can help reduce the incidence of lung, breast, prostate, and colorectal cancers, among other cancers. Low risk of colon cancer has been linked to high-dietary fiber diets, especially those high in fruits, vegetables, whole grains, and legumes. Carcinogens may be eliminated from the digestive system and regular bowel movements are encouraged by fiber. Furthermore, short-chain fatty acids are created when gut bacteria ferment dietary fiber; these compounds have been demonstrated to have anti-inflammatory and anticancer properties in the colon. Sweetened Drinks: Sports drinks, fruit juices, soda, and other sugary drinks have been related to a higher risk of type 2 diabetes, obesity, and several cancers, including pancreatic cancer. A high consumption of sugary drinks can cause insulin resistance, weight gain, and chronic inflammation, all of which can accelerate the development of cancer. A higher risk of cancer, specifically colon, breast, and endometrial cancer, has been linked to sedentary behavior and irregular physical exercise. Physical activity can help lower the risk of cancer by improving immune system function, reducing inflammation, controlling hormone levels, and assisting people in maintaining a healthy weight. On the other side, it has been established that prolonged sitting and inactivity raise the risk factors for cancer development, such as obesity, insulin resistance, and chronic inflammation. The risk of cancer has been linked to exposure to environmental pollutants such as pesticides, industrial chemicals, air and water pollutants, and pollution from these sources. These pollutants may enter the body through the skin, food, or inhalation. Once inside the body, they can accumulate in tissues and organs, resulting in oxidative stress, inflammation, and DNA damage. In summary, a broad range of environmental, behavioral, and dietary variables can raise the risk of cancer when they are present in excess or when they are paired with hereditary vulnerability. These variables are referred to as lifestyle-related carcinogens. A balanced diet and regular exercise, avoiding environmental toxins, stopping smoking, drinking alcohol in moderation, maintaining a healthy body weight, and implementing these

lifestyle-related carcinogen-related practices all help to reduce the risk of cancer. Community-based programs, legislative reforms, and public health interventions can help prevent cancer and improve overall health outcomes by encouraging healthy behaviors and lowering carcinogen exposure. To lower the worldwide cancer burden, specific prevention and treatment techniques pertaining to the molecular processes of cancer formation associated with lifestyle-related factors must be developed. This necessitates continuous research.

10.3.5 Occupational Carcinogens

Occupational carcinogens are substances or agents that can cause cancer in people who are exposed to them in a variety of employment settings. During the course of work activities, these carcinogens can be inhaled, consumed, or absorbed via the skin, increasing the risk of cancer over time. To effectively implement workplace safety measures and preserve workers' health, it is imperative to comprehend the role that occupational carcinogens play in the development of cancer.

Lung cancer and other respiratory disorders, as well as mesothelioma, can be brought on by asbestos exposure. Workers in sectors including manufacturing, shipbuilding, construction, and remodeling may be exposed to asbestos when doing tasks including maintaining, renovating, and demolishing asbestos-containing materials. A volatile organic molecule, benzoene is used to make rubber, plastics, detergents, colors, and other compounds. Long-term exposure to benzene fumes or liquids can raise the risk of lymphoma, multiple myeloma, acute myeloid leukemia (AML), and other leukemias.

Workers may be exposed to benzene through skin contact and inhalation in sectors like rubber manufacture, chemical manufacturing, and petroleum refining. Formaldehyde is a colorless, flammable gas that is utilized in the manufacturing of wood products, textiles, adhesives, and resins. Industries include furniture manufacture, construction, and funeral services may expose workers to formaldehyde fumes or vapors at work. Since there is evidence linking workers exposed to formaldehyde to a higher incidence of leukemia, sinonasal cancer, and nasopharyngeal cancer, the chemical is considered a carcinogen to humans. Naturally present in soil, groundwater, and some industrial operations like metal smelting, mining, and pesticide production, arsenic is a metalloid. Constant contact, ingestion, or inhalation of arsenic increases the risk of developing bladder cancer, lung cancer, skin cancer, and other cancers. Employees in sectors including mining, farming, and semiconductor production could be exposed to arsenic. Colorless vinyl chloride gas is utilized in the manufacturing of vinyl flooring, PVC plastic, and other synthetic materials. Vinyl chloride exposure at work can happen in sectors like chemical processing, polymerization, and plastic production. Vinyl chloride is categorized as a human carcinogen due to evidence pointing to a higher risk of lung cancer and other cancers, as well as liver cancer, namely angiosarcoma of the liver. Diesel engine exhaust is a complex mixture of vapors, gasses, and particulate matter that contains DEPs and PAHs. In industries such as transportation, mining, construction, and agriculture, workers may be exposed to diesel engine exhaust during work. Diesel engine exhaust is classified as a possible human carcinogen due to data linking it to an increased risk of lung cancer, particularly in workers who have been exposed to diesel fumes for an extended duration. Silica is a common mineral found in soil, rock, and sand, as well as construction materials such as brick, concrete, and ceramics. Silica dust exposure at work can occur in industries such as sandblasting, mining, construction, and quarrying. Long-term inhalation of silica dust may increase the risk of lung cancer, particularly among people who have been exposed to respirable crystalline silica over an extended length of time.

Workers in radiography, nuclear power generation, and healthcare are especially sensitive to the cancer-causing effects of ionizing radiation, which includes gamma rays, X-rays, and radioactive isotopes. Ionizing radiation at work increases the risk of acquiring leukemia, thyroid cancer, breast

cancer, and skin cancer, among other malignancies. Employees in radiology, nuclear facilities, and research laboratories may be exposed to ionizing radiation. Cadmium is a heavy metal used in the production of polymers and pigments, batteries, electroplating, and metal refining. Cadmium exposure at work can occur in industries such as mining, metalworking, and battery manufacturing.

Long-term exposure to cadmium dust or fumes increases the risk of developing lung cancer, prostate cancer, kidney cancer, and other malignancies. There is evidence linking shift work, particularly night shift work, to an increased risk of colon, prostate, and breast cancer, among other malignancies. Shift workers are more likely to develop cancer because their circadian rhythm is disrupted and they are exposed to artificial light at night, which can affect immune system function, hormone synthesis, and DNA repair processes. People who work shifts and are sensitive to circadian disruptions may work in the healthcare, transportation, manufacturing, or hospitality industries.

To summarize, occupational carcinogens are a diverse group of substances and agents found in various work situations that have the potential to increase an employee's risk of acquiring cancer. To limit occupational carcinogen exposure and protect employees' health, it is critical to establish effective workplace safety measures such as exposure monitoring, ventilation systems, engineering controls, and PPE. Furthermore, programs for training, medical surveillance, and occupational health and safety laws can help identify and reduce the risk of cancer caused by occupational carcinogens. Employers, legislators, and occupational health specialists can help prevent occupational cancers and improve workplace health outcomes by focusing on worker safety and reducing exposure to carcinogenic substances.

Carcinogens primarily cause cancer by damaging DNA and interfering with normal cellular activities. Overall, by affecting genetic and cellular processes within the body, carcinogens function in a variety of ways to both cause and stimulate the development of cancer.

- **DNA Damage:** Direct damage to DNA by carcinogens can result in mutations that impair regular cell function and encourage unchecked development. For example, the chemicals found in tobacco smoke, such as polycyclic aromatic hydrocarbons (PAHs), can build DNA adducts and lead to mutations in genes, such as the tumor suppressor gene TP53.

- **Mutagenesis:** Carcinogens have the ability to accelerate the rate at which cells mutate, hence hastening the accumulation of genetic changes that drive cancer development. For example, pyrimidine dimers, which are generated by UV radiation from sunlight, are DNA lesions that can induce mutations and skin cancer.

- **Disruption of Cellular Signaling:** Carcinogens can affect cellular signaling pathways necessary for cell division, growth, and apoptosis. Mold-derived aflatoxins, for example, can impair liver cellular signaling, promoting the growth of cancer cells.

10.4 MUTATIONS

The sudden change in developing cell is called mutation. Mutations are changes in genetic material of organism, which can be either DNA or RNA. These alterations can happen on their own or be brought on by a number of different things, including exposure to radiation, chemicals, viruses, or mistakes made when replicating DNA. Chemical and physical agents can alter the hereditary material in a number of ways. Such changes, called mutations, can occur in body cells or in reproductive cells. Those occurring in body cells may kill the cells or lead to uncontrolled growth, a cancer. Nonlethal changes in reproductive cells can be passed on to one's offspring. Chemical substances like benzene and physical agents like UV and other high-energy radiation can both result in mutations. Humans can have

mutations in somatic (skin and bone) cells as well as normal bodily cells. These mutations happen relatively often, but cellular enzymes normally fix them. Since mutations are vital to evolution, genetic abnormalities, and the development of cancer, understanding them is essential.

Mutations are variations in the DNA sequence that can affect how proteins function, how genes are expressed, and how cells function. Comprehending the distinct categories of mutations is crucial, given their pivotal function in genetic diversity, evolution, and the emergence of genetic abnormalities and diseases like cancer. Different parts of the genome, such as individual nucleotides, genes, and chromosomes, are susceptible to mutations. We'll look at the various kinds of mutations, their causes, and their effects in this section. Mutagenicity refers to the ability of a substance to induce genetic mutations in cells. Mutagens are agents that can cause changes in the DNA sequence, leading to alterations in the genetic code. Understanding mutagenicity is crucial as it can have significant implications for human health, including the development of genetic disorders, cancer, and other adverse effects.

The hereditary material of the cell is contained in a molecule called DNA, short for deoxyribonucleic acid. This material is housed in chromosomes found in each cell in the body The DNA not only passes on traits from parents to offspring, it is also controls how cells grow and develop and how they function. DNA can be a target for various chemical and physical agents. Those agents that cause changes, or mutations, in the hereditary material are known as mutagens. The term mutation actually refers to three possible alterations in the hereditary material (1) changes in the DNA molecule itself, (2) alterations of chromosomes that are visible by microscope (for example, deletion or rearrangement of parts of the chromosome), and (3) missing or extra chromosomes

There are several types of mutations such as:

I. Point Mutations

II. Chromosomal Mutations

I. Point mutations: Point mutations are genetic changes that affect just one nucleotide base pair in an organism's DNA sequence. These mutations may significantly impact the structure of proteins, the function of genes, and eventually the organism's phenotype. Point mutations are key to genetic variety, evolution, and the emergence of genetic illnesses, therefore understanding them is essential. Point mutations can be classified into several categories based on the specific type of nucleotide change:

(a) Substitutions' substitution is the process of changing one nucleotide base for another. Three primary categories of substitutions exist:

- **Silent Mutations:** Because of the genetic code's redundancy, silent mutations have no effect on the amino acid sequence of the transformed protein. An amino acid that is encoded, for instance, might not change if a codon's third position is changed
- **Missense Mutations:** In a missense mutation, an amino acid in the protein sequence gets swapped out for another. The impact of missense mutations on protein function can vary depending on the type of amino acid alteration. A missense mutation in the hemoglobin gene, for instance, can cause sickle cell anemia.
- **Nonsense Mutations:** The protein is truncated as a result of nonsense mutations that add an early stop codon to the mRNA sequence. This frequently results in the shortened or non-functional protein being produced. For instance, shortened BRCA1 protein produced by BRCA1 gene mutations can cause ovarian and breast cancer.

(b) Insertions and Deletions (Indels): The addition or deletion of nucleotide bases from the DNA sequence is referred to as an insertion or deletion (indels). These mutations can affect

gene function and protein structure significantly and can happen in different places throughout the genome. Insertions and deletions entail adding or removing one or more nucleotides from the DNA sequence, but they are not strictly point mutations. These mutations may result in frameshifts in the gene's reading frame, which may change the protein's amino acid sequence and possibly cause function loss. For instance, the CFTR gene mutation that results in an inoperable CFTR protein can cause cystic fibrosis

- **Insertions:** The insertion of one or more nucleotide bases into the DNA sequence is known as an insertion mutation. If a frameshift mutation occurs and the number of added bases is not a multiple of three, the gene's reading frame may be disrupted, changing the protein's amino acid sequence. As observed in trinucleotide repeat illnesses like Huntington's disease, insertion mutations can also result in the expansion of repetitive DNA sequences.
- **Deletions:** When a nucleotide base or bases are removed from the DNA sequence, a deletion mutation takes place. Like insertions, deletions can cause frameshift mutations if the number of deleted bases is not a multiple of three. This could lead to the creation of a truncated, non-functional protein or the complete loss of gene activity. Deletions are sometimes associated with genetic illnesses such as Cri-du-chat syndrome, which is caused by a deletion on the short arm of chromosome 5.

II. **Chromosomal mutations:** Changes to the number or arrangement of chromosomes in the genome of an organism are known as chromosomal mutations. These mutations may have a significant impact on cellular activity, gene expression, and an individual's overall phenotype. Since chromosomal mutations are important for evolution, cancer development, and genetic abnormalities, it is imperative to understand them. Chromosomal mutations can be broadly categorized into various groups according to the particular kind of modification.

a. **Deletions:** A chromosome is lost when a fragment is deleted. This can happen when a chromosome breaks and the damaged section is lost, or it can happen when recombination events result in the excision of a segment. Deletions can cause the loss of significant genes or regulatory components and range in size from short segments to whole chromosomal arms. Cri-du-chat syndrome, which is defined by a deletion on the short arm of chromosome 5, is one example of a genetic condition brought on by a deletion.

b. **Duplications:** A chromosomal section that has two copies is called duplication. One chromosome may be duplicated at the expense of another during meiosis if there is an uneven crossing over. Gene dosage effects, in which a gene's increasing copy number causes a change in the degree of gene expression, can be caused by duplications. Charcot-Marie-Tooth disease is one example of a disease brought on by duplications; it is brought on by duplications in the PMP22 gene on chromosome 17.

c. **Inversions:** A chromosomal section within a chromosome can have its orientation reversed, a phenomenon known as an inversion. This can happen when a chromosome breaks and then the broken fragment reattaches in the opposite direction. Genes inside the damaged region may change in order or orientation as a result of inversions, which might impair gene activity. Meiotic pairing and recombination can be impacted by structural alterations in the chromosome that result from inversions. The centromere is involved in pericentric inversions but not in paracentric ones. Genetic illnesses including hemophilia and Prader-Willi syndrome can result from inversions.

d. **Translocations:** A chromosomal segment is translocated when it moves from one chromosome to another. This can happen when two non-homologous chromosomes

recombinate non-homologously, exchanging genetic material in the process. Gene fusions, disruptions in gene function, and the production of chimera genes with different roles can all result from translocations. Because translocations can cause oncogenes or tumor suppressor genes to become dysregulated, they are frequently linked to cancer. For instance, nearly all cases of chronic myeloid leukemia (CML) have the Philadelphia chromosome, which is created by a translocation between chromosomes 9 and 22.

e. Insertions: A DNA segment from one chromosome is inserted into another chromosome during an insertion. Transposable elements, which are DNA sequences that can relocate within the genome, may be the cause of this. By adding extra genetic material to a chromosome or changing the gene sequence within the impacted section, insertions might impair gene activity.

Causes of Chromosomal Mutations: Chromosomal mutations can arise through various mechanisms, including:

a. Errors in Chromosome Segregation: Chromosome abnormalities can arise in the resultant gametes as a result of errors made during meiosis, such as nondisjunction or missegregation of chromosomes. This may lead to trisomy or monosomy in offspring who have an aberrant number of chromosomes.

b. Breakage and Fusion: Breakage and fusion events, in which a chromosome breaks at one or more locations and the fractured ends reconnect to other chromosomes, can also result in chromosomal changes. This may result in the creation of translocations, inversions, duplications, or deletions.

a) Insertions and Deletions: The addition or deletion of nucleotide bases from the DNA sequence is known as an insertion or deletion (indel). These mutations, which can occur anywhere in the genome, have a major impact on gene function and protein structure.

- **Insertions:** An insertion mutation occurs when one or more nucleotide bases are introduced into the DNA sequence. If a frameshift mutation occurs and the number of additional bases is not a multiple of three, the reading frame of the gene may be disturbed, causing the amino acid sequence of the protein to change. As seen in trinucleotide repeat disorders like Huntington's disease, insertion mutations can also result in the expansion of repetitive DNA sequences.

- **Deletions:**When one or more nucleotide bases are deleted from the DNA sequence, a deletion mutation occurs. Deletions, like insertions, can result in frameshift mutations if the number of deleted bases does not equal three. This could result in the production of a shortened, nonfunctional protein or the full loss of gene activity. Deletions are sometimes linked to hereditary diseases, such as Cri-du-chat syndrome, which is caused by a deletion on the short arm of chromosome 5.

b) Inversions and Duplications: Rearranging chromosomal segments results in structural mutations called inversions and duplications:

- **Inversions:** An inversion is the result of a chromosomal segment breaking and reattaching in the opposite direction. Genes within the inverted section may be positioned closer to or away from regulatory elements, which could result in alterations in gene expression. Because inversions change the direction or order of genes within the afflicted segment, they can potentially cause disruptions to gene function. The centromere is involved in pericentric inversions but not in paracentric ones. Genetic illnesses including hemophilia and Prader-Willi syndrome can result from inversions.

- **Duplications:** A chromosomal section that has two copies is referred to as duplication. One chromosome may be duplicated at the expense of another during meiosis if there is an uneven crossing over. Gene dosage effects, in which a gene's increasing copy number causes a change in the degree of gene expression, can be caused by duplications. Charcot-Marie-Tooth disease is one example of a disease brought on by duplications; it is brought on by duplications in the PMP22 gene on chromosome 17.

c) **Translocations:** Translocation occurs when a chromosomal segment travels from one chromosome to another. This occurs when two non-homologous chromosomes recombine non-homologously, transferring genetic material in the process. Translocations can cause gene fusions, changes in gene function, and the formation of chimera genes that play various roles. Translocations are frequently associated with cancer because they can disrupt the regulation of oncogenes or tumor suppressor genes. For example, nearly all instances of chronic myeloid leukemia (CML) have the Philadelphia chromosome, which is formed by a translocation of chromosomes 9 and 22. Mutations are necessary for genetic diversity and evolution, but they can also harm an organism by generating cancer, diseases, and genetic disorders. Recognizing different mutation types and their underlying causes.

10.5 MUTAGENESIS

Mutagenesis is the process of causing genetic mutations and altering an organism's DNA sequence. Understanding the mechanisms of mutagenesis is critical because it sheds light on the origins of mutations, how they occur, and how they impact genetic diversity, evolution, and disease onset. Mutations can occur spontaneously or be caused by a number of outside stimuli, known as mutagens. This section will go over the mutagenesis mechanisms, which include both induced and spontaneous mutations, as well as the procedures involved.

a) **Spontaneous Mutagenesis:** Natural occurrences of spontaneous mutations take place during biological functions, DNA replication, and repair. Intrinsic causes such spontaneous chemical reactions, DNA damage, and errors in DNA replication are the source of these mutations. Spontaneous mutagenesis is facilitated by multiple mechanisms:

- **DNA Replication Errors**: Although they are remarkably accurate in replicating DNA, DNA polymerases are not perfect. Sometimes mistakes happen during replicating DNA, causing the wrong nucleotides to be incorporated into the newly created strand. The DNA sequence may undergo base substitutions, insertions, or deletions as a result of these mistakes. Replication errors can be corrected by systems such as mismatch repair and proofreading; however some mutations may evade detection and continue to exist in the genome.
- **Spontaneous Chemical Reactions:** Changes in structure and function can result from spontaneous chemical reactions involving DNA bases. For instance, guanine bases can oxidize to generate 8-oxoguanine, while cytosine bases can deaminate to form uracil. During DNA replication, these altered bases may cause mispairing, which can result in mutations like GC to AT transitions.
- **DNA Damage:** Endogenous and environmental agents that can harm DNA are continuously present in cells. For instance, oxidative DNA damage, such as base alterations and DNA strand breakage, can be brought on by reactive oxygen species (ROS), which are produced during regular cellular metabolism. In addition to UV exposure from sunshine, which can cause pyrimidine dimer production, other types of DNA damage include spontaneous hydrolysis of DNA bases.

b) Induced Mutagen: External agents known as mutagens, which can include physical agents like radiation and chemicals, are what induce mutations. Mutations can result from these mutagens' interactions with DNA, which can upset its structural integrity. Induced mutagenesis is facilitated by multiple mechanisms:

- **Chemical Mutagens:** Chemicals that interact with DNA to cause genetic mutations are known as mutagens. Alkylating agents, polycyclic aromatic hydrocarbons (PAHs), and heterocyclic amines found in cooked meats, industrial chemicals, and tobacco smoke, respectively—can be some of these mutagens. Chemical mutagens can harm DNA by forming base alterations, DNA crosslinks, and DNA adducts, among other methods.
- **Physical mutagens:** Physical mutagens are elements of the environment, like radiation, that physically alter DNA. Ionizing radiation can cause point mutations, chromosome abnormalities, and DNA double-strand breaks. Examples of this radiation include X-rays and gamma rays. Sunlight-induced pyrimidine dimer production can result in mutations and the development of skin cancer. This is because UV radiation can cause skin cancer. Indirect methods, such as the production of reactive oxygen species (ROS) and interference with DNA repair processes, can also result in DNA damage from non-ionizing radiation, such as microwaves and radiofrequency radiation.
- **Biological Mutagens:**A biological mutagen is a substance that has the ability to produce genetic alterations in living organisms. Mutagens include bacteria, viruses, and microbial toxins, all of which can interact with DNA and disrupt normal biological processes. The human papillomavirus (HPV) is one virus that can cause mutations in critical genes involved in cell formation and proliferation by integrating its DNA into the host genome. Aspergillus fungi produce aflatoxin, which causes DNA adduct formation and mutations in exposed tissues, potentially leading to liver cancer.

10.6 MECHANISMS OF MUTAGENIC ACTION

Mutagens can cause genetic changes in a number of ways, depending on the type of DNA damage they cause as well as their chemical or physical properties. Through chemical alterations such base mutations, DNA strand breakage, or DNA crosslinks, mutagens can directly harm DNA. Changes in the DNA sequence, such as base substitutions, insertions, deletions, or chromosomal rearrangements, may result from this. Mutagens can obstruct DNA polymerase's progress or cause base mispairing, which can both disrupt the replication of DNA.This may induce errors during DNA replication, resulting in mutations in the newly produced DNA strand. Mutagens have the ability to prevent DNA damage from being detected or to inhibit the function of enzymes that repair damaged DNA. This may slow the mending of DNA damage, allowing genetic changes to persist. Certain mutagens can cause cells to create reactive oxygen species (ROS), which can cause oxidative damage to DNA. ROS can cause base changes, DNA-protein crosslinks, and strand breaks, all of which can lead to mutations.

Detection of Mutagenicity: Various assays are available to assess the mutagenicity of compounds and environmental agents, including:

- **Bacterial Mutagenicity Assays**: The Ames test is a bacterial assay used to screen for the mutagenic potential of chemicals by measuring their ability to induce mutations in bacterial cells, usually Salmonella typhimurium or Escherichia coli.
- **Mammalian Cell Assays**: Mammalian cell assays, such as the micronucleus assay and the comet assay, are used to detect chromosomal damage and mutagenicity in mammalian cells exposed to mutagens.

- **Animal Models**: Animal models, such as transgenic mice and rats, can be used to assess the mutagenic potential of compounds in vivo and evaluate their carcinogenicity.

10.7 SUMMARY

Carcinogenesis is a complex and diverse phenomenon that is influenced by a person's genetic composition, lifestyle, and environment. For the purpose of cancer prevention, diagnosis, and treatment, it is imperative to comprehend the mechanisms behind carcinogenesis. Substances or agents with the potential to cause cancer are known as carcinogens. They exist in a variety of forms, such as biological agents, chemicals, and radiation. Carcinogens work by either directly or indirectly causing damage to DNA, which can result in mutations and the growth of malignant cells. Mutagenesis refers to the mechanisms that result in genetic mutations that alter an organism's DNA sequence. Mutations can occur naturally as a result of DNA replication, repair, and cellular activities, or they can be brought about by outside agents called mutagens. Determining the dangers of exposure to toxins, creating cancer prevention plans, and comprehending the genetic causes of illnesses all depend on an understanding of the mechanisms of mutagenesis and the variables that lead to the creation of mutations. Additional research on mutagenesis will help to explain the underlying mechanisms and reduce the negative effects of mutagenic substances on the environment and human health. Epigenetic alterations are just as crucial in carcinogenesis as genetic mutations. Epigenetic modifications such as histone acetylation and DNA methylation regulate gene expression without altering the underlying DNA sequence. Tumor start, development, and progression can be encouraged by epigenetic pathway dysregulation, which can silence tumor suppressor genes or activate oncogenes

10.8 TERMINAL QUESTIONS

Q. 1. What is carcinogen? Discuss the process of carcinogenesis.

Answer:----------

Q. 2. What is the difference between carcinogenic and oncogenic?

Answer:----------

Q. 3. What are the 3 stages of carcinogenesis? Define each step with examples.

Answer:----------

Q. 4. What do you known about mutagenesis? What is the principle of mutagenesis?

Answer:----------

Q. 5. What is the relationship of mutations to carcinogens?

Answer:----------

Q. 6. What is the difference between mutagenesis and mutagen?

Answer:----------

10.9 FURTHER SUGGESTED READINGS

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6. A Textbook of Modern Toxicology: Ernest Hodgson, A John Wiley & Sons, Inc., Publication

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UNIT-11 : TRANSFORMATION OF TOXICANTS

11.1 INTRODUCTION

In the environment, toxicants change in a number of ways, changing their toxicity and chemical makeup. These changes can be brought about by physical, chemical, or biological processes. Physical transformations, such as evaporation, condensation, and dissolution, involve modifications to the physical state of toxicants. The heavy metals can dissolve in water to generate aqueous solutions, and volatile organic compounds (VOCs) can evaporate into the atmosphere from liquid or solid phases. Chemical transformations are reactions that change the molecular makeup of toxicants. Common chemical reactions that have the ability to change toxicants include hydrolysis, photolysis, and oxidation-reduction reactions. Pesticides, for instance, can hydrolyze in water to form less hazardous or more readily degradable chemicals. In a similar vein, photolytic processes that break down chlorinated compounds can be triggered by sunlight. Toxicants undergo biodegradation or metabolism by living organisms, leading to biological changes. Microorganisms change complicated organic compounds into less dangerous ones during the biodegradation process. For instance, bacteria in soil and water can break down hydrocarbons from oil spills, producing carbon dioxide and water as by products. The transformation products that result from these processes could have distinct toxicity profiles from the initial toxicants. While certain transformation products might be less dangerous or even benign, others might be more poisonous. Furthermore, transformation processes may impact a toxicant's bioavailability, which in turn may impair an organism's ability to absorb and accumulate the toxin. Determining environmental dangers and creating efficient mitigation plans require an understanding of how toxicants change. Scientists can forecast the fate and behavior of toxicants in diverse environmental compartments by determining the routes and kinetics of transformation processes. This knowledge is used to develop rules, manage pollution, and protect human health and ecosystems from toxicants' negative impacts.

Objectives:

After readings this unit, the learner will be able to know

- the bioaccumulation and biomagnifications process in living beings
- the biotransformation of chemical or substances from different trophic level

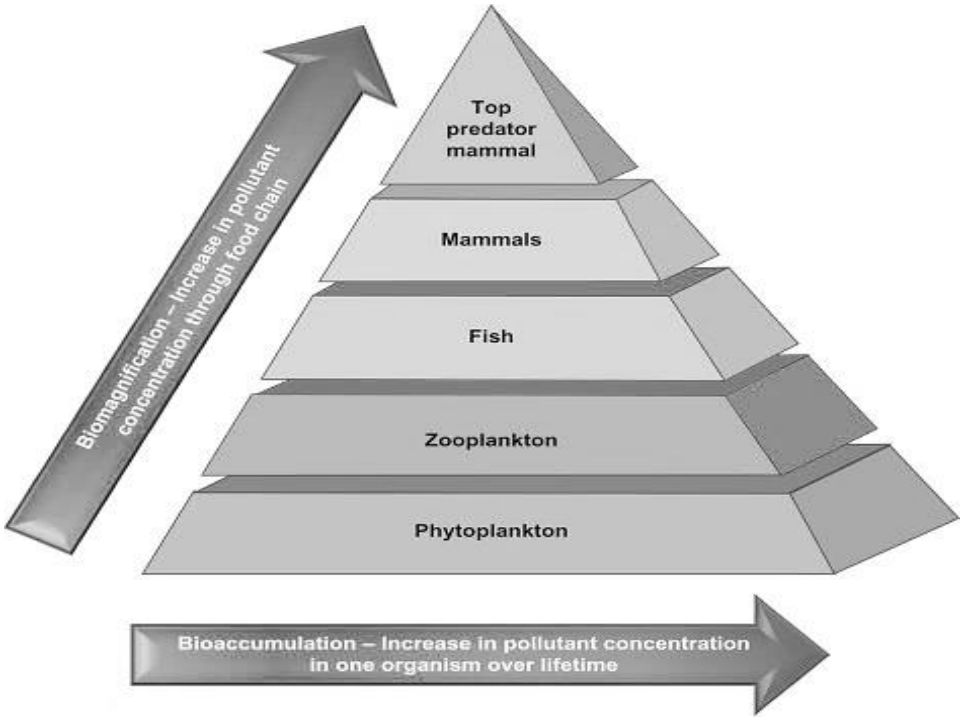
- the biotransformation of DDT and its effects on health
- the toxic material in environment and its effects on human beings

11.2 BIOACCUMULATION

The term "bioaccumulation" describes the slow build-up of substances, usually pollutants or toxins in living things as a result of different exposure routes, including ingestion, absorption, and inhalation. Insecticides, heavy metals, persistent organic pollutants (POPs), and other substances that can deteriorate and remain in the environment are examples of such materials. When organisms absorb substances from their surroundings, bioaccumulation begins. This absorption can occur while eating contaminated foods or coming into direct contact with polluted soil, water, or air. After being absorbed, the chemicals may eventually build up in the body's tissues, particularly in fatty areas where lipophilic compounds have a tendency to congregate. An imbalance between an organism's absorption and excretion of the material leads to bioaccumulation. Although the material may be continuously ingested by organisms through their food or surroundings, there may be restrictions on how well they can metabolize or eliminate it. As a result, the substance's concentration rises within the body of the organism, possibly having negative repercussions. The amount of bioaccumulation depends on the chemical properties of the material, the organism's physiology, the environment, the time and intensity of exposure, and other factors. Highly lipophilic, weakly soluble in water, and biodegradable compounds are more prone to accumulate. In comparison to lower trophic levels, organisms higher up the food chain, including predators, may bio accumulate more pollutants. When discussing metal toxicity, the phrases bioaccumulation and biomagnifications are frequently employed. The term "bioaccumulation" describes the process by which contaminants, such as metals, enter a food chain and build up in the biological tissues of aquatic creatures from sources like food, water, and suspended sediment particles. Chemical bioaccumulation in an organism can be significantly altered by biotransformation. The process by which the concentration of a pesticide or other chemical in an aquatic organism rises above the concentration in the water due to chemical uptake through all accessible pathways (e.g., dietary absorption, transport across the respiratory surface, dermal absorption, and inhalation) is known as bioaccumulation in other words. Chemical Bioconcentration and biomagnifications are combined to form bioaccumulation. Ecosystems as a whole, as well as individual individuals and populations, may suffer from bioaccumulation. Pollutant concentrations that are too high can cause physiological disruptions, reduce the success of reproduction, and weaken an organism's immune system, leaving it more vulnerable to illness and other stresses. Furthermore, as contaminants migrate up the food chain, they have the ability to biomagnify and accumulate, reaching much higher concentrations in top predators.

The bioaccumulation phenomenon has significant impacts for human health. Humans can be exposed to bioaccumulative substances through tainted meat, dairy, and seafood. Prolonged exposure to these substances may have long-term health implications such as cancer, neurological illnesses, and reproductive issues. A rise in a pollutant's concentration from one food chain link to another is known as biomagnifications. A pollutant needs to be physiologically active, soluble in fats, mobile, and long-lived in order for biomagnifications to take place. The concentration of the pollutant rises throughout bioaccumulation to reach the top of the food chain's first organism. Any level of their tropics allows for the buildup of organisms. It is the overall outcome of how chemicals are absorbed, stored, and removed. Parts per million (ppm) is the unit of accumulation measurement. This describes a single particle of a certain material combined with 999999 more particles. Oysters, for instance, can accumulate DDT in their bodies from 700 ppm to 0.001 ppm in seawater. Non-biodegradable metals are taken up by the biotic system and accumulate at a higher level in the ecosystem biota. The chemical keeps building up

until it eventually kills the living thing. Chemicals including mercury, dioxins, DDT, PCBs, and DDT accumulate in fish bodies as a result of the food chain. At the apex of this food chain are people. Chemicals found in fish might build up in our bodies as well if we consume a lot of it. Although the toxins in fish won't instantly make you sick, in certain people they may eventually lead to health issues like diabetes or cancer. However, not everyone will become unwell. Years of eating may not affect some people negatively. After years of consuming fish that contains these toxins, some individuals might be okay. Substances that are persistent, highly stable, and do not degrade over extended periods of time. Persistent chemicals include mercury, dioxins, DDT, PCBs, and others. Regulations include pollutant monitoring, pollution prevention, and control strategies are put into place to lessen the risks related to bioaccumulation. Minimizing the bioaccumulation of hazardous substances and safeguarding the environment and public health require concerted efforts to minimize the release of persistent pollutants into the environment and to advance sustainable practices.



Certain heavy metals' biological amplification and transport in sewage-fed aquatic environments

Kind of bioaccumulation

1. **Organismal bioaccumulation**
2. **Trophic transfer**
3. **Soil accumulation**

1. **Organism bioaccumulation:** The process by which organisms, usually those at higher trophic levels in a food chain, gradually collect toxins or pollutants in their tissues is known as "organismal bioaccumulation." When an organism consumes contaminated food, water, or air, the toxins are stored in its tissues where they are not effectively digested or eliminated, which leads to this buildup. Because bioaccumulation can result in toxic consequences, problems with reproduction, and even population decreases, it can be harmful to both individual organisms and entire ecosystems. Chemicals found in an organism's surroundings may eventually concentrate in the body in this sort of bioaccumulation. Fish swimming in polluted water, for instance, may accumulate pollutants in their fatty tissues.

2. **Trophic transfer:** Trophic transfer in bioaccumulation refers to the movement of poisons or pollutants through different trophic levels of a food chain or web. When lower trophic level species consume polluted food or water, the poisons are absorbed by their tissues. When these creatures are consumed by higher trophic level predators, the accumulated toxins are passed on to them. Predators continue this process by consuming toxic prey, which can lead to more bioaccumulation and potentially higher pollutant concentrations in organisms at the top of the food chain. Trophic transmission is a crucial component in the amplification of toxic substances in ecosystems and can have a serious influence on the health of animals and people that ingest contaminated food. This process involves the transfer of accumulated chemicals or pollutants from one trophic level to another, with an increase in concentration of these substances at each level. Top herbivores and carnivores in the ecosystem, including lions and humans, can, for instance, receive the highest concentration.

3. **Soil accumulation :** The term "soil accumulation" describes the gradual build-up or concentration of toxins or pollutants in soil. This can happen through a number of methods, including direct application of pollutants through human activities like agriculture, industrial processes, or waste disposal, or deposition from the atmosphere, leaching from surface runoff, or both. Pollutants have the ability to attach themselves to organic matter or soil particles once they reach the soil, making removal challenging and possibly leading to long-term environmental issues. Because toxins can be absorbed by plants, make their way into the food chain, or seep into groundwater, accumulating dirt can have a negative impact on ecosystem health, plant growth, and environmental quality. Toxic materials in soil seep from the topsoil and either accumulate or bind to the soil.Factors on which bioaccumulation depends are following

   - Uptake of substance
   - Storage of substance, storage capacity
   - Elimination of substance
   - Hydrophobicity
   - Concentration of pollutant in water
   - Age, sex and type of organism

11.3 BIOMAGNIFICATIONS

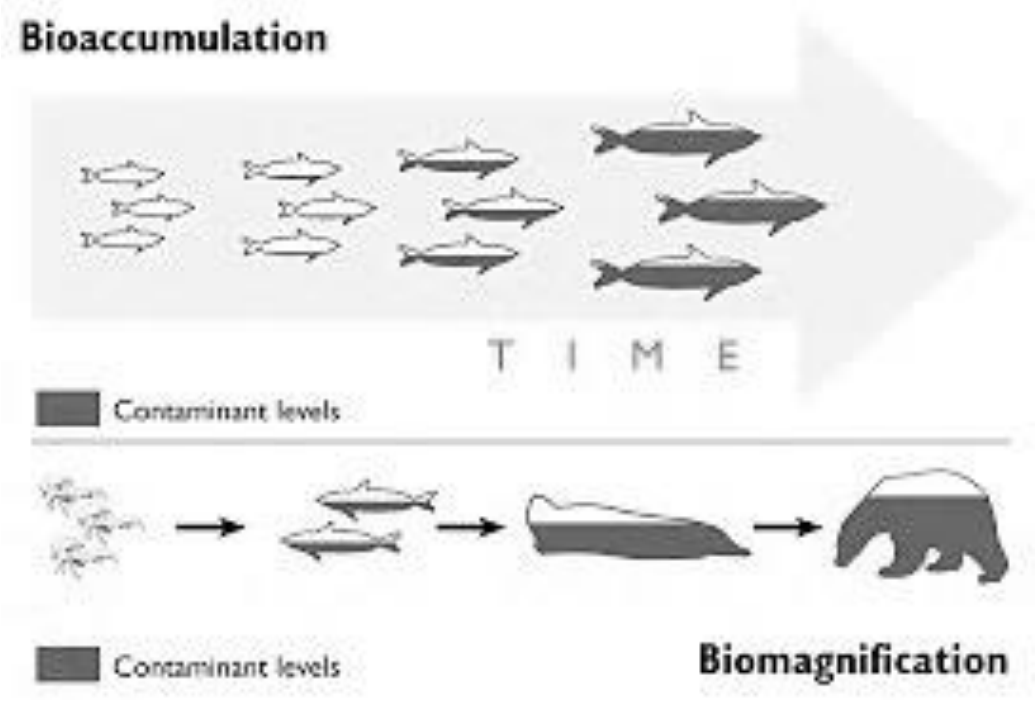
The process known as "biomagnification" is the gradual increase in concentration of some compounds, usually pollutants or toxins, as they move up the food chain. It is the rise of hazardous chemicals or contaminated materials that occurs in food systems. These compounds are usually created from contaminated or intoxicated environments, which lower-order organisms absorb into their own systems. Some examples of contaminants include polychlorinated biphenyl compounds (PCBs), microplastics, heavy metals, and pesticides such as DDT. Because these hazardous compounds are present in a wide range of industrial and chemical products, human contamination is the principal pathway for their introduction into the environment. Primary producers, such as algae, phytoplankton, and plants, absorb pollutants from their surroundings to begin the biomagnification process.

People rarely consider whether the food they eat contains any pollutants. When a customer orders a steak at a restaurant, they don't think about how the cattle was fed, whether it came from contaminated pasture, or whether pesticides were used extensively on the pasture. The animal consumes this contaminated grass, which causes pesticides to build up in its body and then be swallowed by

people. The majority of food industry businesses work hard to regulate their operations to prevent this from happening and give customers confidence that purchasing their goods won't have a detrimental effect on their health

Some types of contaminants include heavy metals, insecticides, industrial chemicals, and persistent organic pollutants (POPs). Because of bioaccumulation, primary consumers such as herbivores and microscopic fish that feed polluted animals end up with higher amounts of contaminants in their tissues than in their environment. Biomagnification refers to the tendency of pollutants to concentrate when they move from one organism to the next. It is the process by which pollutants accumulate and become more concentrated at each trophic level of the food chain, traveling up from one link to the next. "Food web biomagnifications" relate to the trophic enrichment of pollutants within food webs as well as the progressive rise in chemical concentrations with increasing animal trophic rank.

By itself, food-web biomagnifications can increase a bioaccumulative substance's lipid-normalized concentration by 10000-1000000 times. Biomagnifications are ecologically relevant because they expose animals at higher trophic levels to high concentrations. People frequently confuse the phrases "biomagnification" and "bioaccumulation," sometimes using them interchangeably. However, it is vital to differentiate between the two. "Biological magnification specifically refers to increasing the concentration of materials in each higher link in the food chain," says Biology Junction, an online biology journal. Bioaccumulation, on the other hand, is the study of how a specific substance accumulates within a single organism. According to the United States Environmental Protection Agency, bioaccumulation occurs at the base of a food web, generally in basic producers like phytoplankton. Human-produced "Persistent Organic Pollutants" (POPs) are directly absorbed by these photosynthetic sea organisms and retained in their bodies. Ingested toxins accumulate in the tissues faster than they can be digested. Trophic magnification factors (TMFs) and biomagnification factors (BMFs) are used to assess the biomagnification capacity of metalloids and HMs at different tropic levels. BMF is commonly defined as the ratio of HM concentrations in organism-to-organism diets and can be calculated using the formula below.



Ecological and health problems associated with biomagnifications are substantial. Increased levels of contaminants in an organism's tissues can have negative impacts at every trophic level.

Furthermore, excessive concentrations of harmful compounds may bioaccumulation in top predators, including humans and apex predators, posing a risk to their health. For instance, eating tainted seafood exposes people to high concentrations of mercury or persistent organic pollutants, which can harm the nervous system and lead to developmental delays and other health issues.

Larger fish and predatory animals are examples of secondary consumers who eat polluted primary consumers and hence consume more pollutants than their prey. Because these secondary consumers devour a lot of contaminated prey, the number of pollutants in their tissues is constantly increasing. As organisms go up the food chain, pollutant concentrations at higher trophic levels increase. Because top-level organisms can accumulate massive levels of pollutants, biomagnification is particularly dangerous for these species. This phenomenon has been observed worldwide in a number of settings, including aquatic ones. Pollutants such as mercury, PCBs, and DDT have biomagnified in fish populations, placing marine mammals and birds of prey at risk.

Many theories have been proposed to explain biomagnifications. We present the gastrointestinal magnification concept, its latest revisions, and additional non-dietary mechanisms that might provide similar but often contradicting biomagnification findings. Simply put, biomagnification is the concentration of a material increasing in a food chain rather than within an organism. Conservative pollutants are not metabolized.

Consequently, when a polluting organism is consumed, the pollutants are merely transferred to the predator and accumulate in its tissue. Chemicals that collect through biomagnifications in aquatic environments have the potential to eventually become hazardous to higher creatures as well. Generally speaking, "threshold" concentration refers to the lowest substrate concentration needed to support a species' growth. Efforts to mitigate the risks of biomagnifications include reducing the release of pollutants into the environment, implementing pollution control measures, and monitoring contaminant levels in food chains. Sustainable management practices, such as controlling industrial emissions, phasing out the use of persistent pollutants, and promoting ecosystem conservation, are essential for minimizing the impacts of biomagnifications on ecosystems and human health.

The biomagnifications pathway

Biomagnification is the process by which pollutants or toxins accumulate as they move up the food chain, contaminating organisms at higher trophic levels. This pollution build-up route poses significant risks to ecosystems and public health. Primary producers at the base of the food chain, such as algae and plants, absorb toxins from their surroundings via dirty soil or mechanisms such as air and water deposition. Organisms that directly consume these plants or algae may still be at risk, even if the beginning concentrations are low. Pollutants can enter an organism via a variety of pathways, including the mouth, digestive tract, and gill surfaces. Most poisons are immediately absorbed by small aquatic organisms from the water. Certain characteristics of biomagnifications. The pollutant needs to be soluble in fats rather than water and have a lengthy biological half-life (long lifespan) in order for biomagnifications to take place. For instance, DDT. The organism will expel the pollutant if it is soluble in water. Fat-soluble pollutants are held in the fat for a very long period. Therefore, it is customary to quantify the quantity of contaminants present in the fatty tissues of animals like fish. Because female mammal milk contains a high fat content, it is examined for contaminants.Herbivores pick up some of the contaminants in their food as they eat these polluted primary producers. Nonetheless, the concentrations are usually not high enough to harm herbivores straight immediately, though some effects can occur, especially in sensitive species. The main problem arises when top predators or carnivores consume herbivores. The concentration of pollutants increases considerably during this stage, known as biomagnification. This occurs as a result of predators swallowing cumulative toxins from all of the prey they have consumed over their lifetime, in addition to pollutants found in their meal.

Furthermore, the cumulative effect of biomagnification increases as predators devour more food over time. As a result, creatures at the top of the food chain, such as large fish, predatory birds, and mammals, can be found to be heavily contaminated. Pollution levels this high can have a wide range of severe consequences, including reduced immune function, abnormal development, reproductive issues, and even death. When people consume contaminated food from higher trophic levels, such as fish, they become sensitive to the effects of biomagnification. Certain toxins, such as dioxins and PCBs, as well as heavy metals like mercury, can bioaccumulate and magnify in seafood, jeopardizing human health, particularly that of children, pregnant women, and nursing mothers. Pollutants accumulate in tissues and organs because they are difficult for organisms to digest or remove, increasing amounts as one travels up the food chain.

11.4 BIOTRANSFORMATION

The chemical changes that occur in living things as a result of substances such as medications, contaminants, and natural compounds are referred to as biotransformation, or metabolism. In this process, a chemical is enzymatically converted into metabolites, which can differ from the original component in terms of toxicity, excretion ease, and biological activity. The liver is the primary organ involved in biotransformation; however the kidneys, lungs, and intestines also contribute to this process. Hepatocytes are specialized liver cells that include endoplasmic reticulum, which is home to most biotransformation-related enzymes. These enzymes include conjugating enzymes, which help phase II metabolism by attaching functional groups to the metabolites generated in phase I, and cytochrome P450 (CYP) enzymes, which are in charge of the phase I metabolism of numerous substances. Reactions involving oxidation, reduction, or hydrolysis change the substrate molecule's chemical structure during phase I metabolism. In phase II metabolism, these events frequently add or reveal functional groups, increasing the substrate's reactivity and easing the way for later conjugation reactions. Conjugation processes, which attach polar groups to the substrate to increase its water solubility and allow excretion, are commonly involved in phase II metabolism. Examples of these reactions include acetylation, sulfation, methylation, and glucuronidation. Biotransformation main goal is to make it easier for the body to get rid of potentially dangerous toxins. Biotransformation reduces the buildup of lipophilic chemicals in tissues and minimizes their toxicity by making them more water soluble, allowing for their elimination through urine or bile. Reactive metabolites, on the other hand, can occasionally result from biotransformation and end up being more harmful or cancer-causing than the original chemical. Pharmacology relies heavily on biotransformation since it affects the potency and toxicity of medications. Individual variances in medication metabolism and response can be attributed to a variety of factors, including age, sex, genetics, and environmental influences on metabolic pathways. To maximize the benefits of medication therapy and reduce side effects, it is crucial to comprehend how medications are biotransformed.

Based on the order of events and the kind of chemical changes involved, biotransformation, or metabolism, can be divided into two primary categories: phase I metabolism and phase II metabolism.

1. **Phase I Metabolism:** The basic purpose of phase I metabolism is to modify the chemical structure of the substrate molecule using a series of enzyme reactions. These processes, which include oxidation, reduction, and hydrolysis, have the potential to add or modify functional groups. The cytochrome P450 (CYP) enzyme family catalyzes a wide range of oxidation activities and is the primary enzyme system involved in phase I metabolism. These phase II processes produce more polar and water-soluble metabolites, which the body can then remove through bile or urine. Some examples of Phase I reactions are:

   - **Hydroxylation**: Addition of a hydroxyl (-OH) group to the substrate molecule.

- **Oxidation:** Removal of hydrogen atoms or addition of oxygen atoms to the substrate.
- **Reduction:** Addition of electrons or removal of oxygen atoms from the substrate.
- **Hydrolysis**: Cleavage of chemical bonds by water molecules.

2. **Phase II Metabolism:** Conjugation reactions, which occur during phase II metabolism, are the chemical combining of the substrate molecule or its phase I metabolites with endogenous molecules to make them more water soluble and easier to excrete. Functional groups like acetyl, methyl, glucuronic acid, sulfate, or amino groups are added to the substrate molecule by conjugating enzymes. However, in the phase II metabolism adds water-soluble conjugates to improve excretion, while phase I metabolism exposes or adds functional groups to the substrate molecule. All of these biotransformation mechanisms work together to help the body detoxify and get rid of medications, endogenous chemicals, and xenobiotics. Phase II reactions include, for example:

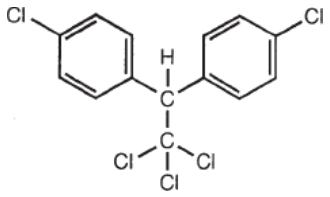
- **Glucuronidation:** Addition of a glucuronic acid group to the substrate molecule.
- **Sulfation:** Addition of a sulfate group to the substrate molecule.
- **Methylation:** Addition of a methyl group to the substrate molecule.
- **Acetylation:** Addition of an acetyl group to the substrate molecule.
- **Amino acid conjugation:** Conjugation with amino acids like glycine or glutamine.

11.5 BIOTRANSFORMATION OF DDT

DDT is a pesticide that belongs to the organochlorine chemical family and has been widely used since II World War. DDT is a white, crystalline material that is very hydrophobic and has a faint chemical odor. It is fairly soluble in most organic solvents, fats, and oils, but almost insoluble in water. The US Environmental Protection Agency (US EPA) classifies DDT as a highly dangerous chemical (LD_{50} 50-500 mg/kg), with a rat LD_{50} of 113 mg/kg. It has been established that DDT has strong insecticidal properties. It operates by activating sodium ion channels in insect neurons, causing the neurons to fire spontaneously (WHO, 1979). As a result, DDT's toxicity and persistence can be attributed to its chemical and physical features, such as its molecular structure containing aromatic moieties and chlorine atoms, high boiling and melting points, and limited solubility in water. Instead of occurring naturally, DDT is formed when sulphuric acid acts as a catalyst in a chemical reaction between chloral (C_2HCl_3O) and chlorobenzene (C_6H_5Cl). In truth, commercial DDT is a combination of several closely related molecules, with o,p-DDT accounting for 15% of the formulation, p,p′-DDT accounting for 77%, and the other compounds accounting for the remainder.

DDT has been used extensively worldwide to manage agricultural pests and arthropod disease carriers. DDT is a hydrophobic and lipophilic chemical that readily builds up in sediment and makes its way into the food chain. As such, it poses a risk to ecosystems and human health. One of the most persistent pesticides is DDT, which may linger in soil for more than 30 years and build up in living things, including humans, through bioaccumulation or biomagnifications as they move up the food chain.

Table 11.1: Chemicalandphysicalpropertiesof1,1,1-trichloro-2,2-bis(*p*- chlorophenyl) ethane (DDT).

Property	
Molecularformula	$C_{14}H_9C_{l5}$
Structure	
Molarmass	354.49g/mol
Density	1.55g/cm³
Meltingpoint	108.5–109°C
Boilingpoint	185–187°C(at7Pa)
Vaporpressure	2.3x 10^{-5}Paat20°C
Watersolubility	0.025ppmat 25°C
Adsorption partition coefficient (K_d)	243,000

Source: Kalloyanova and El-Batawi (1991); Foght*et al.* (2001)

Bth biotic and abiotic factors influence how pesticides behave in the environment. Different herbicides biotransform at very different rates. Recalcitrant pesticides, including dieldrin and DDT, have been shown to linger in the environment for extended periods of time and are known to build up in food chains for decades following their soil application. DDT (dichlorodiphenyltrichloroethane) is biotransformed by a number of enzymatic processes in living things, mostly in the liver. Synthetic pesticide DDT was once widely employed to manage insect pests, but because of its toxicity and environmental persistence, it has been mostly outlawed.

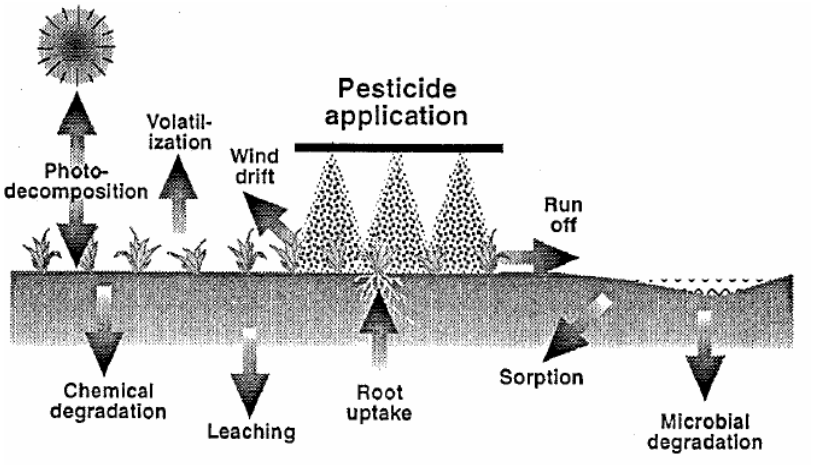


Fig. 11.1 : The destiny of pesticides in the ecosystem.

1. **Phase I Metabolism:** Cytochrome P450 (CYP) enzymes catalyze the oxidative processes that DDT goes through at this phase of metabolism. These reactions generate several metabolites, such as:

- Diphenyldichloroethylene, or DDE, is one of the main DDT metabolites. It is created when one chlorine atom is removed from DDT, leaving behind a less hazardous but yet enduring chemical in the environment.
- Dichlorodiphenyldichloroethane, or DDD, is a different DDT metabolite that is created when DDE is further dechlorinated. Similar to DDE, DDD is more enduring in the environment than DDT despite being less hazardous.
- Dichlorodiphenylmonochloroethylene, or DDMU: two chlorine atoms are lost during the first oxidation of DDT to create DDMU. Though less frequent than DDE and DDD, it is nonetheless detectable.

2. **Phase II Metabolism**: Phase II metabolism involves conjugating the metabolites produced in phase I activities with endogenous molecules to make them more excretable and water soluble. Examples of conjugation reactions are glucuronidation, glutathione conjugation, and sulfation. Eventually, DDT passes through a biotransformation process are less toxic than the parent molecule but nevertheless persistent in the environment. Because these metabolites can accumulate in organisms and biomagnify via food chains, they are dangerous to both human health and ecosystems. Even though DDT is banned in many nations, its metabolites can still be discovered in the environment because of its persistence and legacy pollution.
   - DDE and DDD can be converted to more water-soluble metabolites that can be eliminated in bile or urine by a process called glucuronidation, in which they are coupled with glucuronic acid.
   - Glutathione conjugation is another process that DDE and DDD can go through. This process forms glutathione conjugates, which are then eliminated in bile.

11.6 TOXIC MATERIAL IN ENVIRONMENT

The hazardous substances can come from both natural and human sources can poison the environment. These hazardous substances can seriously endanger wildlife, human health, and ecosystems. Typical hazardous substances discovered in the environment include:

1. **Heavy Metals:** Mercury: Mercury is a metal that is released during mining, coal combustion, and industrial processes. It can build up in water bodies and biomagnify through food chains, which can affect wildlife and humans' neurological and developmental systems.
   - **Lead:** Historically utilized in paint, fuel, and plumbing, lead can pollute water and soil, endangering kidney, cardiovascular, and neurological development.
   - **Cadmium:** This metal, which can build up in soil and water and cause kidney damage and bone diseases, is present in industrial emissions, fertilizers, and batteries.
2. **Organic Persistent Pollutants (POPs):**
   - **Polychlorinated Biphenyls (PCBs):** Found in electrical equipment, PCBs are extremely persistent and have the potential to bioaccumulate in aquatic environments, which can affect human and wildlife development and reproduction.
   - **Dioxins and furans:** These extremely poisonous compounds, which are created during combustion processes, can lead to immune system malfunction, cancer, and reproductive issues.

3. **Herbicides and Pesticides:**

   - **Organochlorine Pesticides:** These pesticides, which include dieldrin, chlordane, and DDT, can bioaccumulate in organisms and persist in the environment, endangering both human health and animals.
   - **Organophosphate and carbamate pesticides:** These agricultural pesticides have the potential to contaminate food, water, and soil, which can have both immediate and long-term negative impacts on health.

4. **Air Impurities:**

   - **Particulate matter (PM):** Particulate matter (PM) can aggravate asthma and other respiratory illnesses and cause respiratory and cardiovascular problems. PM is produced by combustion processes, industrial operations, and automobile emissions.
   - **Nitrogen oxides (NOx) and sulfur dioxide (SO2):** During the combustion of fossil fuels the gas emitted. These gases are responsible for acid rain, smog, and respiratory issues in both people and animals.

5. **VolatileOrganic Compounds (VOCs):** VOCs are emitted by solvents, automobile emissions, and industrial operations. Examples of these include xylene, toluene, and benzene. VOCs can cause neurological, respiratory, and cancerous effects by contaminating air and water.

11.7 SUMMARY

The environment causes physical, chemical, and biological modifications in toxicants that alter their chemical structure, toxicity, and fateThese changes, which are influenced by external factors, are critical in determining the potential dangers that poisons pose to ecosystems and public health. Biotransformation is the enzymatic conversion of molecules in living organisms, and the liver is the principal site of this activity. Phase I and phases II reactions are involved, and it mostly happens in the liver. Phase I processes increase the polarity of the chemical by oxidation, reduction, and hydrolysis. Phase II processes improve solubility in water for simpler excretion, such as conjugation with amino acids, sulfate, or glucuronic acid. The body's reaction to foreign chemicals, drug metabolism, and detoxification all depend heavily on biotransformation. Drug metabolism, detoxification, and the body's removal of xenobiotics are all dependent on biotransformation. These toxic substances could have a major and long-term influence on ecosystem quality, biodiversity, and human health. To protect ecosystems and public health, toxic material emissions must be monitored, managed, and limited.

11.8 TERMINAL QUESTIONS

Q. 1. What is the meaning of bioaccumulation?

Answer:----------

Q. 2. What causes bioaccumulation?

Answer:----------

Q. 3. Write about biotransformation and types.

Answer:----------

Q. 4. Write about Biotransformation mechanism of DDT.

Answer:----------

Q. 5. Toxic material in environment and its effects on human beings.

Answer:----------

11.9 FURTHER SUGGESTED READINGS

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2. Environmental Toxicology, third edition, Sigmund F. Zakrzewski, Published by Oxford University Press, Inc. New York, New York 10016

3. Environmental Toxicants, Human Exposures and Their Health Effects, Third Edition, Morton Lippmann, Published By John Wiley & Sons, Inc., Hoboken, New Jersey.

4. Toxicology in Occupational and Environmental Setting, Wolfgang Dekant, Institute of Toxicology, University of Wuerzburg, Germany.

5. A Textbook of Modern Toxicology, Ernest Hodgson, Published By John Wiley & Sons, Inc., Hoboken, New Jersey.

6. A Textbook of Modern Toxicology: Ernest Hodgson, A John Wiley & Sons, Inc., Publication.

7. Principles of Environmental Toxicology, I. Shaw, J. Chadwick, CRC Press.

8. Occupational Toxicology, Chris Winder, Neill H. Stacey, CRC Press.

UNIT-12 : OCCUPATIONAL TOXICOLOGY

Structure

12.1 INTRODUCTION

The study of harmful substances that employees may come into contact with at work is known as occupational toxicology. The personnel themselves, the experimental animals, or other test systems utilized in the studies could all have negative impacts. Define and comprehend the agent of interest's toxicity. The term "occupational" is preferred over "industrial," as the latter may imply chemical exposure in factories; however, this would not always include jobs like farming, which may expose one to pesticides, or office work, which may involve problems like photocopiers in enclosed areas. Events like the thalidomide tragedy and chemical poisoning of the environment have raised public awareness of theharmful effects of chemicals on human health. This has included acknowledging that occupational exposures have an impact on one's health. In this regard, a casual look at the International Agency for Research on Cancer's (IARC) Group 1 carcinogen list ought to be sufficient evidence. We cannot afford to be complacent in our efforts to reduce substance-related illness, as seen by the epidemic of asbestos-related cancer that is still present in some nations and will become apparent in others in the near future. By taking into account the quantity of chemical entities available, one can gain an appreciation of the range of issues that occupational toxicology faces. It is feasible to obtain a decent understanding of the quantity of chemical substances, and this is not too difficult.

12.2 OCCUPATIONAL TOXICANTS

Chemicals that are present in the work environment and have the potential to be harmful to employees' health are referred to as occupational toxicants. These substances exist in a variety of forms, such as dust, vapors, fumes, gases, and liquids. To protect employees' health and safety, occupational toxicology seeks to recognize, evaluate, and reduce the hazards connected to exposure to these toxicants. Depending on the substance's nature, the amount and length of exposure, and an employee's susceptibility, the presence of occupational toxicants in the workplace might present serious dangers to those who work there. Toxicant exposure can happen by injection, ingestion, skin contact, or inhalation; in many work environments, inhalation is the most frequent method of exposure. Numerous compounds, including heavy metals (including lead, mercury, and cadmium), solvents, pesticides, industrial chemicals, carcinogens, irritants, and sensitizers, can function as occupational toxicants. Depending on their toxicity and the degree of exposure, these compounds can have a wide range of harmful health effects, from acute poisoning to chronic disorders. Lead exposure, for instance, can harm the nervous system, whereas asbestos exposure can result in lung cancer and mesothelioma. Occupational toxicants can have a variety of health impacts, including as cancer, respiratory issues, skin rashes, allergic reactions, reproductive issues, and organ damage. Additionally, some toxicants may have long-term impacts that take years to manifest, making it difficult to recognize and manage possible health problems in the work place. When it comes to determining the hazards connected to occupational toxicants and creating plans to reduce those risks, occupational toxicologists are essential. In order to do this, it may be necessary to carry out risk assessments, keep an eye on workplace exposures, put control measures in place (such as engineering controls, administrative controls, and personal protective equipment), and instruct and teach employees on safe handling techniques. To prevent workers from being exposed to occupational toxicants, regulatory bodies like the Health and Safety Executive (HSE) in the UK and the Occupational Safety and Health Administration (OSHA) in the US develop guidelines and standards. Employers are required by these regulations to take precautions to guarantee that workers are not exposed to levels of toxicants that exceed acceptable exposure limits (PELs) for a variety of substances. Employers are required by law and morality to give their workers a safe workplace in addition to complying with regulations. In order to do this, it is necessary to recognize and manage the risks related to occupational toxicants, monitor and record workplace exposures on a regular basis, provide suitable training and safety gear, and put in place efficient emergency response plans in the event of spills or accidental exposures.

12.3 EXPOSURE LIMITS

Occupational toxicant exposure limits refer to the highest permissible concentration or level of exposure to a certain toxin in the workplace for a given amount of time, as determined by regulatory or suggested norms. These restrictions are in place to shield employees from the harmful health impacts of being around hazardous materials.

1. **Permissible Exposure Limits (PELs):** These permissible exposure limits are regulatory thresholds established by US organizations like the Occupational Safety and Health Administration (OSHA). For example, an 8-hour time-weighted average or a short-term exposure limit set out the maximum permissible concentration of a material in the air averaged over a given duration. Businesses must make sure that employees aren't exposed to toxicants in excess of certain thresholds.
2. **Threshold Limit Values (TLVs):** Developed by the American Conference of Governmental Industrial Hygienists (ACGIH), TLVs are suggested exposure limitations. TLVs, akin to PELs,

denote airborne particle concentrations that the majority of workers can repeatedly encounter without experiencing detrimental health consequences. There are several categories within TLVs, including ceiling limit, short-term exposure limits (STEL), and time-weighted average (TWA).

3. **Recommended Exposure Limits (RELs):** The National Institute for Occupational Safety and Health (NIOSH) and other organizations propose certain exposure limits. These restrictions, which are supported by scientific data, are meant to shield employees from the harmful health effects of prolonged exposure to particular compounds. RELs are given as recommendations to safety experts and businesses; they may not be the same as PELs or TLVs.

The scientific evidence that is now available, toxicological data, epidemiological studies, and risk assessment procedures are the foundations for determining occupational toxicant exposure limits. These bounds are evaluated and modified on a regular basis to take into account modifications to regulatory requirements as well as advancements in scientific knowledge. In order to prevent overexposure and safeguard employees' health and safety, employers must evaluate workplace exposures to toxicants, implement suitable control measures to guarantee compliance with exposure limits, provide workers with the necessary training and protective gear, and carry out routine monitoring and surveillance.

12.4 OCCUPATIONAL HAZARDS

Risks or hazards that exist in the workplace and have the potential to endanger employees' health, safety, or well-being are known as occupational hazards. Numerous elements, including chemical, biological, physical, ergonomic, and psychosocial ones, can give rise to these risks.

1. **Physical Hazards:** These comprise dangers including vibration, noise, radiation, temperature extremes, and mechanical hazards like falling objects or moving machinery. Physical risks can result in fractures, burns, wounds, or loss of hearing.
2. **Chemical Hazards:** These include exposure to dangerous materials such gases, vapors, fumes, dusts, mists, and toxic chemicals. These substances can cause poisoning, respiratory issues, dermatitis, cancer, and neurological disorders, among other acute or long-term health effects.
3. **Biological risks:** Exposure to microorganisms like bacteria, viruses, fungus, and parasites can result in biological risks. Those who work in the food industry, healthcare, and agricultural sectors are most vulnerable. Among other health problems, allergies, and infectious disorders can be brought on by biological risks
4. **Ergonomic Hazards:** These concerns pertain to how work tasks, tools, and workspace arrangements are designed. Due to jobs demanding awkward postures, severe exertions, or repetitive actions, poor ergonomics can result in musculoskeletal disorders (MSDs), repetitive strain injuries, back pain, and other physical discomforts.
5. **Psychosocial Hazards:** These risks result from social and organizational elements in the workplace, including a lack of social support, an excessive workload, job insecurity, workplace violence, and bullying and harassment. Stress, anxiety, sadness, burnout, and other mental health problems can be brought on by psychosocial hazards.

To protect employees' health, safety, and wellbeing at work, it is essential to recognize, evaluate, and manage occupational hazards. This entails carrying out risk assessments, putting control measures in place (such as engineering controls, administrative controls, and personal protection equipment), educating and training employees, and creating efficient safety policies and procedures. To address

occupational dangers and improve workplace safety, regulatory bodies like the Health and Safety Executive (HSE) in the UK and OSHA in the US provide standards and guidelines. Employers are required by law and morality to reduce risks, provide a secure workplace, and shield workers from damage. In order to avoid mishaps and injuries, employees also have a responsibility to recognize dangers, adhere to safety procedures, and report hazardous situations.

12.5 RISKS ASSOCIATED WITH HAZARDOUS SUBSTANCES

Given their potential to inflict harm upon exposure, hazardous substances pose considerable dangers to both human health and the environment. Toxic, combustible, corrosive, and reactive compounds are among the many chemicals that fall under this category. For hazardous compounds to be managed and their effects mitigated, it is essential to understand the risks involved. A summary of the dangers connected to dangerous drugs is as follows:

1. **Health Risks:** Exposure to dangerous substances can result in a range of negative health consequences, from acute symptoms to long-term illnesses. These effects are contingent upon various elements, including the substance's toxicity, the mode of exposure (e.g., ingestion, dermal contact, and inhalation), the length and intensity of exposure, and the sensitivity of the individual. The following are some health risks linked to dangerous substances:
2. **Acute Poisoning:** Prolonged exposure to elevated levels of specific chemicals may result in acute poisoning symptoms, including nausea, vertigo, dyspnea, and unconsciousness.
3. **Chronic Health Effects:** Prolonged exposure to dangerous substances can cause long-term neurological impairment, dermatitis, cancer, reproductive issues, respiratory illnesses, and organ damage (liver or kidney damage, for example).
4. **Sensitization and Allergic Reactions:** People may become sensitized to some dangerous substances, which can cause allergic reactions when they are exposed again. A few examples are specific compounds found in textiles, industrial goods, and cosmetics.
5. **Environmental Risks:** Hazardous materials can also seriously endanger wildlife, water bodies, ecosystems, and other aspects of the environment. Hazardous compounds provide many environmental dangers, which include:
6. **Contamination:** Air, soil, and water contamination can result from the improper disposal or release of dangerous materials into the environment. In addition to disrupting natural habitats, this pollution can pollute food and water sources and damage ecosystems.
7. **Bioaccumulation and Biomagnification:** Certain dangerous compounds have the ability to build up in living things and intensify as they move up the food chain. This can result in higher concentrations in apex predators and a higher risk of toxicity for natural populations.
8. **Habitat Destruction:** Plant, animal, and microbe populations can be impacted by pollution and contamination from hazardous substances, which can lead to habitat degradation and biodiversity loss.
9. **Safety Risks:** Hazardous substances pose safety risks in the workplace, particularly in industries where handling, storage, and transportation of chemicals are involved. Safety risks associated with hazardous substances include
    - **Fire and Explosion Hazards:** Flammable and combustible substances can pose fire and explosion risks if not handled properly. Ignition sources such as sparks, flames, and static electricity can trigger fires and explosions in the presence of certain chemicals.

- **Chemical Reactivity:** Reactive substances can undergo hazardous reactions when exposed to heat, air, water, or incompatible materials. These reactions can release toxic gases, generate heat or pressure, and cause chemical spills or explosions.
- **Storage and Handling Accidents**: Improper storage, handling, or transfer of hazardous substances can result in accidents such as spills, leaks, and exposures. These accidents can endanger workers, nearby communities, and the environment.

Hazard identification, exposure monitoring, thorough risk assessment, and control measure implementation are necessary for managing the hazards related to hazardous compounds. This covers giving employees the right instruction, personal protection equipment (PPE), and emergency response procedures in addition to handling, labeling, and disposing of chemicals in the right way. International standards and regulatory organizations offer rules and regulations that reduce the hazards related to hazardous materials and encourage safe handling procedures across a range of industries.

Risk assessment and management are critical processes used to identify, evaluate, and mitigate risks associated with various activities, processes, or substances. Effective risk assessment and management help organizations identify potential hazards, prioritize risks, and implement control measures to prevent or minimize harm to people, property, and the environment. Here's an overview of risk assessment and management guidelines

12.6 RISK ASSESSMENT AND MANAGEMENT GUIDELINES

The goal of occupational hygiene, a multidisciplinary profession, is to safeguard employees' health and wellbeing by detecting, evaluating, and controlling workplace dangers. Physical, chemical, biological, ergonomic, and psychosocial workplace risks are all included in its scope of recognition, assessment, and management. By putting in place efficient control mechanisms and encouraging a safe and healthy work environment, occupational hygiene seeks to avoid diseases, injuries, and other health effects associated to the workplace. Important elements of workplace sanitation consist of followings:

1. **Identification of Hazards:** Finding possible risks connected to the activity, procedure, or material is the first stage in risk assessment. This entails methodically locating potential danger areas, such as chemical, biological, physical, ergonomic, or psychosocial risks. The following methods can be used to identify hazards: process mapping, checklists, brainstorming, and historical data analysis.
2. **Risk Analysis:** Following hazard identification, each hazard's possible negative effects are evaluated for likelihood and severity. Quantifying the likelihood of an event and its effects are key components of risk analysis. Both qualitative and quantitative approaches, such as risk matrices and risk rating, as well as probabilistic risk assessment and fault tree analysis, can be used to accomplish this. By ranking hazards according to importance, risk analysis helps identify where resources should be allocated.
3. **Risk Evaluation:** Following a risk analysis, the findings are assessed to ascertain whether the hazards found are tolerable or call for additional action. Comparing the projected risks to predetermined standards, such as organizational policies, stakeholder expectations, or legal requirements, is the process of risk appraisal. Higher-than-acceptable risks might need to be addressed right away, while lower-risk ones could be controlled with continuous observation and control mechanisms.
4. **Risk Control:** This refers to putting policies in place to get rid of, lessen, or manage hazards that have been recognized to a manageable level. Engineering controls, administrative controls,

procedural controls, and personal protective equipment (PPE) controls are the four primary categories of control measures. Redesigning equipment or processes, putting safety standards and procedures into place, offering monitoring and training, and equipping employees with personal protective equipment are a few examples of control measures.

5. **Monitoring and Review:** To ensure the efficacy of control measures and spot developing risks, risk management is a continuous process that needs to be regularly monitored and reviewed. Monitoring entails keeping tabs on shifts in risk tolerance, adherence to safety precautions, and the efficiency of risk mitigation techniques. Frequent evaluations of risk assessments and control measures aid in finding weaknesses, determining what has to be changed, and updating risk management strategies accordingly.

6. **Communication and Consultation:** Throughout the risk assessment and management process, effective communication and consultation are crucial. This entails involving stakeholders in order to obtain feedback, exchange information, and work together on risk management initiatives. These stakeholders include staff members, contractors, regulators, and the community. Establishing trust, raising risk awareness, and facilitating cooperation in the implementation of control measures are all aided by open and honest communication.

7. **Record-Keeping and Documentation:** It's critical to keep records of every step of the risk assessment and management procedure, including the identification of hazards, risk analysis, control strategies, outcomes of monitoring, and review findings. Thorough documentation guarantees responsibility, streamlines adherence to legal mandates, and establishes a foundation for ongoing enhancement.

12.7 OCCUPATIONAL HYGIENE

Organizations may systematically identify, evaluate, and manage risks to safeguard the environment, communities, and employees' health and safety by adhering to these principles. Safer workplaces, more operational effectiveness, and increased organizational resilience in the face of uncertainty and change are all impacted by effective risk assessment and management.

In order to safeguard employees' health and wellbeing, occupational hygiene is a multidisciplinary profession that focuses on locating, evaluating, and controlling workplace dangers. It includes identifying, assessing, and controlling potential risks in the workplace that are chemical, biological, ergonomic, and psychosocial. Occupational hygiene aims to avoid infections, injuries, and negative health impacts associated to work by putting in place efficient control mechanisms and encouraging a safe and healthy work environment.

a. **Hazard Identification:** Occupational hygienists identify potential hazards present in the workplace through comprehensive assessments and surveys. This involves identifying sources of exposure to physical agents (e.g., noise, vibration, radiation), chemical substances (e.g., toxic gases, solvents, dusts), biological agents (e.g., bacteria, viruses, fungi), ergonomic factors (e.g., repetitive motions, awkward postures), and psychosocial stressors (e.g., workload, job insecurity).

b. **Risk Assessment:** After identifying potential dangers, occupational hygienists evaluate the risks of being exposed to those risks. This entails estimating the probability and impact of harmful health impacts depending on variables like exposure levels, frequency, duration, and individual susceptibility. Risk assessments aid in the prioritization of dangers and the selection of suitable risk-reduction controls.

c. **Exposure Monitoring:** To gauge the presence of potentially dangerous materials or agents in the workplace, occupational hygienists carry out exposure monitoring. Biological samples (blood, urine, etc.), air samples, or environmental samples may be collected in order to measure exposure levels and evaluate adherence to exposure limits and legal requirements. Data from exposure monitoring can be used to assess risk and gauge how well control strategies are working.

d. **Control Measures:** Occupational hygienists recommend and put into practice control measures to lessen or eliminate workplace risks based on the findings of risk assessments and exposure monitoring. Engineering controls (such as ventilation, isolation), administrative controls (such as work procedures, training), personal protective equipment (such as respirators, gloves), and the replacement or removal of hazardous materials are a few examples of control measures. Prioritizing control measures is done using the hierarchy of controls, with a focus on removing dangers wherever possible at their source.

e. **Training and Education:** Occupational hygienists educate and train employees, managers, and supervisors on the dangers of workplace hazards and the value of putting control measures in place. This entails promoting safe work practices, educating people on the appropriate use of personal protection equipment, and increasing knowledge of potential health implications.

f. **Regulatory Compliance**: Occupational hygienists ensure compliance with occupational health and safety regulations, standards, and guidelines established by regulatory agencies such as OSHA, NIOSH, and ACGIH. This includes conducting audits, inspections, and assessments to identify areas of non-compliance and implementing corrective actions to address deficiencies.

All things considered, occupational hygiene is essential for preserving the health and safety of employees since it detects, evaluates, and eliminates workplace risks that could lead to exposures, diseases, or injuries. Occupational hygienists help to create safer and healthier work environments for all employees by putting best practices and scientific concepts to use.

12.8 INDUSTRIAL HYGIENE

The goal of the field of industrial hygiene, sometimes referred to as occupational hygiene, is to ensure the health and safety of workers by finding, assessing, and mitigating workplace dangers. Its main goal is to stop occupational diseases, accidents, and exposures by identifying and controlling the different physical, chemical, biological, ergonomic, and psychological risks that exist in industrial environments. Key components of industrial hygiene include:

a. **Hazard Identification:** Using a variety of techniques, including workplace inspections, hazard surveys, and exposure monitoring, industrial hygienists systematically identify possible dangers in the workplace. Physical agents (such as vibration, noise, heat, radiation), chemical substances (such as toxic gases, solvents, metals), biological agents (such as bacteria, viruses, fungi), ergonomic factors (such as heavy lifting, repetitive motions), and psychosocial stressors (such as workload, shift work) are a few examples of potential hazards.

b. **Risk Assessment**: After identifying potential dangers, industrial hygienists evaluate the risks of coming into contact with those risks. This entails estimating the probability and impact of harmful health impacts depending on variables like exposure levels, frequency, duration, and individual susceptibility. Risk assessments assist in identifying the most important hazards and the best management strategies to successfully reduce risks.

c. **Exposure Monitoring:** To gauge the concentrations of potentially dangerous materials or agents in the workplace, industrial hygienists carry out exposure monitoring. Biological samples (blood,

urine, etc.), air samples, or environmental samples may be collected in order to measure exposure levels and evaluate adherence to exposure limits and legal requirements. Data from exposure monitoring can be used to assess risk and gauge how well control strategies are working.

d. **Control Measures:** Industrial hygienists recommend and put into practice control measures to lessen or eliminate occupational risks based on the findings of risk assessments and exposure monitoring. Engineering controls (such as ventilation, isolation), administrative controls (such as work procedures, training), personal protective equipment (such as respirators, gloves), and the replacement or removal of hazardous materials are a few examples of control measures. Using the hierarchy of controls, you can set priorities. Prioritizing control measures is done using the hierarchy of controls, with a focus on removing dangers wherever possible at their source.

e. **Training and Education:** Industrial hygienists instruct employees, managers, and supervisors on the dangers of workplace hazards and the need of putting control measures in place. This entails promoting safe work practices, educating people on the appropriate use of personal protection equipment, and increasing knowledge of potential health implications.

f. **Regulatory Compliance:** Occupational hygienists make sure that rules, guidelines, and standards related to occupational health and safety are followed. These regulations are set by regulatory bodies like the American Conference of Governmental Industrial Hygienists (ACGIH), NIOSH (National Institute for Occupational Safety and Health), and OSHA (Occupational Safety and Health Administration). This entails carrying out evaluations, audits, and inspections to find non-compliance areas and putting remedial measures in place to fix any shortcomings.

g. **Emergency Preparedness**: To handle possible workplace catastrophes such chemical spills, fires, or releases of hazardous materials, industrial hygienists create and carry out emergency response plans and procedures. To guarantee an efficient reaction to crises, this entails educating employees on emergency protocols, carrying out drills and exercises, and collaborating with emergency response organizations.

12.9 HAZARD CONTROL

"Hazard control" is the process of identifying, assessing, and implementing measures to reduce or eliminate workplace risks in order to protect workers' health and safety. Effective hazard control strategies cover a range of hazards, including chemical, biological, physical, ergonomic, and psychological factors, in order to prevent accidents, diseases, and injuries. The following are important hazardous control strategies:

a. **Engineering controls**: Engineering controls are making changes to the machinery or work environment in order to get rid of or lessen dangers at their source.

- **Substitution:** Switching out risky materials or procedures with less dangerous ones. For example, replacing hazardous chemicals with safer ones.
- **Enclosure:** To control risks like noise or airborne pollutants, barriers or enclosures are placed around machines or processes.
- **Ventilation:** To collect and eliminate airborne pollutants from the workplace, local exhaust ventilation systems should be implemented.

b. **AdministrativeControls:** To lessen exposure to risks, administrative controls concentrate on altering work practices, rules, and procedures. As examples, consider:

- **Work rotation:**Switching up jobs performed by employees helps reduce extended exposure to ergonomic risks or repetitive motions.
- **Job scheduling:**To lower the possibility of mishaps or exposures, high-risk jobs should be scheduled at times when fewer employees are present.
- **Education and training:**supplying workers with knowledge, guidance, and instruction on emergency protocols, safe work practices, and hazard awareness.
- **Signage and warning labels:**To inform employees of possible risks and to convey safety instructions, post signs, labels, and warnings.

c. Personal Protective Equipment (PPE): PPE refers to the clothes, tools, and gadgets that employees wear or use to guard against risks. As examples, consider:

- **Respiratory protection:** using breathing devices, respirators, or masks to prevent inhaling dangerous gases, dusts, or vapors.
- **Eye and facial protection:** To guard against impact, chemical splashes, and airborne particles, use safety glasses, goggles, or face shields.
- **Earmuffs:** earplugs for hearing protection to lessen exposure to loud noises and avoid hearing loss.
- **Protective gear:** aprons, boots, coats, or gloves to prevent cuts, abrasions, and chemical splashes, among other physical dangers.

d. Behavioral Controls: These measures entail encouraging safe conduct and cultivating a safety-aware culture in the workplace. As examples, consider:

- **Safety coaching and training:** Continuing education and feedback are given to promote safe work practices and address risky behavior.
- **Safety incentives and recognition programs:** Honoring staff members who uphold safety procedures and show a dedication to the cause.
- **Reporting and investigation:** To support inquiry, analysis, and remedial action, it is recommended that employees report risks, near misses, and occurrences as soon as possible.

Organizations can effectively mitigate workplace hazards and create safer, healthier work environments for their people by employing a combination of engineering controls, administrative controls, PPE, and behavioral controls. It is vital to conduct periodic assessments, oversee, and revisions of risk mitigation strategies to guarantee their efficacy and accommodate evolving circumstances or novel threats.

12.10 SUMMARY

A specialized area called occupational toxicology studies harmful compounds that are present in the workplace and their possible consequences on human health. It entails evaluating the risks to one's health, exposures, and hazards related to different chemicals, physical agents, and biological agents that one may come into contact with at work. Occupational toxicology's main objective is to safeguard employees' health and safety by detecting, assessing, and controlling the hazards associated with toxic substance exposure at work. This entails figuring out how employees might be exposed to dangerous materials by injection, ingestion, skin contact, or inhalation as well as evaluating the possible health impacts of these exposures. All things considered, controlling occupational toxicants is crucial to

protecting employees' health and wellbeing and averting accidents and diseases at work. Employers can make their workplaces safer and healthier for their staff members by educating them about the dangers of exposure to harmful substances and putting in place the necessary controls. Through the identification, evaluation, and control of workplace hazards, industrial hygiene plays a critical role in safeguarding the health and safety of workers in industrial environments, thereby preventing occupational illnesses, injuries, and exposures. Industrial hygienists make workplaces safer and healthier for all workers by putting best practices and scientific concepts to use. Toxicology, epidemiology, industrial hygiene, and risk assessment are among the fields that occupational toxicologists draw from for their thorough assessments of workplace dangers. For the purpose of assessing the possibility and seriousness of negative health consequences linked to occupational exposures, this may entail doing risk assessments, toxicity tests, and exposure assessments.

12.11 TERMINAL QUESTIONS

Q. 1. What is occupational toxicity? Discuss occupational toxicant.

Answer: ----------

Q. 2. What is the exposure limit level? Discuss the TLV exposure limit?

Answer: ----------

Q. 3. What activities do you need to undertake to address the problems of chemical hazards in the short and long term?

Answer: ----------

Q. 4. What systems, policies and programs do you need to put in place to ensure that chemical safety issues are being effectively managed?

Answer: ----------

Q. 5. What possibilities can you think of for methods of monitoring exposure?

Answer: ----------

Q. 6. What do we need to know about the chemical to decide if such suggestions are feasible?

Answer: ----------

12.12 FURTHER SUGGESTED READINGS

1. Occupational toxicology 2nd edition edited by Chris winder and Neill Stacey.

2. Occupational Toxicology, Chris Winder, Neill H. Stacey, CRC Press.

3. Environmental Toxicology, third edition, Sigmund F. Zakrzewski, Published by Oxford University Press, Inc. New York, New York 10016.

4. Environmental Toxicants, Human Exposures and Their Health Effects, Third Edition, Morton Lippmann, Published By John Wiley & Sons, Inc., Hoboken, New Jersey.

5. Toxicology in Occupational and Environmental Setting, Wolfgang Dekant, Institute of Toxicology, University of Wuerzburg, Germany.

6. A Textbook of Modern Toxicology, Ernest Hodgson, Published By John Wiley & Sons, Inc., Hoboken, New Jersey.

7. A Textbook of Modern Toxicology: Ernest Hodgson, A John Wiley & Sons, Inc., Publication

8. Principles of Environmental Toxicology, I. Shaw, J. Chadwick, CRC Press.

ROUGH WORK

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