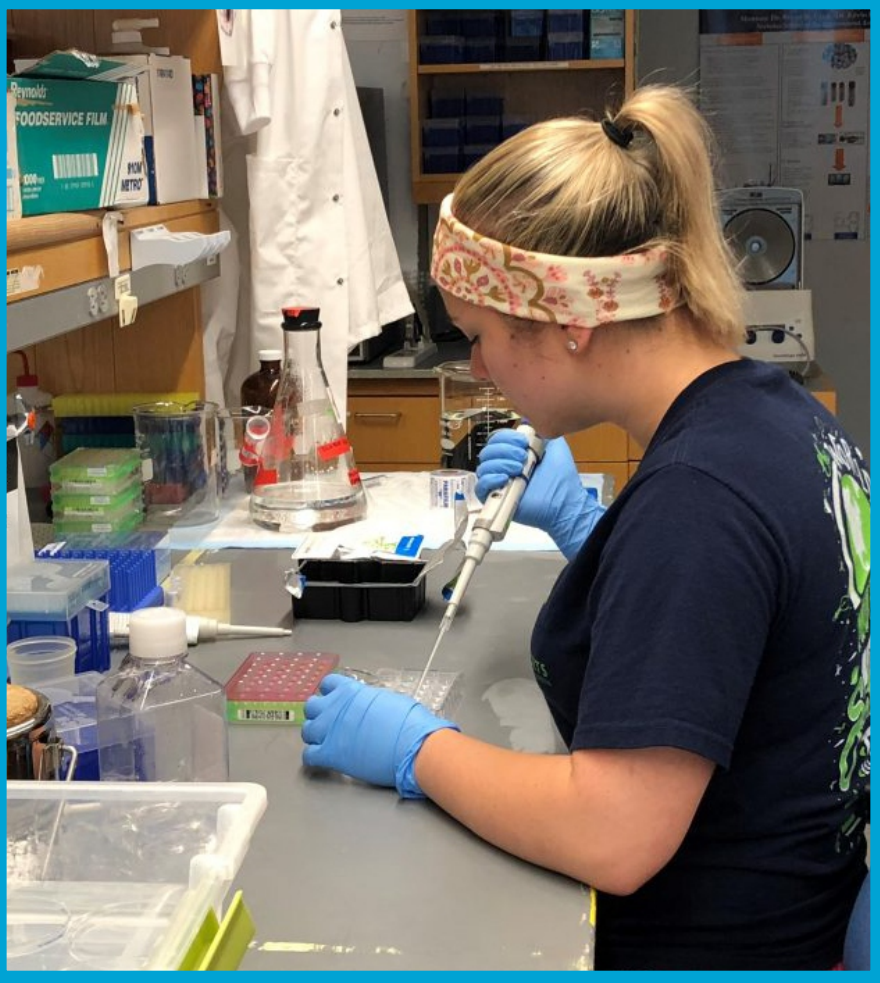
Environmental Toxicology



Mayur Porwal

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Wisdom Press
NEW DELHI

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This edition published by Wisdom Press,
Murari Lal Street, Ansari Road, Daryaganj,
New Delhi - 110002.

ISBN: 979-8-89161-318-8

Edition: 2022 (Revised)

Wisdom Press

Production Office: "Dominant House", G - 316, Sector - 63, Noida,
National Capital Region - 201301.
Ph. 0120-4270027, 4273334.

Sales & Marketing: 4378/4-B, Murari Lal Street,
Ansari Road, Daryaganj, New Delhi-110002.
Ph.: 011-23281685, 41043100.
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CONTENTS

CHAPTER 1

REVIEW OF PHARMACOLOGIC CONCEPTS

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ABSTRACT:
Science in the modern day admits that such a rigid distinction is unjustified. Paracelsus understood in the sixteenth century that "the right dose differentiates a poison from a remedy." Numerous chemical compounds or mixes have a wide range of effects, from positive to neutral to harmful. Their impact varies on the species and size of the organism, its nutritional state, the type of exposure, and a number of other associated elements in addition to the amount of the chemical to which an organism is exposed. An excellent illustration is alcohol. Alcohol may be safe when used in moderation and is occasionally even prescribed by doctors. But an overdose results in drunkenness and, in the worst circumstances, death. Similar to that, vitamin A is necessary for the majority of higher species to operate normally, but an excess of it is very harmful. If a chemical's biological effect is dose-dependent, there must be a quantifiable range between concentrations that have no effect and those that have the greatest impact. The observation of an impact, whether advantageous or detrimental, is made more difficult by the fact that systems that seem to be homogenous are really heterogeneous. Even an inbred species will have distinct variations in behavior in reaction to substances.

KEYWORDS:
Alveoli, Dosage, Gases, Substances, Toxicity.

INTRODUCTION

Early scientific understanding identified two main categories of substances: those that are helpful (such meals and medications) and those that are dangerous (those that result in illness or death). These were classified as poisons.An effect that is achieved in one person won't always be duplicated in another. Therefore, statistical techniques of assessment will be required for any accurate calculation of the hazardous potency of a substance[1], [2].

Assessment of Toxicity

An observable and well defined end result must be found in order to assess a compound's toxicity for a biological system. As an end goal in bacterial systems, turbidity or acid production that reflects the growth or growth inhibition of a culture may be employed. Colony count may be utilised in specific circumstances, such as in the research of mutagenesis. The same is true for measurements of viable cells, cell protein, or colony count in cell cultures. The death of an animal is the in vivo experiment's most easily apparent end goal, and it is usually employed as a starting point for assessing a chemical's toxicity. There are other issues with toxicology than the death of animals or the inhibition of cell development. Depending on the experiment's objectives, a variety of additional end points could be used. Examples of such options include the suppression of a particular enzyme, sleep patterns, the emergence of tumours, and the delay before an action takes effect[3], [4].

Dose must be stated in terms of concentration rather than absolute quantity since the toxicity of a chemical depends on the size of the organism exposed (1). (The entire quantity delivered is usually referred to as the whole dosage in medical literature and pharmacokinetics.) In

vitro systems employ molar units (millimolar, micromolar, nanomolar) or weight units (milligramme, microgram, nanogram, etc.) per millilitre of maintenance medium. In trials on animals, dosages are measured in weight, molecular units, or square metres of body surface area per kilogramme of body weight.

As an example, a simple experiment is created to ascertain a chemical's lethality in mice. The test substance is given to several groups of animals, typically 5–10 animals per group, with each subsequent group getting an increasing dosage. Each group's total number of deceased animals is kept track of. The proportion of animals who died at each dosage, less the percentage that perished at the immediately lower dose, is then plotted versus the dose's logarithm. The quantal dose-response curve, also known as the Gaussian distribution curve, is produced using this plot and.

The dosage that will kill 50% of the animals is known as the LD50, and it is shown by the point at the top of the curve. LD16 is equal to the mean minus one standard deviation (SD), while LD2.3 is equal to LD50 minus two SD. The LD for the mean plus one SD is LD84, while the LD for the mean plus two SD is LD97.7. ecological toxicology 1M is usually pronounced as "molar" and stands for moles per litre. So, mM stands for millimolar, mM for micromolar, and nM for nanomolar. Lethal dosage is abbreviated as 2LD. Depending on the kind of experiment, other terminology may also be employed. Inhibitory concentration is denoted by IC, and effective dosage by ED. The cumulative proportion of dead animals is often displayed against the logarithm of the dosage since this sort of figure is not particularly useful [5], [6].

Bliss, who investigated the impact of pesticides on insects, is credited with the invention of the semi logarithmic plot. At the smallest dosage and the highest dose, he saw that certain insects were always dead and others were always alive. Additionally, he noticed that increasing the dosage by a given amount always enhanced the impact. A logarithmic dosage scale, as opposed to a linear one, was recommended by a mathematical model that reflected these circumstances.

The impact in this section is proportional to the dosage logarithm because the centre of the curve is almost linear. The two extremities of the curve never reach 0 and 100% effect but asymptotically get closer to them. As a result, it is impossible to establish the threshold dosage, or the level below which there is no impact, by experimentation.

The confidence limits of the data points are highest in the centre section and lowest at the flat regions of the curve, according to analysis of the curve in these flat segments, even a minor difference between the actual value and the predicted value results in a significant dosage estimate inaccuracy. Toxicologists must understand that the only valid data points are those that lie along the straight section of the curve.

Transformation of Probit

The probit transformation (for probability), a new method of visualizing the dose-response curve, was presented by Bliss (1). Effect is shown in this figure as a profit unit, with the LD50 value being 5. Each +SD increases the scale by one point, and each -SD decreases it by one.

Pharmacologic Concepts Reviewed

Quanta dose. The frequency is the proportion of animals who died after receiving each dosage. 3The two positions, one on each side of the mean, within which 95% of the data points would fall if the experiment were to be repeated 100 times are known as confidence bounds. The 95% confidence interval is the distance between these positions. It matches the median.

DISCUSSION

A compound's potency, as measured by its LD50, is a relative notion that only has significance when comparing the potencies of two or more different compounds. When two substances' dose-response curves are parallel, it is simple to compare them; the substance with the lower LD50 value is the more powerful one. As LD values differ, two substances, however, may have a reversed toxicity relationship. Compound A is more harmful than compound B at LD50 values, but less toxic at LD20 concentrations, as seen in Figure 2.4.A dose-response curve's slope plays a significant role in determining the margin of safety. A little dosage increase may result in a big change in toxicity if the slope is steep. Therefore, the margin of safety increases as the slope becomes less. It's important to distinguish this definition of the margin of safety from the one used in clinical toxicology, where the margin of safety refers to the difference between an effective (curative) dosage and a hazardous one. The therapeutic index is defined as the ratio of LD50 to ED50. Both potency and effectiveness must be taken into account when determining a compound's toxicity. Due to the fact that their dose-response curves never reach 100% of the effect, certain substances may have great potency, as measured by their LD50, but poor effectiveness[7], [8].

Reversible Toxicology

The ability of a harmful impact to be reversed should also be taken into account. A chemical's toxicity is often largely reversible. The person will recover when the toxin is eliminated by excretion or rendered inactive by metabolism, unless the damage to the afflicted organs has advanced to the point where it threatens the organism's ability to survive. The poison may still be present in the tissue, although in certain circumstances the impact may endure longer. A toxin's irreversible inactivation of an enzyme results in the loss of an organism's essential activities. Even when there is no evidence of free poison in the body, the organism will not recover until enough of the compromised enzyme has been synthesised for the first time. Intoxication with organophosphates, which bind to acetylcholinesterase basically permanently, is a common illustration of such an effect. In rare instances, a toxin's activity may deprive an organism of a crucial substance, even when there is no permanent inactivation of an enzyme, and recovery must wait for the resynthesis of this substance. This is the case with reserpine, which works by depleting sympathetic nerve terminals' stores of catecholamine; the time needed to do so is longer than reserpine's persistence in the tissue.There is a biphasic dose-response relationship for substances that are needed in tiny levels for an organism to operate normally but that are hazardous at large doses, as seen in Figure 2.5. This group includes the vitamins A, niacin, selenium, and several heavy metals like copper and cobalt. Such compounds have a typical range of values. Concentrations over this range are hazardous and, in severe circumstances, potentially fatal. If the concentration falls below this level, the organism has a deficit that affects typical processes and might be fatal[9], [10].

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Strong acids and bases are examples of substances that might cause harm in a non-specific manner by simply denaturing protein and dissolving the tissue. Chemical burns are the name given to such lesions. Toxins often affect the tissue by interacting with certain parts of it, which throws off regular metabolism. Paul Ehrlich (4) first put up the idea of particular receptors at the beginning of the 20th century. According to his theory, a chemical must find a receptor site and a particular target region in order to exert biological effect.

There are several known receptors, and they are all proteins. Enzymatic activity is present in a few of the proteins. For instance, acetyl-cholinesterase is a receptor for organophosphates, and di-hydro folate reductase is a receptor for anti-folates. The receptors for steroid hormones are examples of receptors that act as "transport vehicles" across cellular membranes (5). Certain receptors may be exclusive to certain tissues or they may be found in all the cells of an organism. Plasma proteins regularly bind substances in circulation, sometimes in extremely tight bonds. The proteins involved are not thought of as unique receptors, despite the fact that this binding is often specific for a particular chemical. Such interactions do not produce biological activity; they only stop the substance from getting to the target cells.

Toxins' Entry Method

Percutaneous, respiratory, and oral ingestion are the three main ways that xenobiotics enter the human body from an environmental perspective. Interstitial fluid fills the extracellular space in multicellular organisms. Thus, after passing through the first cellular barrier (such as skin, intestinal mucosa, or the lining of the respiratory system), a substance enters interstitial fluid regardless of how it enters the body (with the exception of intravenous delivery). The substance leaves the interstitial fluid, permeates the capillaries, and enters the bloodstream, where it is transported throughout the body.

Percutaneous Route

The skin creates a barrier of defence between the rest of the body and the outside world. Chemicals were formerly supposed not to permeate skin, according to conventional wisdom. This viewpoint is no longer valid in light of more current findings. Although most compounds only penetrate the skin slowly, this route of entry is crucial for both human and animal exposure to harmful toxins. The skin is made up of three layers: the epidermis, which is the outermost protective layer; the dermis, which is the middle layer; and the hypodermis, which is the deepest layer and is made up of a combination of adipose tissue and connective tissue. The skin also has epidermal appendages that extend into the dermal layer, including hair follicles, sebaceous glands, and sweat glands and ducts. Diffusion from the epidermis into the dermis, entrance via sweat ducts, and penetration through hair follicle orifices are the three potential pathways for percutaneous absorption. Although the latter pathways provide relatively simple access to the vascularized dermal layer, it is thought that absorption via the epidermal cells is the primary method of toxin entrance due to its enormous surface area.

The stratum corneum, the epidermis' outermost membrane, is the major barrier to the percutaneous entry of water and xenobiotics. Keratinocytes that have dried and flattened are layered in this membrane in various thicknesses. The stratum corneum lacks vascularization and metabolic activity. Although it is not vascularized, the lower basal layer of the epidermis has a high metabolic activity and may bio transformxenobiotics. Every chemical that enters the stratum corneum does so passively over a number of cell layers. The chemical characteristics of a xenobiotic affect the site of entrance. Protein filaments are thought to

allow polar molecules to pass through cell membranes whereas nonpolar ones do not penetrate via the lipid matrix (for further information, read the chapter's section on cellular absorption). The stratum corneum becomes more permeable to polar compounds when it is hydrated. Electrolytes penetrate mostly in a nonionizedstate; hence permeability is influenced by the pH of the fluid applied to the skin. The stratum corneum is easily penetrated by several lipophilic chemicals, including carbon tetrachloride and organophosphate pesticides. The permeability of the skin is increased by pretreating it with solvents such dimethyl sulfoxide, methanol, ethanol, hexane, acetone, and, in particular, a combination of chloroform and methanol (6). The elimination of lipids from the epidermis, which would change its structure, is most likely what causes this impact. Skin permeability varies from person to person. Depending on the diffusivity and stratum corneum thickness, it differs across species and even within species. Generally speaking, gases may permeate the skin more easily than liquids and solutes. Solids don't really penetrate. They may, however, dissolve into the skin's secretions and then be taken up as solutes. The stratum corneum is the rate-limiting response in the time-dependent process of percutaneous absorption. As a result, the length of exposure to a xenobiotic is crucial. Therefore, it is crucial to clean up spills as soon as possible. Similar to gastric absorption in terms of kinetics, percutaneous absorption happens more quickly.

Breathing Route

The three parts of the respiratory system are the nasopharyngeal, tracheobronchial, and pulmonary. Mucous glands are dispersed throughout the ciliated epithelium that lines the nasopharyngeal canal. This area's function is to filter out big inhaled particles and raise the warmth and humidity of the air being breathed. The trachea, bronchi, and bronchioles make up the tracheobronchial area. These are branching, progressively smaller channels that connect the nasopharynx with the lungs. They are lined with goblet cells, which secrete mucus, and ciliated epithelium. These cells perform what is known as the mucociliary escalator, which is the movement of foreign substances from the deepest regions of the lungs to the oral cavity, where they may either be ejected with sputum or eaten. The airways become narrower but the overall surface area gets bigger when the tracheobronchial conduits branch. Alveolar ducts, tiny tubes seeded on both sides with alveoli, respiratory bronchioles, small tubes approximately 1 mm long and 0.5 mm wide, and collections of alveoli (also known as alveolar sacs), make up the pulmonary area.

Alveoli are little bubbles that range in size from 150 to 350 mm and are where the exchange of gases between the environment and the blood occurs. The human lung has a total alveolar surface area of 100 m2 during deep intake and 35 m2 during expiration. Squamous alveolar lining cells, also known as Type I pneumocytes, surfactant-producing cells, also known as Type II pneumocytes, and freely floating phagocytic macrophages are three cell types that should be noted. Along with manufacturing surfactants, which are necessary to keep the alveoli inflated, type II pneumocytes play a role in wound healing. Gases and solutes may readily diffuse between blood capillaries and alveolar lining cells because of this close contact.Xenobiotics that are inhaled may injure respiratory tissue or reach the bloodstream and cause systemic toxicity to cause their negative effects.

The nasopharyngeal and tracheobronchial regions, to a considerable degree, eliminate gases that are readily water-soluble. Although this elimination safeguards the lower respiratory system, it does not stop harmful gases from entering the bloodstream. Poorly water-soluble gases reach the alveoli while being partly diluted by the nasopharyngeal region's humidity. The quantity of a poison in the air and the little volume of respiration determine how much of

the toxin is transported to the lungs (in gaseous form, as liquid aerosols, or as particles). The minute volume is the result of the tidal volume (i.e., the average respiratory volume, which is around 500 mL) and the respiratory rate (about 15 breaths per minute).

According to Fick's law (8), gases easily pass across alveolar membranes:

D ¼ cd S=MW1=2 Pa and Pb are the partial pressures of the gas in the inspired air and the blood, respectively, while A and d are characteristics of the lung (surface area and thickness of the membrane, respectively). D is the diffusion rate (g/cm2/per second); cd is the diffusion coefficient (cm2=s); S is the solubility of the gas in blood; MW is molecular weight. The qualities of the gas are represented by the first two expressions in this equation, while the characteristics of the lungs are represented by the third expression.

According to this equation's analysis, D is positive and gas is taken in by the blood as long as Pa is greater than Pb. Equilibrium between the gas in the alveoli and the blood has been reached when Pa 14 Pb, D 14 0 and no net gas exchange occurs. D becomes negative when Pb exceeds Pa, indicating that the person was taken out of the harmful environment. Gas diffuses from the blood into the alveoli in this scenario and is expelled during expiration.

The solubility of the gas in blood is a significant element that also affects diffusion rate. When S is high, the diffusion rate is rapid and the gas leaves the alveoli rapidly. The pace at which gas is supplied to the alveoli in this instance is the limiting element in gas delivery to the blood. Gas delivery is increased by deepening or speeding up breathing to increase minute volume.

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Because the diffusion rate is sluggish when S is modest, blood flow (or cardiac output) rather than minute volume becomes the toxicity's rate-limiting component. Aerosolized liquid toxins may potentially go to the alveoli. If they are lipid-soluble, they passively diffuse through alveolar membranes with ease. The size of the particles affects the toxicity of particulate pollution. Particles bigger than 5 mm are deposited in the nasopharynx and either driven into the oral cavity where they are ingested or ejected in sputum, or they are evacuated by sneezing. The tracheobronchial area receives deposits of particles that measure 2 to 5 mm. They are ejected in the sputum or ingested after being cleared by the mucociliary escalator. Alveoli get particle deposition of 1 mm or less. The free or phagocytized particles may then be transported to the tracheobronchial area, where the mucociliary escalator removes them from the respiratory system.Alternately, loose and phagocytized particles may reach the lymphatic system by slipping through tiny (0.8–1.0 nm) gaps between alveolar lining cells. However, the latter is a laborious and ineffective procedure. Polycyclic aromatic hydrocarbons (PAHs), some of which are carcinogenic, are often adsorbed on combustion-related particles. These hydrocarbons that have been adsorbed may dissolve in the alveolar fluid and reach the bloodstream as solutes via oral

Orally consumed substances start to be absorbed in the mouth and oesophagus. However, this area's retention period is often so brief that no appreciable absorption occurs. Compounds are combined with food, acid, gastric enzymes, and microorganisms in the stomach. All of these have the potential to change a chemical's toxicity, either by affecting absorption or by changing the substance itself (Compared to blood capillaries, the lymphatic capillaries are far more permeable to big molecules, such as proteins.) Prior to entering the circulatory system, some xenobiotics that are absorbed in the gastrointestinal cells may undergo biotransformation; the remaining xenobiotics are delivered as the parent substance. The

substances that are absorbed may reach the bloodstream either via the lymphatic system, where they ultimately drain into the bloodstream, or through the portal circulation, where they are transported to the liver[11], [12].

CONCLUSION

It has been shown that the quantitative levels of toxicity vary depending on whether substances are ingested with food or on an empty stomach. In the small intestine, food is absorbed to the greatest extent. For several nutrients including carbohydrates, amino acids, calcium, and salt, the gastrointestinal tract has specialised carrier systems. Some xenobiotics reach the cells via these pathways, whereas others do so by passive diffusion. Only nonionized forms of lipid-soluble organic acids and bases may be absorbed by passive diffusion. The Henderson-Hassel Bach equation4 states that only between nonionized forms can equilibrium be reached on both sides of the cell membrane. Review of Pharmacologic Concepts the bodily fluids' pH levels are as follows: 1.0 for gastric juice; 6.5 for small intestine contents; 7.4 for plasma and interstitial fluid; and 6.8–7.8 for urine. For acids, pKa 14 pH log for bases, pKa = 2:2a log (ionized/non-ionized) ph.Through pinocytosis, particles with a diameter of several nanometers may be taken up from the digestive tract and transported into the bloodstream.

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CHAPTER 2

STORAGE OF CHEMICALS IN THE BODY

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ABSTRACT:
The capacity of certain substances or their metabolites to be stored in the body must be taken into account. A substance will often build up in the body after repeated consumption if the rate of its biotransformation or excretion is slower than the rate of absorption. The buildup and persistence of alcohol in the blood during extended drinking is the finest illustration of this phenomena. An average 12-ounce beer can, 5-ounce glass of wine or one shot of 86-proof liquor is metabolized by the human body once per hour. A 140–160-pound person's blood alcohol level increases by 20 mg% each drink, per hour displays the amount of alcohol in the blood after ingesting one drink per hour or two drinks per hour, respectively. The intake of alcohol is significantly quicker than its metabolism when two drinks are drunk per hour, which causes the alcohol levels to rise quickly. One drink per hour is advised in order to maintain legally acceptable blood alcohol concentrations while driving.

KEYWORDS:
Cycto-chrome, Enzymes, Glutathione, Liver, Substances

INTRODUCTION

The body stores certain substances in particular tissues. By effectively removing the substance from circulation, such storage lowers the compound's toxicity. When the storage receptors become saturated, which happens when repeated dosages of a dangerous drug are taken in and stored, toxicity suddenly ensues. In rare circumstances, a chemical with an affinity for the same receptor may displace a stored drug from its storage receptor. The displacement of anti-diabetic sulfonylureas by sulfonamides and the potential of antimalarial medications like quinacrine (Atabrine) and primaquine to displace one another (15) are examples of this phenomenon. In these situations, there is a particular risk that the substances may have evaded detoxification metabolism while being retained in the body, making their release hazardous and delayed[1], [2].

Halogenated hydrocarbons, DDT (dichloro-diphenyl-trichloroethane), PCBs (polychlorinated biphenyls), and other lipophilic substances may be without injury to the exposed organism, fat is deposited. These poisons do, however, have a tendency to build up in the food chain. When a creature at the bottom of the food chain eventually reaches its storage limit, the poison may be discharged into the bloodstream and milk. Another risk is that fat reserves are mobilised for energy when an animal is starving, as occurs to wild animals regularly in the winter.

The resultant discharge of toxic substances might result in illness or death.Living things are somewhat safeguarded by their reserve functional capacity in addition to the potential long-term inactivation of xenobiotics owing to storage in diverse tissues. The lungs, liver, and kidney are a few examples of organs that might sustain some damage without showing any obvious symptoms. In these circumstances, only histology examination may show the harm[3], [4].

Metabolism Phases

Most xenobiotics' effects result in either excretion or metabolic inactivity. On the other hand, certain substances need to be metabolically activated in order to have any biological effect. Most often, specialised enzyme systems carry out these biotransformation, including the activations and inactivations. These enzymes' primary function is to make the removal of xenobiotics easier. Water-soluble substances may often be expelled in their natural forms without needing to be metabolised. Lipophilic substances may be eliminated by biliary excretion or through the kidneys if they undergo metabolism to become more polar and hence more water-soluble.

Xenobiotics typically undergo two steps of metabolism. The majority of the time, phase 1 entails oxidative reactions, while phase 2 includes conjugation (combination) with extremely water-soluble molecules. Sometimes the byproducts of biotransformation are unstable and break down to release highly reactive substances like free radicals, potent electrophiles, or extremely stressed three-member rings with a propensity for nucleophilic ring opening (epoxides, azaridines, episulfides, and diazo-methane; the chemical reactions must take place via enzymatic processes in which the substrate is activated while attached to the enzyme in order for order to be maintained inside the cells.

A stable product is only released when the required reaction has occurred. Freely moving reactive substances are undesirable because they randomly react with macromolecules like DNA, RNA, and proteins. DNA modification results in improper transcription and replication. Erroneous signals are generated via RNA modification, which in turn results in the production of aberrant proteins, which changes both regulatory and enzymatic function.

Bio-transformations in Phase 1

A group of related enzymes (usually known as mixed-function monooxidases) or cytochrome P-4501 are responsible for phase 1 processes. The fundamental processes that cytochrome P-450 enzymes catalyse include oxygen introduction into a molecule. Most of the time, the oxygen is kept in the final product, although this does happen sometimes. A prosthetic group with porphyrin-bound iron serves as the oxygen carrier (Figure 3.2, centre). These enzymes primarily catalyse the hydroxylation process.

The fundamental fact is that two single electrons are transported to the P-450-substrate complex in two distinct processes, despite the fact that other publications suggest somewhat different methods.

The reduced form of nicotinamide-adenine dinucleotide phosphate (NADPH) is where these electrons come from. In order for NADPH to perform reductions, a hydride ion—a hydrogen atom carrying two electrons—must be transferred (2). A step-down mechanism is required for the transmission of a single electron since the transfer of both electrons would occur simultaneously. To accomplish this single-electron transfer, cytochrome P-450 is joined with the enzyme cytochrome P-450 reductase, which contains two prosthetic groups: Flavin mononucleotide (FMN) and Flavindiacetate (FD)[5], [6].

The endoplasmic reticulum (ER), which is a part of the cell, contains both the cytochrome P-450 and cytochrome P-450 reductase enzymes. The phospholipid's function is to make it easier for the two enzymes to interact. The outer nuclear membrane and the ER, a network of membranes inside the cell, are one continuous membrane. The ER is broken down into tiny vesicles known as microsomes when cells are homogenised, and they may be extracted by

fractional centrifugation. By treating a microsomal sample with sodium dodecyl sulphate, cytochrome P-450 may be solubilized (5). The liver is where cytochrome P-450 and its reductase are mostly found. These enzymes are nonetheless detectable in the kidney, lungs, gut, brain, and skin [7], [8].

Another oxidising enzyme system that competes with cytochrome P-450 for the oxidation of amines is found in the endoplasmic reticulum. Historically known as mixed-function amine oxidases, this class of enzymes includes FAD as a prosthetic group. Although it was formerly believed that this system was solely specific for amines, it now seems that it also metabolisesxenobiotics that include sulphur. In Figure 3.7A, Figure 3.7B, and Figure 3.7C, respectively, mixed-function amine oxidases convert primary amines into hydroxylamines and oximes, secondary amines into hydroxylamines and nitro compounds, and tertiary amines into amine oxides. Additionally, they oxidisethiols into RS-SR compounds (Figure 3.7E) and thioethers into sulfoxides and sulfones (4).The reduction of carbonyl, nitro, and azo groups is also carried out by soluble xenobiotic-reducing enzymes in mammalian systems. Esterases hydrolyze esters and amides into the appropriate carboxylic acids, alcohols, or amines. In Burger's Medicinal Chemistry, soluble xenobiotic-metabolizing enzymes are covered in great detail.

DISCUSSION

Epoxides' Disposition

Epoxides are often found as end products or intermediates in cytochrome P-450 catalysed processes. They are prone to react in the cell with macromolecules, especially DNA, since they are fundamentally unstable; these reactions result in mutations or cancerous alterations. The stability of the epoxide and its suitability as a substrate for epoxide-metabolizing enzymes determine whether or not they react with macromolecules. Epoxides that are very unstable and have a half-life of a few minutes or less don't pose much of a threat since they will break down before they can interact with DNA. The very stable epoxides are likely to undergo an enzymatic conversion to innocuous molecules and will only react with DNA very slowly, if at all. Epoxides are eliminated via two enzymatic and two nonenzymatic reactions. Epoxides are transformed into trans-diols by an enzyme called epoxide hydrolase, also known as epoxide hydrase (Figure 3.8A). The trans-diols may then be conjugated as shown in the next section. The second step includes the enzyme glutathione S-transferase and glutathione (Figure 3.8B). A trans-(hydroxy)glutathione conjugate, the last byproduct, is finally divided into its equivalent mercapturic acid derivative.The two nonenzymatic reactions are the SN1-type rearrangement and the SN2-type addition of water, which produces a trans-diol[9], [10].

Conjugations Phase

By means of various conjugations, the lipophilic molecules that phase 1 processes transform into polar, somewhat more hydrophilic products may be further transformed into extremely water-soluble materials. From a chemical perspective, conjugations may be further classified into nucleophilic conjugations and electrophilic conjugations (the conjugating agent is an electrophile). Glycine, glutamine, sulphate, acetate, and glucuronide are all components of electrophilic conjugations. Glucuronidase, an enzyme found in lysosomes and in gut microbes, hydrolyzes the glucuronide conjugates into aglycons.

Sulphate is used to conjugate phenols (arenols), steroids, and N-hydroxy species. These processes use cytoplasmic sulfotransferases as the enzymes, and 30-phosphoadenosine 50-

phosphosulfate (PAPS), a mixed anhydride of sulfuric and phosphoric acid, as the cofactor. shows the conjugation of the sulphate. Sulfatases may easily target the sulphate conjugates and break them down to their basic components. Only amines may be conjugated with acetate, and this process is carried out by the cytoplasmic enzyme N-acetyltransferase. Normal primary metabolism involves the acetylation of oxygen and sulphur, but not in the metabolism of xenobiotics. S-Acetyl Coenzyme A serves as the acetyl donor

Conjugation with amino acids (glycine and glutamine) is only possible with carboxylic acids, particularly aromatic ones, and is carried out by mitochondrial enzymes (N-acetyltransferases). Before being conjugated, the carboxylic acid has to be activated by coenzyme A and adenosine 50-triphosphate (ATP) (7). S-adenosylmethionine (SAM) serves as a cofactor for the cytoplasmic enzyme methyl transferase, which catalyses methylations.

Glutathione

Most tissues contain the -glutamyl-cysteinyl-glycine tripeptide known as glutathione, although the liver has the most (170 mg of reduced glutathione per 100 g of liver tissue) (Figure 3.13). In cellular metabolism, glutathione serves a number of significant functions. When it comes to xenobiotic metabolism, both enzymatic and nonenzymatic processes are involved. It functions as a low-molecular-weight scavenger of reactive electrophilic xenobioticsnonenzymatically. It will likely compete with proteins, RNA, and DNA for electrophiles as long as its concentration is high enough. A group of isozymes with a wide substrate specificity for electrophilic substrates, collectively known as glutathione S-transferase, catalyse the enzymatic processes involving glutathione. (Isozymes are enzymes that share catalytic activities while having diverse chemical compositions.) 10% of the soluble liver protein is made up of at least five isozymes. Aliphatic and aromatic epoxides, as well as aromatic and aliphatic halides, and glutathione react with one another when catalysed by glutathione S-transferase.The conjugated product undergoes further hydrolysis during which glutamyl and glycyl residues are eliminated. Next, acetyltransferase performs N-acetylation of the product. Mercapturic acid, which is the final product and is readily eliminated in urine, is very water-soluble.

Additionally, organic nitrate reactions with glutathione are catalysed by glutathione S-transferase. The mercapturic acid route is not used in these processes, however. Instead, they cause the oxidation of glutathione to its S-S dimer and the conversion of organic nitrate to inorganic nitrite (Figure 3.15). Nitroglycerin, a vasodilator used to treat myocardial ischemia, is quickly rendered inactive as a result of this interaction. Dietary nitrites produced in such reactions may interact with amines and produce carcinogenic nitrosamines as a result.

Glutathione peroxidase is a catalyst for another process that does not go via the mercapturic acid route. In this process, glutathione is oxidised while highly reactive peroxides are reduced to alcohols. It is clear how crucial glutathione is as a detoxification agent. Its depletion predisposes to hepatotoxicity and mutagenicity by other exogenous agents, whether caused by genetic predisposition or sustained large loads of xenobiotics. Table 3.1 lists several instances of substances that reduce liver glutathione levels in rats.

Isozyme Induction and Inhibition

A process known as "enzyme induction" occurs when a xenobiotic increases the production of an enzyme. The phenomenon was first noted in experiments on the N-demethylation of aminoazo dyes in rat livers. The capacity of the liver to demethylase the dyes was improved by dietary variables or pretreatment of the animals with different compounds (9). The process

of induction is carried out by a cytoplasmic receptor-inducer complex (10), which then interacts with the right gene to boost the enzyme's output. Haugen and his colleagues showed that there are many isosymes of cytochrome P-450, and that certain substances may induce these isosymes.

They extracted cytochrome P-450 from rabbit liver microsomes and demonstrated that at least four different forms exist (11). By using gel electrophoresis, the mixture of isozymes may be divided into different bands. Two of them—designated LM2 and LM4 (LM stands for liver microsomes, and the subscript denotes the band's sequential number)—were homogeneously purified. LM2, whose induction by phenobarbital (PB) has been shown, has a molecular weight of 50,000. With a molecular weight of 54,000, LM4 is induced by -naphthoflavone (Figure 3.16). Since it has been shown that 3-methylcholanthrene (3MC) may also activate LM4 and that this enzyme prefers aromatic hydrocarbons as a substrate (12), it is also known as aromatic hydrocarbon hydroxylase (AHH). Additionally, this isozyme absorbs light at a peak wavelength of 448 nm when paired with CO rather than 450 nm as the other isozymes do. Animals treated with PB have a substantial expansion of smooth endoplasmic reticulum, an increase in liver weight, and an increase in the activity of certain isozymes. On the other hand, pretreatment with 3MC increases liver weight but little affects endoplasmic reticulum. While 3MC promotes both hepatic and extrahepatic P-450 enzymes, PB does not activate extrahepatic cytochrome P-450 (6).

There are 12 known cytochrome P-450 isozymes as of right now. They all demonstrate quantifiable substrate preferences while having roughly the same catalytic activities and using the same substrates. They are called CYP followed by a number, a letter, and sometimes another number, depending on their preferred substrate and function, such as hydroxylation, N-hydroxylation, N-demethylation, or O-de-ethylation. For instance, CYP 1A1, 1A2, 2A1, 2B1, and so forth (13) Additionally, the molecular weight and electrophoretic mobility of isosymes might differ.

Their reactions to certain inducers also vary amongst them. In addition to having different preferences for substrates, cytochrome P-450 isozymes also have site- and stereoselective activity. Figure 3.17 (12) provides an illustration of the site selectivity. A notable example of stereoselective action is the hydroxylation of the rodenticide warfarin (Figure 3.18). Warfarin possesses two stereoisomers, (R) and (S), as a result of the asymmetric carbon (denoted by the asterisk).

Table 3.2 shows the relative levels of warfarin hydro- xylation (R/S) in rats after 3MC and PB were used to induce P-450. Understanding site selectivity is essential for determining the risk of exposure to possible mutagens and carcinogens, as will become clear later in this chapter.

Inhibitors

Cytochrome P-450 inhibitors may be irreversible or reversible. Reversible inhibitors are often P-450 substrates that undergo sluggish metabolism. They block the enzyme's active site, which slows down the breakdown of other xenobiotics.

Environmental P-450 Inducing Agents

Several environmental factors have an impact on cytochrome P-450. According to a study (14) the pesticide DDT [1,1,1-trichloro-2,2-bis(p-chlorophyll) ethane] (Figure 3.21, top) reduced the amount of time that animals spent sleeping after being given

hexobarbitalanaesthesia when fed to rats at a rate of 50 mg/kg per day. This alteration indicates P-450 induction. DDT also decreased the quantity of breast tumours that dimethylbenzanthracene generated (15). This outcome may be caused by the stimulation of epoxide hydrolase (see the part after this one in this chapter), glutathione S-trans-glutathione, or the P-450 isozyme responsible for the noncarcinogenic hydroxylation of dimethylbenzanthracene[11], [12].

CONCLUSION

The drug SKF 525-A, also known as 2-diethyla-minoethyl 2,2-diphenylvalerate, is an example of a reversible inhibitor (Figure 3.19). By hydroxylating the benzene rings and dealkylating the nitrogen, this molecule is slowly metabolised and is rather strongly bound to the LM2 isozyme (inhibition constant Ki 14 10-6). The reversible inhibitor -naphthoflavone is another example (Figure 3.20). -naphtho- flavone, a related substance, induces LM4.Tetrachlorocarbon (CCl4) is one substance that inhibits P-450 in an irreversible manner. It works by triggering the peroxidation of lipids, which then compromises the integrity of cell membranes and results in the loss of P-450. Animals given hexobarbitalanaesthesia may have their increased sleep duration measured to determine the impact of an inhibitor. Cytochrome P-450 inactivates hexobarbital, hence inducers of P-450 decrease sleep duration while inhibitors of P-450 lengthen it.

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CHAPTER 3

FACTORS INFLUENCING TOXICITY

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ABSTRACT:
The size of the organisms is one evident distinction that influences toxicity. In comparison to a much bigger animal, a little insect requires far less venom to kill it (all other things being equal). The weight of an animal and its surface area also have an inverse connection; the smaller the animal, the greater its surface area per gramme of weight. As a result, while a person (70 kg) has 350 times the weight of a rat (200 g), they only have 55 times the surface area. A rough formula for calculating an animal's surface area (S) is as follows: Weight (kg)2/3/10 S(m2) 1/4. When contemplating the selective elimination of an uneconomic species, such as certain insects, by spraying an area with pesticide, this sort of assessment is crucial. The objective is to manage the insects without endangering people, animals, or the environment. It is also necessary to take into account other elements, such as the rate of percutaneous absorption. For instance, it has been shown that DDT (dichlorodiphenyltrichloroethane) is far more hazardous to insects when applied topically than it is to mammals when given as an injection. In addition to the discrepancy in surface area to body weight, this toxicity is partly caused by the fact that the insect's chitinous exoskeleton is more permeable to DDT than exposed human skin

KEYWORDS:
Animals, Acid, Genetic, Influence, Species, Toxicity

INTRODUCTION

The chance of different responses to hazardous chemicals increases with the number of species that have evolved apart from one another. (1). Of course, the majority of mammalian skin is covered with fur outside of the laboratory, providing the animals with extra protection. The reasoning above is not intended to suggest that pesticide spraying without limits is ecologically sound (particularly because chlorinated hydrocarbons are fat-soluble and weakly biodegradable). Lack of insect species selectivity, leaking into water-sheds and groundwater, and bioaccumulation in the food chain are issues with their usage. In Chapter 11, these issues will be covered in further depth[1], [2].

Metabolic Routes

Another justification for obtaining selective toxicity may come from the variations in metabolic pathways across species. The use of sulfonamides in chemotherapy is an excellent illustration of this sort of selectivity. We know that most animals, including humans, need an external source of folic acid. Tetrahydrofolic acid, a crucial cofactor involved in the de novo manufacture of purine and pyrimidine nucleotides, is produced by the organism's conversion of folic acid to tetrahydrofolic acid. On the other hand, certain gram-negative bacteria are unable to absorb folic acid that has already been generated. Instead, they have the ability to make dihydropteroic acid, a precursor to tetrahydrofolic acid, from 6-hydroxy-methyl-7,8-dihydropteridine and p-aminobenzoic acid (2). Due to their structural resemblance to p-aminobenzoic acid (see Figure 2.10 in Chapter 2 for further information), sulfonamides block

this reaction (3). These cofactors for tetrahydrofolic acid are therefore unavailable to these bacteria. This deprivation then inhibits the development of microorganisms. Because they are unable to continue this synthetic process, humans are unaffected. Sulfonamides may have harmful side effects in humans, although these side effects are unrelated to the molecular mechanism through which they work. Instead, they tend to precipitate in the kidney due to their poor solubility in urine.

Enzyme Function

In certain circumstances, even if the enzymes that carry out specific reactions may be different, metabolic pathways may be the same for many species. The inhibitory activity of two drugs towards the enzyme dihydrofolate reductase derived from various species was compared by Hitchings and Burchallprovides a summary of this experiment's findings. When contrasted to the relative insensitivity of mammalian enzymes to both chemicals, it is clear that the enzyme from the two bacterial strains has a high sensitivity to tri-methoprim and no sensitivity to pyrimethamine. Pyrimethamine is nonetheless efficient against plasmodia, the parasites that cause malaria, while not being selective for bacteria. Use of trimethoprim is limited to bacterial illnesses[3], [4].

Systems that MetaboliseXenobiotics

Different xenobiotic-metabolizing systems may potentially play a role in selective toxicity. For instance, cytochrome P-450 transforms the pesticide malathion (Figure 4.3) into malaoxon, which inhibits acetylcholinesterase. When administered topically to houseflies, it is roughly 38 times more lethal than when given orally to rats (5). Mammals have very active esterase, which hydrolyze the ester groups to render malaoxon inactive. Esterases are also present in insects, however they function considerably more slowly than human enzymes do.

Using synthetic pyrethroids as pesticides is an intriguing example of selective toxicity. This class of chemicals is generated from pyrethrins, which are naturally occurring poisons extracted from Chrysanthemum flowers (Figure 4.4). The pyrethroids' toxicity against insects is quite specific. Permethrin, one of these members, has an LD50 that is 1400 times greater for rats than for the desert locust (6). It's possible that this is because pyrethroids seem to be more harmful to cold-blooded creatures than to warm-blooded ones since their toxicity rises with decreasing temperature. Thus, their specific toxicity towards insects may be caused by temperature dependency (7). The fact that pyrethroids are particularly hazardous to fish in the lab lends credence to this idea. Another explanation is that pyrethroids rapidly bio inactivate in humans but not in insects, which is accomplished by hydrolyzing the ester bond.

DISCUSSION

Acute toxicity determination, subchronic toxicity determination, and chronic toxicity determination are the three different kinds of toxicity studies performed on animals. Chapter 5 discusses the determination of chronic toxicity, which often relates to carcinogens. Determining the LD50 is a step in acute toxicity investigations. A chemical is administered to groups of animals (5–10 males and an equal number of females) at three–six different dosage levels. It is tallied how many animals pass away in a 14-day period. Any changes in the animals' behaviour are observed, as well as their weight. All animals, including those in the control group, are checked for pathological abnormalities once the experiment is over and the survivors are killed.

Daily administration of the substance being evaluated to groups of men and females at three dosage levelsthe maximum tolerated dose (MTD), the lowest observable adverse effect level (LOAEL), and the no observable adverse effect level (NOAEL)results in subchronic toxicity studies. The selection of MTD ensures that it does not exceed LD10. Two species and typically two exposure routes are examined, one of which is identical to the anticipated human exposure. The examinations last anything from five to ninety days. There include behavioural changes, weight changes, and mortality. Prior to, midway during, and after the experiment, blood chemical readings are taken. The animals are then all sacrificed for pathological research.

Species Variations

The objective is to reduce species differences when forecasting human toxicity using data from animal assays. Unfortunately, it is usually difficult to do this. There may be significant metabolic variances across species, even within a same class, like mammals. Although sometimes qualitative differences are found, quantitative differences mostly exist.For instance, the only animals that need vitamin C are primates, guinea pigs, fruit-eating bats, and birds. These animals lost the ability to produce ascorbic acid at some point in their evolutionary progression; other it can be synthesized by mammals and birds. The severe reaction to the antitumor medication methotrexate is another example.

Methotrexate is not poisonous to guinea pigs and rabbits, while being very hazardous to people, mice, rats, and dogs. These instances highlight the significance of selecting the right animal model. The majority of toxicity evaluations are conducted on mice or rats due to their relative availability and simplicity of upkeep. In rare instances, animals like dogs, cats, or primates are utilised, particularly when studying pathology. Whatever the animal model, extrapolating the findings to people requires care due to the possibility of significant quantitative variations between humans and the model. For this reason, before approving phase 1 clinical trials, the Food and Drug Administration (FDA) requires a toxicity assessment in two unrelated species (often rats or mice and dogs). (Phase 1 clinical studies are intended to examine a novel drug's toxicity in human subjects.) An examination of the NCI (National Cancer Institute) carcinogenicity assay results from 190 chemicals that were evaluated in two species, mice and rats, may further demonstrate the variety of response to harmful substances. solely 44 of them were determined to be carcinogenic in both species, as opposed to 54 that were solely carcinogenic in either mice or rats [5], [6].

Explicit Mode

It is crucial that test animals be exposed to the alleged toxin in a way that mimics the predicted human exposure in any assessment of the toxicity of environmental and industrial compounds. When a legal dispute threatens to outlaw or severely limit the use of a harmful chemical, this issue gains significant significance. For instance, the tobacco industry disregarded early tests that showed cigarette tar was carcinogenic since the tar was painted on the test animals' skin. Human exposure cannot be compared to this application.

Tests for carcinogenicity in animal models provide a unique challenge. Within the practical constraints of the size of the population studied, it is required to employ rather high doses of the suspected carcinogen to produce a significant number of tumours over the lifespan of mice or rats. This high dose may or may not replicate the real-world circumstances of workplace exposure to carcinogens. In any event, it doesn't accurately mimic the widespread exposure of the population to environmental carcinogens over an extended period of time.

The extrapolation of the dose-response curve for small doses, although possible for big doses, remains totally speculative. These factors make it challenging to determine the risk of exposure to environmental carcinogens[7], [8].

According to current U.S. government policy, there is no threshold dosage for carcinogens (a level below which there is no chance of developing cancer); all exposure, regardless of amount, is regarded as harmful. No additive shall be deemed to be safe if it is found to induce cancer when ingested by man or animal, or if it is found, after tests which are appropriate for the evaluation of the safety of food additives, to induce cancer in man or animal. This amendment, known as the Delaney Clause, was passed by the U.S. Congress in 1958. Practically speaking, the Delaney amendment primarily addresses pesticide residues in processed foods that cause cancer. The federal government and the U.S. Congress have been pushing since the beginning of 1993 for risk assessment to replace the Delaney amendment, which would allow residues of carcinogenic pesticides in processed foods only if they pose a negligible risk—one additional cancer per million people over a 70-year lifetime was considered a negligible risk. Modern analytical technologies enable identification of considerably smaller residues than was conceivable in 1958 when the Delaney Clause was created, which was used to justify the change in policy. Therefore, the Delaney Clause's rigorous interpretation caused extra difficulty for the agricultural and food-processing businesses while offering little safety for the general population. The Delaney Clause's amendment has generated debate. The Agricultural Chemical Manufacturers Association and the food-processing sector favour the replacement of the Delaney Clause with risk assessment, although many environmental organisations are against it. The Food Quality Protection Act was enacted into law in August 1996. A new requirement known as "reasonable certainty that no harm will result from aggregate exposure to the pesticide chemical residue" was introduced in this legislation to replace the Delaney Clause [9], [10].

Individual Differences in Xenobiotic Response

Individual differences within a species' reaction to xenobiotics may result from environmental factors, from an individual's or a group's genetic make-up, or even from the age of the individuals.

Environmental and hormonal influences

It has been shown that nutrition may have an impact on a xenobiotic's metabolism (see reference 9 in Chapter 3). Concurrent exposure to other xenobiotics, such as medications or environmental pollutants, may be another risk. In the chapter before this one, we discussed xenobiotic-metabolizing enzyme induction and inhibition. One chemical's metabolism might be accelerated or slowed down by exposure to another substance that also happens to be a cytochrome P-450 inducer or inhibitor, or any of the conjugating enzymes. There is a lot of evidence to suggest that a person's hormonal balance influences how they react to poisons. This syndrome shows itself in various reactions within a person depending on the time of day, in addition to distinct responses between men and females. These fluctuations result from varying blood corticosterone concentrations, which themselves rely on the circadian rhythm, also known as the cycle of light and dark (10).

Genetic Variables

Any biological system that seems to be homogenous is really heterogeneous, as was mentioned in even though every person is kept in the same environment and given the same food. The quantal dose-response curve demonstrates how most people within a system react

similarly to chemical damage. A tiny percentage of people are always either unusually sensitive to the insult or exceptionally resistant to it, depending on which end of the curve you look at. These people possess the hereditary traits known as hypersensitivity (located at the left end of the bell curve) and hyposensitivity (located at the right end of the bell curve). It is not believed that genetic mutations are the cause of the hyper- and hyposensitivities. They just represented the common genetic variance seen in populations. In certain instances, a multi-phasic curve is produced when a large population sample is screened for specific features and the findings are shown as a quantal dose-response plot. The major peak in the hypothetical figure shown in Figure 4.5 denotes the "normal" population, whereas the lesser peak denotes the modified population. The alleged acetylation polymorphism is a kind of genetic mutation. Isoniazid (INH), antritubercular medication, stops working by acetylating, a process that is carried out by N-acetyltransferase. Certain demographic groups in both humans and animals have a hereditary deficit of this enzyme[11], [12].

A triphasic curve is produced when blood levels of INH are assessed in a sizable population sample 6 hours after the administration of a standard dosage of the medication and the findings are shown as a quantal dose-response relation. As a result, there are three populations: the fast acetylators, who had little to no INH in their blood, the slow acetylators, who had significantly higher levels of the drug left, and the very slow acetylators, who had the highest levels of the drug left, which constitute the population under the third peak (11). The absence of N-acetyltransferase seems to be a hereditary characteristic that runs in families. The frequency of occurrence of this trait varies by race; it is most common among blacks and Caucasians, less common among Japanese and Chinese, and least common among Eskimos. Acetylation polymorphism is but one illustration of how changed xenobiotic metabolising ability might result from genetic changes. Ted Loomis' Essentials of Toxicology (11) provides a thorough discussion of this topic. When genetic changes take place in reproductive cells, genetically changed populations are created. The kids won't survive if the mutation causes a lack of an enzyme that is essential for regular metabolism. Therefore, the only mutant populations that can be seen are those where the deficient enzyme is not required for life. These people live normal lives, but when they are exposed to a drug or xenobiotic, they may suffer harm.

Effect of Age

In general, young people are more resistant to the harmful effects of xenobiotics than are growing or ageing organisms. This greater susceptibility is most likely caused by the fact that young people do not yet have fully established levels of detoxifying enzymes, and that these levels have diminished in ageing people. Children's underdeveloped immune systems and weakened immunity in ageing organisms might potentially be contributing factors. The heritable components that affect an organism's features or characteristics are known as genetic variables, sometimes known as genetic factors or genetic determinants. Physical characteristics like height and eye color, illness susceptibility, behaviours, and other characteristics may all be included in these qualities. An organism's DNA, a molecule that contains the genetic data required for life and reproduction, is where genetic variations are encoded.

Many Genetic Variations

There are many different kinds of genetic variables, each having unique traits and patterns of inheritance. The following list includes some of the most significant genetic factors: SNPs, or single nucleotide polymorphisms, are the most prevalent genetic variations in the human

genome. In order to do them, a single nucleotide base (A, T, C, or G) must be swapped out at a particular location in the DNA sequence. SNPs are crucial in medical genetics and personalised medicine because they may affect characteristics and disease susceptibility. CNVs stand for copy number variations, which are differences in the number of copies of a certain DNA region within a genome. They may include greater structural alterations or even the duplication of minor sequences. CNVs may significantly affect a person's phenotype, affecting things like vulnerability to illness and developmental abnormalities.

Indels, or small-scale genetic changes, are caused by the insertion or deletion of a few base pairs from the DNA sequence. These mutations may cause gene disruption, alter how proteins work, and increase genetic diversity within a population. Larger changes to the genome, such as translocations, inversions, and chromosomal rearrangements, are referred to as structural variants. These occurrences may trigger genetic abnormalities or aid in the development of certain traits.

Gene mutations:

Gene mutations are changes to a particular gene's sequence. These mutations, which may result in both advantageous adaptations and genetic disorders, can be acquired from parents or appear spontaneously. The BRCA1 and BRCA2 mutations linked to breast cancer risk are two such examples.Epigenetic modifications are heritable changes in gene expression that do not entail changes to the DNA sequence itself, while not being purely genetic differences. DNA methylation and histone alterations are examples of epigenetic changes that may affect gene activity and affect characteristics and illnesses.

Genetic Variables in Genetics: Their Importance

Genetic factors are crucial to our comprehension of genetics and have a number of important ramifications. Genetic variables adhere to the Mendelian rules of heredity, which were defined by Gregor Mendel. They contribute to the understanding of how qualities are handed down across generations and the reasons why certain traits are dominant and others recessive.

Genetic Conditions:

Numerous genetic conditions, such as cystic fibrosis, sickle cell disease, and Huntington's disease, are brought on by certain genetic factors. For diagnosis, treatment, and genetic counselling, it is crucial to comprehend the underlying genetic variables.

Pharmacogenetics:

In pharmacogenetics, a person's genetic composition affects how they react to pharmaceuticals. Genetic factors are important in this field. Genetically-based pharmacological treatment adaptation may enhance therapeutic effectiveness and minimise side effects.

Genetic factors influence the genetic diversity both within and across populations, according to population genetics. Population genetics investigates how genetic traits evolve over time as a result of phenomena such as migration, genetic drift, and natural selection. Genetic variations are the basis for evolution, according to evolutionary biology. Natural selection affects genetic diversity, causing adaptability and species divergence through time. We can better understand how species develop and adapt to changing environments by studying genetic factors. Genetic factors are at the heart of personalised medicine, which bases treatment choices on a patient's genetic profile. Genetic testing has the ability to reveal illness

risk factors, direct treatment decisions, and forecast therapeutic outcomes. DNA profiling and identification in forensic science are made possible by the application of genetic factors. The individuality of genetic elements in a person's genome is what allows DNA fingerprinting to work.

Genetic Variables and Their Effects on Medicine:

Genetic factors play a significant role in medicine, providing information on illness susceptibility, treatment outcomes, and preventative measures. Here are some significant ramifications:

Disease Risk Assessment:

Genetic testing may help those who are more vulnerable to developing certain illnesses, such hereditary malignancies or cardiovascular conditions. By using this information, proactive monitoring and preventative interventions are possible.

Targeted Therapies:

In oncology, therapy choices are influenced by genetic factors. With targeted medicines, side effects are reduced and results are improved by taking advantage of certain genetic abnormalities in cancer cells.

Pharmacogenomics:

Genetic factors affect how people metabolizes and react to medications. Pharmacogenomics adjusts medicine prescriptions to a person's genetic profile, improving therapeutic effectiveness while minimising side effects.

Prevention:

Genetic factors may reveal a tendency to diseases like diabetes or Alzheimer's. With this information, people may make lifestyle adjustments and take precautions to lower their risk.

Family Planning:

Couples with known genetic risk factors for hereditary disorders may use prenatal testing and assisted reproductive technology to plan their kids[13], [14].

CONCLUSION

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CHAPTER 4

CHEMICAL CARCINOGENESIS AND MUTAGENESIS

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ABSTRACT:
Adults who have polyposis of the colon, a hereditary disorder that usually results in colon cancer, are a good example. The hereditary disorder xerodermapigment sum, which is characterised by a weak DNA excision repair system (see the discussion later in this chapter), represents the third type. When exposed to UV radiation, those who are prone to skin cancer get it. It's possible that genetic predisposition contributes to the population's varying vulnerability to the cancer-causing effects of cigarette smoking. The causes of the fourth category of cancers are unknown, thus very little can be written about them. Between 60 and 90 percent of all cancers are likely to fall under Groups 2 and 3 combined (i.e., cancer caused by environmental factors, whether or not there is a hereditary predisposition). In this view, the environment includes not just air, water, and soil, but also things like food, drink, lifestyle choices, professional exposure to chemicals, medications, and pretty much every element of how people interact with their surroundings. According to this definition, it is possible to avoid exposure to probable carcinogens and alter lifestyle choices in order to significantly reduce the risk of developing cancer. Therefore, it is not unexpected that a significant portion of environmental toxicology involves the study of chemical carcinogenesis.

KEYWORDS
Bases, Cancer, Carcinogens, DNA, Genetics

INTRODUCTION

About 200 disorders that are characterised by abnormal cell development go under the umbrella term "cancer." The following categories may be used to categorise the causes of cancer, according to Kundson:

1. Genetic propensity

2. Environmental aspects.

3. The addition of environmental variables to genetic predisposition

4. Unknown elements

Childhood malignancies like retinoblastoma (a genetically predisposed malignancy of the retina), neuro-blastoma (a malignancy of the brain), and Wilmstumour (a malignancy of the kidney) are typical instances of the first category. An overview of the estimated environmental cancer mortality or incidence in the United States is provided the information in this table should only be regarded as a rough approximation. Depending on the researchers and how they gathered the relevant facts, there are wide variations in the estimations. A more thorough discussion of this topic may be found in the Office of Technology Assessment study on cancer risk. These figures don't apply to the current situation because of the extended latent period of cancer. Data that is revealed in 20 years may show a quite different picture. For instance, according to data from the National Cancer Institute, lung cancer incidence

among American men decreased in 1988 for the first time in many years. However, since the 1960s, the number of people who smoke, the main cause of lung cancer, has consistently decreased[1], [2].

Cigarette use is the leading factor in all environmental cancers. According to estimates, there were 168,000 new instances of lung cancer in 1992 and that tobacco smoking resulted in $52 billion in yearly medical costs and lost income on average. The majority of lung cancer cases were brought on by smoking, but additional factors such as passive smoking (being exposed to other people's tobacco smoke), industrial carcinogen exposure at work, and radon exposure in homes also increased the risk of developing lung cancer[3], [4].

Although the mortality due to direct inhalation of carcinogens may be modest, the figures on cancer mortality related to air pollution may be deceptive. The indirect effects of air pollution might have a big impact. Many air pollutants, such as polycyclic aromatic hydrocarbons (PAHs), which are dumped on land or in bodies of water, enter the food chain and are thus categorized as cancers brought on by dietary factors rather than air pollution. Additionally, carcinogens that are breathed may travel to the digestive system through the mucociliary escalator. Most people in certain occupations, such as coke-oven and coal-tar pitch workers, are affected by the highest incidence of cancer directly linked to inhaling air pollutants, which occurs in highly industrialized areas. Such occupational exposure to PAH may be 30,000 times higher than that of the general public. It is important to discuss the comparatively high cancer death rate linked to food. No direct epidemiological evidence has been produced connecting any specific food or dietary contaminant to human cancer, with the exception of the linkage between liver cancer and the intake of crops infected with afflation. But a lot of carcinogens have been discovered in food.

Pre-carcinogens include nitrates, which are added to meat as preservatives. Although nitrates aren't inherently carcinogenic, salivary enzymes convert them to nitrites, which are then found in vegetables, fruits, and drinking water. Nitrates are often found in these substances as a consequence of nitrate fertilizers seeping into groundwater. When meat or fish is fried, broiled, or smoked, PAHs are created. Additionally, PAHs, polychlorinated biphenyls (PCBs), and other organic contaminants may be present in fish or shellfish from contaminated waterways. The absence of a link between eating certain foods and developing cancer does not prove that there is none. Obesity and cancer-related mortality have been linked. It is unknown if this outcome is directly related to fat or whether obesity is a reflection of a certain lifestyle that promotes cancer[5], [6].

Multiple Stages of Cancer Development

The experiments of Berenblum and Shubik (4) are where the idea of a multistage development of cancer first emerged. These researchers examined the carcinogenic potential of benzo[a]pyrene (BP) and 9,10-dimethylbenzanthracene (DMBA) in mice. Only one mouse developed a tumour when the skin of 45 mice was exposed to a single application of a 1.5% solution of DMBA in liquid paraffin. However, 20 out of 45 mice developed tumours when the single administration of DMBA was followed by the application of 5% croton oil in liquid paraffin twice weekly for 20 weeks. When croton oil was used twice a week for two weeks before the DMBA therapy, no tumours were seen.

The current paradigm of cancer start, promotion, and progression was developed in response to more information from epidemiological and laboratory investigations. An agent that is genotoxic (the term is defined later in this chapter) interacts with cellular DNA to induce

initiation. The cell is permanently altered when a DNA harm occurs and is not repaired. An animal may harbour such a latently premalignant cell throughout the majority of its normal lifespan without ever giving rise to a cancerous tumour.

DISCUSSION

The latent phase in humans may last 20 years or more. The latent time is inversely linked to the initiator dosage, claim some researchers (5). Others challenge the accuracy of this supposition. Even after a delay of up to a year (6), exposure of a premalignant cell to a promoter causes the cell to become permanently malignant. Promotion is a gradual process, and exposure to the promoter has to be maintained for a while. This need explains why the risk of developing cancer decreases quickly after quitting smoking as tobacco smoke seems to include both initiators and promoters. Numerous promoters have been found thus far. The phorbol esters, a class of diterpenes derived from croton oil, are the most thoroughly studied examples. Colon cancer development has been demonstrated to be promoted by bile acids. When humans are exposed to the carcinogens in cigarette smoke, alcohol serves as a promoter. Smokers seldom get oral or upper gastrointestinal cancer, but those who also consume alcohol are more likely to have these types of cancer. several inducers of cytochrome P-450, such as phenobarbital, DDT, and butylatedhydroxytoluene (BUT, an antioxidant food additive), as well as several hormones, if they are present in excess, have been identified as promoters[7], [8].

Uncertainty surrounds the promoters' manner of operation. Their impact on cellular membranes might partially explain their activity. Studies using phorbol esters suggest that they might play a role in the repression and depression of genes. Another idea that is supported by experimental data is that cells may "communicate" with one another by sending tiny growth-regulating molecules across the so-called gap junction. Promoters may stop this intercellular communication, as shown by studies in cell culture. These growth-inhibiting restrictions may be broken by such interference, allowing a latently premalignant cell to go on to develop into a cancerous tumour. Some substances may increase the activity of a carcinogen even if they are not necessarily carcinogenic on their own when given before or alongside one. Cocarcinogens are the name given to such substances. Certain promoters, including phorbol esters (8, 9), are cocarcinogens as well.

Sometimes it's difficult to tell these two groups apart. The primary distinction is that promoters are engaged in processes that happen after the neoplastic conversion, while carcinogens amplify this conversion. Catechol’s are typical examples of cocarcinogens. catechol, which are found in tobacco smoke, enhance the carcinogenic effects of PAHs, the main tobacco carcinogens. Similar to how cigarette smoke increases cancer risk, asbestos does the same. Pleural and peritoneal mesotheliomas are brought on by asbestos exposure alone, whereas lung cancer is not. However, asbestos exposure significantly raises the risk of lung cancer among smokers.

Different Carcinogens

The two types of carcinogens are genotoxic and epigenetic. Mutagens are often chemicals that interact either directly or indirectly with DNA. Because they have the capacity to change the genetic code, they are classified as genotoxic. Strong electrophiles, molecules made of or containing highly stressed heterocyclic three- or four-member rings, such as epoxides, azaridines, episulfides (see Chapter 3), and lactones, are examples of directly acting genotoxic carcinogens. The nucleophilic ring opening of these cyclic compounds is a

propensity. Many xenobiotics enter the body as harmless substances and turn into carcinogens following metabolic activation, Precarcinogens are the name given to such xenobiotics.

Less commonly than those that act directly on the body, indirectly acting genotoxic agents may cause cancer. When they interact with non-DNA targets, oxygen or hydroxy radicals such O.- (superoxide), O.OH, H2O2, and 1O2 (singlet oxygen 2) are released. By interacting with DNA, these activated organisms may disrupt DNA strands or harm purine or pyrimidine bases. The manner of ionising radiation's carcinogenic action is essentially this sequence. However, certain chemicals with the quinoid structure or those that are activated to create quinoids are thought to function by generating free radicals, either directly or indirectly, such as via oxygen or hydroxy radicals. Numerous studies have been done on the molecular basis of how genotoxic carcinogens work. There is a plenty of knowledge on how they interact with DNA. More information on this topic will be covered in a later chapter [9], [10].

Review of Chromosomal Structure and DNA

A quick overview of DNA and chromosomal structure is necessary before talking about mutagenesis and how chemicals interact with DNA. Purine and pyrimidine bases, sugar (deoxyribose), and phosphate make up DNA's three major building blocks. The two related purines are guanine and adenine, whereas the three related pyrimidines are cytosine, thymine, and uracil. Only thymine and cytosine, out of the three pyrimidines, are found in DNA, but only cytosine and uracil are found in RNA. Each base may occur in either its lactim or lactam tautomeric form. The bases are planar as a result of the pi electron clouds. These two prerequisites are crucial for the DNA double helix's structural integrity. The bases can only be stacked on top of one another with planarity, and the bases can only be properly paired with the appropriate tautomeric configurations.

The nucleosides which connect purine or pyrimidine bases to the C-10 of deoxyribose or ribose, respectively, in DNA or RNA, are the next higher tier of organisation in DNA. The sugar is connected at position N-1 in pyrimidines and N-9 in purines. The glycosides bond has a fair amount of acid lability. The nucleosides are collectively referred to as either ribosides or deoxyribosidesdepending on the kind of sugar. Individually they are named adenosine (A) or deoxyadenosine (dA), guano- sine (G) or deoxyguanosine (dG), cytidine (C) or deoxycytidine (dC), thymidine (T) (no "d" prefix is required since it occurs exclusively as a deoxyribose), and uridine (U), which occurs only as a riboside.Steric hindrance limits the sugar's free rotation around its N-9 or N-1, depending on the situation, and C-10, leading to the possibility of its two conformations, syn and anti. The anti-configuration is preferred in naturally occurring nucleosides. Nucleotides are created when the 30 or 50 hydroxyls of the sugar are esterified with phosphoric acid. They are each given an own designation, such as adenosine monophosphate (adenylate) (AMP) or deoxyadenosine mono-phosphate (dAMP), and so on. Deoxythymidilate is known as TMP in line with the nomenclature used with nucleosides.

The purine and pyrimidine bases of each deoxyribose protrude outward from the C-10, making DNA a polymer made up of a chain of 20 deoxyriboses linked together by a 30,50phosphodiester bonds. Such a chain has a polarity, with one end terminating in 50-OH and the other in 30OH.The quantity of dA was always equal to that of T, and the amount of dG was always equal to that of dC, Chargaff and colleagues discovered in the late 1940s (12). This was despite the fact that the content of individual nucleotides differed across DNA species. Watson and Crick (13) postulated the double-stranded DNA model in response to

this discovery and X-ray diffraction data from the DNA molecule. The two DNA chains in this model have opposing polarity, meaning that one runs in a 50–30 direction and the other in a 30–50 direction. Between the bases, hydrogen bonds keep the chains together. As a result of the bases' predominance in tautomeric forms and the anti-configuration of deoxyribose, dA can only couple with T and dG can only pair with dC. The binding force between dG and dC is 50% more than that between dA and T because there are three hydrogen bonds in the dG-dC pair as opposed to two in the dA-T pair. The dG-dC combination is thus smaller than the dA-T combination. The buoyant density of DNA increases with the dG-dC concentration. In the helix, the bases are layered on top of one another. DNA in its natural, B-form, has 10 base pairs per turn, or 3.4 nm, in length.

DNA melts or denaturates in response to changes in temperature or salt content. The two chains separate as a result of this process. Hyperchromicity of denaturation, the term for this ripping apart, is followed by a rise in the optical density of DNA.

The major groove and minor groove, which are visible in the double helix's three-dimensional structure, are two grooves. Specific proteins interact with DNA in these grooves. The so-called sense strand, one of the double helix's DNA strands, is the only one that stores genetic information. The antisense strand is the other strand, which merely acts as a replication template. As the synthesis of the new strands complements the old strands in a direction of 50 to 30, the strands are pushed apart during replication.

A specific nucleotide sequence is transcriptionally transcribed using the sense strand as a template to create messenger RNA. A specific sequence of amino acids is translated into proteins from the message stored in mRNA. A codon is a group of three nucleotides that codes for a particular amino acid in DNA. Four bases are accessible, and each codon has three bases, resulting in 64 potential messages, which may produce 20 amino acids. As nonsense codons, three of themat least two of which code for the end of the amino acid chaindo not code for any amino acids. It seems that numerous distinct triplet’s code for the same amino acid since the remaining 61 triplets’ only code for 20 amino acids. Degeneracy of the genetic code is the term used to describe this occurrence.

A gene is a sequence of codons that contains roughly 1000 base pairs and is in charge of producing a particular protein. Chromosomes are constructed from genes. An average chromosome has 108 base pairs. It includes a significant quantity of protein in addition to DNA. Chromatin is chromosomal material that has been removed from the nucleus of eukaryotic organisms. It is made up of double-stranded DNA, about equal amounts of basic proteins (histidines), less acidic proteins (non-histones), and trace amounts of RNA

The five different kinds of histones include H1, H2A and H2B, which are lysine-rich, H3, and H4, which are arginine-rich. DNA strands are folded (referred to as "super packed") by histones. The first electron microscopic analysis of chromatin showed that it is made up of spherical nucleosomes, which have a diameter of 12.5 nm, and DNA filaments that link them.

A further look into the structure of nucleosomes revealed that the double-stranded DNA is coiled twice, completely, around an H2A, H2B, H3, and H4 octamer core. 140 base pairs make up this supercoiled configuration. There are straight DNA segments (often 20 base pairs or more) at both ends of the coil. These sections, known as linker DNA, join the nucleosomal granules together. H1 is found near the coil's entry and exit. The chromatin becomes soluble when histone H1 is deleted since it is the least firmly bound histone. For the majority of eukaryotic species, the histones are identical or quite similar. No matter where the

different parts come from, chromatin forms spontaneously when histones and DNA are combined. Due to the creation of chromatin, the double-stranded DNA is folded to 1/7 of its original length.

The nonhistone proteins seem to be engaged in the regulatory roles of gene expression, while histones are associated to the packing of nuclear material at the lower structural level of chromosomes. They conceal or reveal certain DNA regions as necessary for transcription. The nonhistone proteins may also act as scaffolding proteins to organise chromosomal DNA at a more advanced level (16). Although the precise folding of the secondary structures, or the chains of nucleosomes in a chromosome, is unknown, electron microscopic analysis suggests that a thin fibre with a diameter of 5–10 nm folds into a heavier fibre with a diameter of 25–30 nm. Light microscopy is a useful tool for studying chromosomal structure. Mammalian chromosomes manifest as X-shaped structures during the metaphase stage of cell division.

The centromere, which connects the X's two sides, is also known as the sister chromatid. For each chromosome, the centromere's location is unique. "q" stands for the chromatids' long arms and "p" for their short arms. Chromosomes exhibit a distinctive pattern of horizontal bands when stained with quinacrine or Giemsa stain. Although it differs across species, this banding is very repeatable within species[11], [12].

Mutagenesis

It is now well accepted that some gene mutations cause cancer. The majority of cancers are caused by intricate interactions between carcinogens and the body's genetic system; a tiny proportion may be brought on by inherited genetic defects. The majority of genetic damage in our contemporary lifestyle is caused by the interaction of environmental chemicals with human and animal genetic systems, despite the fact that some of the harmful carcinogens are produced as free radicals during normal metabolism.

There are three categories of visible genetic lesions:

1. Point mutations, which are modifications to DNA

2. Clasto-genesis, or alterations in chromosomal structure, such as the breaking off of a chromosome's arm or its translocation

CONCLUSION

The mechanism of action of epigenetic carcinogens is much less understood. The term "epigenetic" refers to any carcinogens that are not categorised as genotoxic, therefore many different processes may be at play. Metal ions (nickel, beryllium, chromium, lead, cobalt, manganese, and titanium), solid-state carcinogens (asbestos and silica), immunosuppressant (azathioprine and 6-mercaptopurine), promoters, and the recently discovered xenoestrogens are just a few examples of the compounds that make up the epigenetic carcinogens. Promoters receive extra consideration. In addition to well-known promoters like phenobarbital and tetradecanoylphorbol acetate (TPA), other environmental pollutants also fall under this category. These include PCBs, tetrachlorodibenzo-dioxin (TCDD), and pesticides containing chlorinated hydrocarbons (DDT, aldrin, chlordane, etc.). It has been shown that each of these causes liver cancer in rats

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CHAPTER 5

EXPLORING THE CONCEPT OF MUTAGENESIS

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ABSTRACT:
Base substitution or frame-shift mutation are both examples of point mutation. Transition (when a purine is switched for another purine, such as A for G or vice versa, or a pyrimidine is switched for another pyrimidine, such as C for T or vice versa) and trans-version (when a purine is switched for a pyrimidine or vice versa) are two forms of base substitution. Six base substitutions are allowed in total: two transitions (AT-GC and GC-AT) and four trans-versions (AT-TA, AT-CG, GC-CG, and GC-AT). It is anticipated that a single base swap would have minimal impact. First of all, the incorrect integration of a base into DNA may not have any impact whatsoever on the inclusion of the correct amino acid into a protein due to the degeneracy of the genetic code. Second, even if the incorrect amino acid is included, the enzyme's activity won't be impacted unless it happens to be located in the active site. Cryptic mutations are base substitutions that do not result in changes to the amino acids of proteins or alterations that do not affect the activity of enzymes. It is possible, nevertheless, that the base substitution will result in the creation of a nonsense codon, which signifies the end of protein production.

In this scenario, an incomplete enzyme will be created, which might have negative effects. When base pairs are inserted or removed and their number is not three or a multiple of three, frame-shift mutation results. In this instance, the triplet coding is completely misinterpreted leading to a significant alteration in the protein structure. By looking at chromosomes morphologically, point mutations cannot be found. A mutant progeny may be produced if a point mutation takes place in reproductive cells. Point mutations that cause heritable illnesses may have a paternal or maternal ancestor. Contrary to the chromosomal abnormalities that will be detailed, point mutations are more common as a father becomes older.

KEYWORDS:
Autosomes, Chromosomes, DNA,Mutation, Mutagenesis.

INTRODUCTION

The average person has 46 chromosomes, including two sex chromosomes, XX in females and XY in men, and 22 pairs of autosomes, which are identified by numbers ranging from 1 to 22.

The usual human karyotype is known as this combination. Chromosome abnormalities may be investigated in bone marrow, peripheral lymphocytes, or cell culture.Because they are visible under a light microscope during mitosis, the chromosomes are best characterised at this time.

The identification of chromosomal fragments is made possible by the banding that develops after staining. As a result, it is possible to identify breaks, gaps, unstained segments, sister chromatid swaps, and combinations of two chromosomes or their portions. Some evidence points to chemical damage as the cause of clastogenesis, at least sometimes. There is evidence that sister chromatid exchanges and intercalator-induced DNA strand breaks are related [1], [2].

Aneuploidization

Uneven chromosomal distribution during cell division is referred to as aneuploidization. Although this phenomenon contributes to a huge number of genetic illnesses, it is still unclear what exactly causes aneuploidization and how it works. There hasn't been discovered any other contributing component outside the impacts of X-rays.To identify the kind of chromosomal abnormality, use the following code. The first number in the karyotype denotes the total number of chromosomes present, and the second number, followed by + or 0, denotes the presence of any extra or missing chromosomes. This code designates Turner syndrome as (45, X0) and Down syndrome as (47, 21+). One sex chromosome is absent in the latter situation, while chromosome 21 is trisomized in the former.Although the likelihood of aneuploidy rises with maternal age, live births with aberrant chromosomal patterns are generally rare (23–30%) compared to the frequency of occurrence. The majority of abnormal pregnancies end spontaneously. The review by Thilly and Call (Interaction of Chemicals with DNA) covers this topic in great detail[3], [4].

Alkylation

Due to the abundance of heteroatoms, such as nitrogen and oxygen, which carry pairs of free electrons, DNA is susceptible to nucleophilic substitution. Except for N-9 in purine and N-1 in pyrimidine bases, almost all endo- and exocyclic nitrogens are vulnerable to electrophilic attack. The oxygen in bases and the nonesterified phosphate oxygens that make up the backbone of DNA strands are both oxygens. Purines' acidic C-8 also develops nucleophilic characteristics by dissociating its hydrogen into a proton. The superscript in position notation indicates an exocyclic atom.The nucleophilicity of the atom being substituted, the site's accessibility, and the size of the alkylating agent all affect the favored replacement site in the base molecule. The Swain-Scott equation relates the electrophilicity of the alkylating agent and the nucleophilicity of the site of substitution to the rate of reaction for small alkylating agents, when steric hindrance is not a concern. Only the strongest nucleophiles and alkylating agents with a high Swain-Scott s value react through the SN2 mechanism. Small s molecules react with both strong and weak nucleophiles via the SN1 mechanism [5], [6] .

The N-7 and C-8 of guanine are preferred by the bulky electrophiles in general (but not always), and they are preferentially integrated into the linker, rather than the core, DNA (10). Every N and O in purine and pyrimidine bases, as well as non-esterified O in the phosphates, are possible objects for interaction with tiny alkylating agents (such as N-nitroso compounds), which react through carboniumlions (11, 19). The relative nucleophilicity of the hetero atoms in the purine bases is shown by the amount to which adenine and guanine were alkylated by methylnitro- sourea (MNU), as shown in Table 5.3. It is important to note the N-7 of guanine's very high nucleophilicity.Some alkylation produce changed but stable products that last forever or until they are removed during the repair process. Other alkylations, on the other hand, result in unstable adducts that later go through a number of rearrangements. Depending on the kind of substituent and location of alkylation, effects of alkylation may range from a comparatively benign base replacement to a very harmful DNA strand break or base removal. Guanine's tautomeric form changes when it is methylated or ethylated at position O6, making it resemble adenine. Thus, 6-methylguanine will link with thymine (or uracil) during the replication of DNA or transcription of messenger RNA instead of cytosine. As previously mentioned, a base substitution may result in a visible or subtle mutation.

The effects of replacing N-7 or N-3 of purines have substantially more severe effects. According to Table 5.3, the most reactive atom in guanine is N-7, while the most reactive

atom in adenine is N-3. Aflatoxin B1 interacts with guanine's N-7 upon metabolic activation to 2,3-epoxide, N-7-substituted purines are unstable and may break down in two different ways. The pyrazine ring opening (reaction I) results in a rather stable compound that compromises the genetic code's accuracy. A gap in the nucleotide sequence caused by the depurination (reac- tion II), which may also happen with N-3-substituted purines, results in a frameshift mutation.

The cyclic furanose and the open aldose are the two forms of free deoxyribose that are in equilibrium with one another (like other sugars). There is only the furanose form in DNA due to the bases' glycosidic bond. Depurination establishes balance between furanose and aldose Base-catalyzed rearrangement may occur with aldose causing a strand break at position 30, etc. Alternately, a neighbouring amino group and the free aldehyde may create a Schiff base and cross-link. The DNA will get even more distorted as a result of both of these processes[7], [8]

DISCUSSION

Acetylaminofluorene (AAF) is activated to a potent electrophile. The positively charged nitrogen rotates guanine around its glycoside bond by reacting with the nucleophilic C-8 of guanosine. Between stacked bases, the planar AAF intercalates, and guanine slips out such that it protrudes outside the helix. Base displacement is the term used to describe this movement (19). Thus, a nucleotide sequence gap is produced, leading to a frameshift mutation.Following activation to 7,8-dihydrodiol-9,10-epoxide (Chapter 3), the pervasive environmental carcinogen benzoate pyrite creates a covalent link between the hydrocarbon's C-10 and the exocyclic nitrogen of guanine. Only the trans isomer of 7,8-dihydrodiol-9,10-epoxide interacts with DNA in vivo; the other stereoisomers, cis- and trans-epoxy (with respect to 7-hydroxy), do not. According to the cis-isomer's instability may be to blame for this impact. A frameshift mutation was found to result from benzonapyrite alkylation (19). It has not been determined whether this mutation comes from its interaction with guanine or from the purported alkylation of phosphate. Table 5.4 shows the relative reactivities of four alkylating agents with the N-7 of guanine in comparison to those of phosphate oxygens[9], [10].

Values are non-dimensional and relative, please note. From reference 20, with modifications. Due to the resonance between the two free oxygens, an initial assault on the phosphate's OH group is challenging. However, after the alkylation has occurred, the electron locations are fixed, which substantially facilitates the subsequent alkylation of the trimester. Following this second assault, the first alkyl group is either removed, maintaining the status quo, or a strand break occurs between the phosphate and the 30-OH of the deoxyribose. The alkyl group may be removed from the phosphotriester by alkali-catalyzed hydrolysis, which also causes strand scission.Because the ligases created to mend strand breaks can only link 30-phosphate with 50-OH, but not 30-OH with 50-phosphate Intercalating Agents, this sort of scission cannot be repaired.

A few aromatic or heterocyclic planar molecules have the capacity to squeak between DNA's stacked bases. Intercalation is the term for this kind of contact. The helix is stretched out and distorted locally as a consequence of intercalation, lengthening the helix every turn. In, a few examples of intercalating agents are shown. These compounds may all be identified by their sizes, which are about equivalent to the diameter of the double helix of DNA and correspond to three condensed aromatics (or heterocyclic) rings. According to one research (17), intercalators obstruct topoisomerase II's ability to function. For processes like replication and

transcription, topoisomerase II catalyses brief double-strand breaks in DNA. Although strand scission happens when inter-collators are present, topoisomerase II is still tightly linked to the nicked DNA and precludes strand ligation.

Ultraviolet Radiation's Effect

Strand breaks are brought on by free radical production from X-rays and shortwave UV light. However, nearby pyrimidines get dimer zed by UV light with wavelengths approximately 290 nm, which is in the region of light absorption for pyrimidine's. The DNA helix is unwound as a consequence of this dimerization, and the hydrogen bonds between the dimer zed pyrimidine's and their corresponding purines are broken.

Breast Cancer and Xenoestrogens

The female hormones, estrogen and progesterone, have lately garnered attention as epigenetic carcinogens. About 40% of all malignancies in women are thought to be hormonally mediated. Although the exact mechanism by which these hormones function as carcinogens is unknown, it seems that timing and duration of exposure have a significant impact on the likelihood of developing breast cancer. The probability that a woman may get breast cancer seems to increase with the length of time between the start of her menstrual cycle and menopause. This information might help to explain why there are racial differences in the incidence and death rates of breast cancer. For instance, from 1986 and 1988, the United States had a death rate from breast cancer of 22.4 per 100,000 individuals, compared to 4.7 in China. In accordance with this, Chinese girls experience menarche at the age of 17, while American females do it on average at 12.8.Between 1980 and 1988, the incidence of breast cancer in the United States rose by nearly 3% per year, from 84.8 per 100,000 in 1980 to 109.5 per 100,000 in 1988 (3). Other industrialized nations have seen a comparable growth. Mammography's enhanced detection capabilities may somewhat explain the observed increase, but they cannot fully account for the pattern. A recent research found a link between the prevalence of breast cancer and the quantity of DDE [1,1-dichloro-2,2-bis(p-chlorophyll) ethylene], the main metabolite of the pesticide DDT, in women's serum.

The discovery of numerous synthetic molecules that bind to estrogen receptors in 1994 was made despite their structural dissimilarity. "Xenoestrogens" is the term used to describe them. The majority of them are either industrial waste products such certain PCBs, alkyl phenols, and PAH, or pesticides like DDT, DDE, Ketone, and dihedron. They either replicate the physiological hormone or counteract its effects. They wreak havoc on women's endocrine systems in either situation.The String Cornell Cancer Research Laboratory's H. Leon Brad low and former U.S. Department of Health and Human Services scientific advisor Devra Lee Davis proposed a mode of action for xenoes- taunts. There are two mechanisms to metabolize the natural estrogen, estradiol: conversion to 2-hydroxyestrone and to 16-hydroxyestrone (Figure 5.19). The latter has a strong estrogenic activity and destroys DNA, while the former has a mild estrogenic activity and is not carcinogenic. These researchers claim that xenoestrogens block the route that results in 2-hydroxyestrone synthesis and direct metabolism towards the creation of 16-hydroxyestrone.

It shouldn't be inferred from the explanation above that exposure to xenoestrogens or natural oestrogens is the sole factor in breast cancer development. The aetiology of breast cancer is very complicated, and carcinogenesis may result from a variety of pathways, according to Wolff and Weston. For instance, 5–10% of occurrences may be attributed to family history alone. Although specific connections between xenoestrogen exposure and carcinogenesis are

rare, they do exist as a possible risk factor for breast cancer. Studying this association is challenging since the tumour initiation event may have happened years before a tumour became visible, and timing of exposure, genetic modulation, and inhibition or encouragement of a tumour development may have all been important aspects. Additionally, nutrition is a risk factor, albeit its specific function is not fully understood. Radiation exposure and alcohol use are the two risk factors for breast cancer that have the most clear-cut definitions[11], [12].

Effect of Low-Frequency Electromagnetic Fields on Cancer

Although the data mentioned above supports the melatonin hypothesis, the authors warn that their study had significant flaws and that more research is required to conclusively demonstrate that there is a link between electromagnetic-field exposure and breast cancer. The effects of electromagnetic fields on human health have been extensively reviewed.

Repair Mechanism for DNA

Only if DNA damage brought on by chemicals or radiation is successfully repaired before or right away after genome replication will it result in mutation. Properly is key since improper repair might result in mutation on its own. Premutagenic change refers to the first modification of a DNA base brought on by alkylation or dimerization. Only when the damage is incorrectly fixed or not repaired at all is the mutation corrected. DNA may be repaired in a number of ways. Excision repair is the kind that is most clearly explained. Two distinct mechanisms may be involved in excision repair. The lesion is repaired with new nucleotides by utilising the intact strand as a template in the case of thymidine dimers by creating a nick in the DNA strand close to the damaged location, releasing the nucleotides, and repairing the lesion. If just one base is broken, the repair entails removing the base and then cutting similar to the first instance, the strand and resynthesis of the damaged section. Excision repair often works quite faithfully. A species' capacity for DNA excision repair and lifespan have been demonstrated to be positively correlated. We don't fully understand other forms of repair that commonly follow DNA replication. Some of them are prone to mistakes and might be the cause of cancer growth and mutation. Some sources claim that a unique methyl transferase may carry out specific repairs, including the demethylation of O6- methyl guanine. No matter how effective or ineffective the repair mechanism is, mutation will happen if the frequency and severity of injuries exceed what the system can handle or if the healing mechanism is weak or inhibited.

Tumor-suppressing genes and oncogenes

Malignancy develops as a result of gene mutations, as was previously indicated. But not all genetic mutations result in cancer. Genes in charge of controlling cell replication must be altered for the mutation to result in malignant development. Proto-oncogenes and tumour suppressor genes are the two different categories of genes that control growth. There are several different types of proto-oncogenes. Some of them encode for growth factor-responsive proteins that protrude from the cell's outer membrane. Some of these encode intracellular proteins that control cell development. others regulate the division of cells. Proto-oncogenes become oncogenes when any of these genes are altered, which may lead to uncontrolled cell growth.Tumoursuppressor genes, as opposed to oncogenes, produce proteins that prevent the growth of cells. Tumoursuppressor gene mutations are recessive and only cause aberrant development when both alleles are affected, in contrast to proto-oncogene mutations, which are dominant and may cause cell proliferation.

A. G. Knudson's research on genetically predisposed tumours inspired him to suggest the two hits theory, which holds true for both acquired and hereditary malignancies. This indicates that at least two mutations must take place in a single cell for a normal cell to become a cancer cell. Additional mutations in the daughter cells of the mutant cell cause them to proliferate more quickly, and the cells suffer structural modifications revealing aberrant chromosomes.

Although mutations in tumour suppressor genes and proto-oncogenes are directly responsible for the transformation of carcinogenic cells, changes in other genes may enhance the likelihood that malignancies may arise. For instance, a mutation in the gene that produces CYP1A1, an enzyme that transforms PAH into carcinogens (see Chapter 3), may result in an accumulation of the carcinogenic form of PAH, increasing the likelihood that proto-oncogenes may mutate. Similar to this, a change in the gene for the synthesis-Glutathione transferase might result in a rise in the amount of electrophilic alkylating agents.

CONCLUSION

Low-frequency electromagnetic fields, such as those created by power lines, household appliances, and electronic gadgetry, have been a source of worry over the last ten years. This worry was sparked by reports of higher cancer incidence clusters, particularly pediatricleukemia, among residents living close to electricity lines. Numerous epidemiological investigations were conducted in response to this worry. A slight correlation between exposure to low-frequency electromagnetic fields and childhood leukemia and other cancers was found in some of them, but not in others. Animal tests also produced conflicting findings. The ani- mal experiments were challenging because the effect varied on the frequency, waveform, and angles between the applied field and the earth's magnetic field, and there was no apparent dose-response impact. According to a more recent epidemiological research that looked at records of breast cancer deaths in women, electrical workers had a 38% higher mortality rate than women in other professions (32). There are theoretical underpinnings to the link between breast cancer risk and exposure to low-frequency electromagnetic fields. It has been noted that electromagnetic fields inhibit the pineal gland's ability to produce the nighttime hormone melatonin. As an estrogen antagonist, melatonin inhibits this hormone's capacity to promote tumour growth.

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CHAPTER 6

THE ADVANTAGES OF ENDOCRINE DISRUPTERS

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ABSTRACT:
Thalidomide a prescription medicine for use during pregnancy as a sedative and to treat nausea, was created in 1957 and has since gained widespread usage in Europe and Australia. But soon it had to be taken off the market because some kids of thalidomide-using mothers were born severely deformed, with missing or undeveloped limbs. There was no correlation between the impact and the total dosage of the medicine given to pregnant women who took thalidomide. The impact instead relied on timingthe point in the pregnancy when a drug was consumed. Only when thalidomide was administered between the fifth and eighth week, while the organs were growing, did the malformations appear. As a synthetic estrogen analogue, diethylstilbestrol (DES) was first created in 1943. It was often administered to expectant mothers for the prevention of miscarriages in the decades that followed. Nevertheless, a 1952 epidemiological research carried out at the University of Chicago found no difference in the frequency of miscarriages in women who took DES and those who did not. Many doctors continued to prescribe the medication despite this finding far into the 1960s. Two independent case-control epidemiological investigations conducted in 1971 revealed that vaginal cancer occurred at an exceptionally early age of 15 to 22 in girls born to moms who used DES.

KEYWORDS:
Animals, Development, Disruptors, Endocrine, Hormones.

INTRODUCTION

Although the p values for statistical significance in both studies were fairly excellent, several researchers questioned the validity of the case-control study approach in the incidence of abnormalities of the reproductive organs, such as T-shaped uteri in women and aberrant testicles, genital tumors, low sperm counts, and abnormal sperms in males, was substantially higher than the incidence of vaginal cancer, according to a number of later investigations. Additionally, there were some signs that women exposed to DES in utero had greater than average gay and bisexual inclinations [1], [2].

Unbalanced Hormones

Correct hormonal balance is crucial for the healthy development of a foetus, as shown by the cases of thalidomide and DES and as confirmed by later investigations with environmental pollutants. Males and females both have oestrogens and androgens, but in differing amounts. Any deviation from the ideal balance of sex hormones might cause an abnormal Thalidomide and diethylstilbestrol structures, respectively due to a skewed ratio of females to males among the newborns in terms of sexual development. As a result, prenatal or early postnatal exposure to an overabundance of natural hormones, hormone mimickers, or antagonists upsets the foetuses' whole endocrine balance, which results in aberrant development. VomSaal did a good job of documenting the significance of a healthy hormonal balance during in utero development. He demonstrated that in mice, female foetuses that were

sandwiched between two male foetuses had testosterone levels in their blood and amniotic fluid that were much greater. Male aggression and a lack of pheromones that would make them sexually desirable to males were present in the adult mice that emerged from these foetuses.

It has only recently come to our attention what makes a fertilized egg develop into a male or female. In essence, the procedure seems to be rather easy. The mother's eggs have an X chromosome in them. An X or a Y chromosome might be present in the father's sperm. If an X-chromosome-carrying sperm and an egg are combined, the subsequent embryo will be female. The likelihood of a male embryo is increased when a sperm bearing the Y chromosome fertilizes an egg, but the gender of the growing embryo is not determined for some time. The last problem is reliant on hormonal signals gathered throughout embryonic development. Hormonal imbalance is likely to cause changed sex ratios or aberrant sexual development that, in severe situations, may lead to hermaphrodites.Although the majority of research focused on substances that interact with estrogen receptors, thyroid and androgen functions may also be impacted. Compounds that disturb the equilibrium of hormones are known as endocrine disrupters[3], [4].

Characteristics of Hormone Disruptors

Endocrine disrupters have been identified as a significant number of structurally and functionally unrelated compounds to far. Not only do they not physically match the hormones they mimic or whose activity they interfere with, but they also typically do not have any structural similarities. In other words, unlike carcinogens, where a structure-activity link can often be identified, chemicals having hormonal actions do not have the same relationship. Colborn et al. discovered 44 substances with endocrine-disrupting properties that are extensively distributed in the environment. In addition to certain heavy metals, PCBs, dioxins, plasticides (alkylphenols and bisphenol-A, and other industrial chemicals or by-products, they also contained herbicides, fungicides, insecticides, and nematocides. Many of these substances are fat soluble, resistant to degradation, and have high vapour pressures, making them simple to transfer with air flow [5], [6] .

Comparison of the chemical compositions of several endocrine disruptors and natural oestrogen.

Endocrine disrupters may act directly or indirectly. The direct-acting substances either imitate natural hormones or block their function when they come into contact with hormonal receptors. The indirect-acting prevent sterol, the building block of sex hormones, from being made. At parts per trillion, they function in a manner similar to that of natural hormones. The mechanism that breaks down xenobiotics may need to activate some of them. The plasma protein cannot bind hormonal mimics, which increases the effective dose of the mimic even though it may be less potent or occur at a lower concentration than the natural hormone. Plasma levels of natural hormones are tightly regulated by binding any excess to plasma protein, which temporarily renders the hormone inactive. The dose-response curve for many environmental endocrine disruptors has an unusual form, resembling an inverted U[7], [8].

Endocrine disrupters are particularly dangerous since the harm they inflict is permanent and may not show up for many years. Graph 6.3. Nonylphenol, a plasticizer added to polystyrene plastics, is shown in the top structure, whereas bisphenol-A, a plasticizer added to polycarbonate plastics, is shown in the bottom structure exposure. Furthermore, the harm

does not only affect the reproductive system. The brain, skeleton, thyroid, liver, kidney, and immune system are possible targets in both sexes, as are the internal and external genitalia.

DISCUSSION

Large amounts of different chemicals started to infiltrate the environment after World War II. Some, including pesticides and chemical fertilisers, were used on deliberately, while others were industrial byproducts that either leaked unintentionally or were dumped in open pits. Chemical reliance was increasing, which was an indication of development.Silent Spring by Rachel Carson (10) did not make the risks of chemical environmental pollution widely known until 1962. The greatest concern with regard to human health was cancer. Since then, most industrialised nations, including the United States, have outlawed the use of several persistent, lipid-soluble substances including PCBs and chlorinated insecticides (DDT, aldrin, chlordane, toxaphene), yet their legacy still exists. They either come from nations where they are still in use or are residues from their earlier usage that have been transported by air currents.Endocrine disruptors have been implicated in several instances of harm to animals worldwide. The relationship between polluted water and ill or improperly developing animals'mammals, fishes, birds, or reptilesis highly repeatable, even if a causal relationship cannot always be shown. Despite decades of study on endocrine disruptors, only scientists were aware of their existence and potential effects on the environment. The general public, if not the government authorities, did not become aware of the potential environmental and health effects of endocrine disruptors until the 1996 release of the book Our Stolen Future by Colborn[9], [10].

Fish and Birds That Eat Fish

Coho and chinook salmon from the Great Lakes were found to have thyroid disease in 1981, and this pathology looked to have an environmentalaetiology. Male fish have also been documented to have feminised instances. It has been noted that male fish that gathered near effluents from waste-water treatment facilities developed vitellogenin, a protein that typically only appears in female fish and is essential for the formation of the egg yolk. A variety of substances known to be estrogenic in animals were evaluated by the authors of this paper, and they found same fish also produced oestrogen from them.

The effluents from waste-water treatment facilities are known to include several of these estrogenic compounds (12). The natural and synthetic oestrogens (estradiol and ethinyl estradiol, respectively) were shown to be the substances responsible for the feminization of male fish, according to a more recent research carried out in the United Kingdom. These substances, which make up the majority of the contraceptive pill's active component, were discovered in extremely small amounts in waste-water treatment plant effluents.

Colborn, in a thorough study, offered historical evidence in favour of the theory that bald eagle reproductive failures are caused by organochlorine pesticides that were introduced to the Great Lakes after World War II. There has also been evidence linking the contamination of the Great Lakes with organochlorine chemicals, particularly PCB, with immunosuppression in Caspian tern and herring gull fledglings. Researchers for the International Joint Commission found that colonial fish-eating birds from the Great Lakes had embryo mortality, edoema, and malformations syndrome. Indirect evidence revealed a link between the illnesses reported and the TCDD contamination of Lake Ontario. The fact that the improvement in Lake Ontario herring gull reproduction corresponded with the drop in organochlorine chemicals, notably TCDD and PCB, served as further support for this

causal relationship (16). Similarly, Donaldson et al. hypothesised that among other things, a decline in organochlorine levels in the Great Lakes' waters is responsible for the bald eagle population's recovery in the Canadian Great Lakes.

An experiment in which DDT was injected into gull eggs at quantities equivalent to those observed in contaminated seabird eggs may have provided more proof of the harmful effects of organochlorine chemicals on fish-eating birds. These eggs produced male birds that exhibited feminization traits, including the development of ovarian tissue and oviducts (18).

Mollusks

Several species of mollusks, both in the United States and the United Kingdom's Connecticut coast harbors and marinas, have males that are more masculine than females. Offshore in the shipping lanes of the North Sea, same phenomena were also seen. Tributyltin tin (TBT), an antifouling substance used in paint for boats and ships to inhibit the growth of barnacles, has been identified as the source of this aberrant sexual development.

Oceanic Mammals

The findings of necropsies conducted on the bodies of stranded beluga whales from highly specialised laboratories were first reported in 1988 by researchers at the University of Montreal parts of the St. Lawrence River that are contaminated. There were significant multisystemic lesions in two animals. One of these two cases had a herpes-like particle and a severe necrotizing dermatitis.

There were five distinct tumour types in the other four animals. High tumour incidence was correlated with high benz(a)pyrene-DNA adduct concentrations. These animals' tissue contained large levels of organochlorine chemicals as well. Others (20) have also noted the occurrence of tumours in beluga whales from the St. Lawrence (20). A thorough analysis of the pathophysiology of the declining St. Lawrence River beluga whale population has been published. They came to the conclusion that "St. The danger of long-term exposure to toxins found in their ecosystem may well be represented by Lawrence belugas, who may also serve as an excellent model for anticipating potential health issues in populations of highly exposed humans in the future.

Common seals off the coast of the Netherlands that were consuming fish from contaminated waters had reproductive failure. The number of seals decreased from more than 3000 to fewer than 500 between 1950 and 1975.

The levels of PCB in the tissue of seals from the northern and western parts of the Wadden Sea were compared by the authors of this study. The levels were really different. Thus, the PCB entering the sea from the Rhine was blamed for the reproductive failure.The 1988 North Sea seal extinction was attributed to suppressed immunity. A virus similar to distemper, to which healthy animals were resistant, was the underlying cause. The animals succumbed to the infection, however, when their immunity was weakened, perhaps as a result of exposure to endocrine disruptors.

Reptiles

The herbicide dicofol was extensively spilled in Florida in 1980 at the Tower Chemical Company, which is close to Lake Apopka. The spill site was included to the EPA's Superfund list. Six-month-old female alligators from Lake Apopka were found to have plasma oestrogen concentrations that were almost twice as high as those from unpolluted lakes. Additionally,

their ovarian morphology was aberrant. The male alligators' testosterone levels were low, their testicles were disorganised, and their penises were unusually tiny. The incapacity of the species to reproduce was presumably caused by abnormal sexual development in both males and females.

Species of Land Animals

Many of the Florida Panthers still alive today have been shown to have a number of problems, including low sperm counts, unusual sperm, thyroid issues, immunosuppression, and inherited cardiac problems. When the youngsters were 11 years old, many IQ and achievement tests were given to them.

The exposed kids had lower IQ scores than the controls and had reading comprehension skills that were at least two years behind. In addition to having problems in their immune systems, many youngsters in Inuit towns in northern Quebec suffered from persistent ear infections, according to Canadian health officials. The typical food of those who inhabit the arctic area, which mostly consists of fish and marine animals, may be related to these symptoms. A few investigations showed significant dietary absorption of organochlorine chemicals as well as significant PCB, DDE, and dieldrin contamination of mother's milk. Organochlorine chemicals were introduced into the arctic marine food chain by air transport from the industrialised areas farther south.

Men in the United States and industrialised nations of Europe have a steadily declining sperm count and motility, according to studies from France, Denmark and the United States. According to the Parisian research between 1973 and 1992, sperm concentration decreased by 2.1% year, and sperm motility decreased by 0.6%.

The American research examined regional variations in sperm concentration. They claimed that non-Western nations did not experience the fall in sperm count that was seen in the United States and Europe. The Danish researcher presented a mechanism of action and hypothesised that the rising prevalence of male reproductive disorders may be linked to foetal exposure to endocrine disruptors.

Endocrine disrupters have been identified as a significant number of structurally and functionally unrelated compounds to date. Not only do they not structurally match the hormones they mimic or whose activity they interfere with, but they also typically do not have any structural similarities. In other words, unlike carcinogens, where a structure-activity relationship can frequently be identified, chemicals having hormonal actions do not have the same relationship. Colborn et al. discovered 44 substances with endocrine-disrupting properties that are widely distributed in the environment. In addition to some heavy metals, PCBs, dioxins, plasticides (alkylphenols and bisphenol-A, and other industrial chemicals or by-products, they also contained herbicides, fungicides, insecticides, and nematocides. Many of these substances are fat soluble, resistant to degradation, and have high vapour pressures, making them simple to transfer with air flow.

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The indirect-acting prevent sterol, the building block of sex hormones, from being made. At parts per trillion, they function in a manner similar to that of natural hormones. The system that breaks down xenobiotics may need to activate some of them. The plasma protein cannot

bind hormonal mimics, which increases the effective dose of the mimic even though it may be less potent or occur at a lower concentration than the natural hormone. Plasma levels of natural hormones are tightly regulated by binding any excess to plasma protein, which temporarily renders the hormone inactive. Many environmental endocrine disruptors have an unusual dose-response curve with an inverted U shape[11], [12].

CONCLUSION

Many of these flaws were first attributed to a lack of genetic variety, but recent research seems to show that environmental toxins including mercury, DDE, and PCB may be key factors in the extinction of the species (25). Endocrine disruptors' effects on people have not been studied as thoroughly as they have in animals.

In some instances, the causal relationship has been shown conclusively, and in others, there was a strong chance that such a relationship existed. Jacobson et al. conducted the most important investigation in this field. These researchers compared 71 control newborns whose mothers did not eat fish to 242 children born to moms who ate PCB-contaminated fish from Lake Michigan. In comparison to the controls, the experimental group had modest behavioral deficits such motor immaturity, a larger startle reaction, and more unusually weak reflexes. The baby's birth weight and head circumference were similarly negatively correlated with the mother's fish intake

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CHAPTER 7

THE DETAILED ANALYSIS OF RISK ASSESSMENT

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ABSTRACT:
This chapter's discussion will mostly center on carcinogenicity and mutagenicity, with endocrine disruptors also being taken into account. Epidemiological studies were used to determine the carcinogenicity of several substances. Epidemiological studies, however, take a long time before any results can be drawn due to the lengthy latency period of cancer. Additionally, they cost a lot of money. Animal bioassay is yet another technique that might be used. Although these bioassays are very helpful in predicting the risk of developing human cancer, they can take up to 2 years and at least 600 animals to complete.

In terms of both time and money, this procedure is likewise too expensive to be taken into account for extensive screening. For these reasons, a low-cost, quick test technique is required for a first assessment of possible mutagens and carcinogens. Experience in the past has demonstrated that some of these substances, while not lethal unless consumed in large amounts, may be mutagenic and carcinogenic with prolonged exposure to minute levels, or may interact with the immunological or reproductive systems of people and animals. To safeguard human health, it is important to establish that substances—such as cosmetics, food, and pesticides—to which people are routinely exposed won't be harmful over the long term.

KEYWORDS:
Animals, Carcinogens, Exposure, Humans, Risks.

INTRODUCTION

Risk assessment is to determine the extent of potential adverse effects on both human health and the environment from exposure to chemicals found in the environment. Whether assessing risks to human health or the environment, the Environmental Protection Agency (EPA) follows a four-step process:

1. Hazard analysis

2. Dose-response analysis

3. Exposure evaluation

4. Risk identification

Risk Assessment

The amount of chemicals currently in use is astounding. According to data compiled by Hodgson and Guthrie in 1980 (1), there were at that time 1500 active ingredients in pesticides, 4000 active ingredients in therapeutic drugs, 2000 additives to drugs to improve stability, 2500 additives to foods with nutritional value, 3000 additives to foods to extend product life, and 50,000 other chemicals in common use. The chemical and pharmaceutical industries have expanded, thus these sums must now be significantly higher[1], [2].

Test for Bacterial Mutagenesis

There are several bacterial mutagenesis test variants, but the Ames test is by far the most widely applied. Salmonella typhimurium strains that were genetically altered to be unable to synthesize the amino acid histidine and hence require histidine for growth are used in this test. The assay measures the frequency of back mutations to a parent strain that is not histidine-dependent. On agar plates, the bacteria are planted along with the test substance and a minimal growth media that contains just enough histidine to induce a background growth. Countable colonies are produced by the organisms with back mutations. Scores for spontaneous mutations are recorded on control plates. Increasing doses of the mutagen can be used to trace a dose-response curve. Since bacteria lack an activating mechanism for metabolic activation, which is required for many putative mutagens and carcinogens, the plates also include a liver microsomal preparation (post mitochondrial supernatant, PMS).

Different mutant strains with various genetic make-ups have been created. This variant distinguishes between frame-shift mutation and base substitution. Additionally, supersensitive strains lack a lipopolysaccharide covering and a DNA repair system. They are therefore more sensitive to external chemicals.Experimental testing of the Ames assay's predictive reliability revealed that 85% of the known carcinogens were found to be positive. Less than 10% of substances labelled as non-carcinogens had positive tests. According to a more recent study (3), the chemical class of the chemicals studied had a significant impact on how predictable the Salmonella test was. Because of this, only 40% of the chlorinated carcinogens were shown to be mutagens, compared to 75% and 100% of the mutagen tests for the cancer-causing amines and nitro chemicals, respectively, were positive. Escherichia coli, which lacks a DNA repair mechanism, is used in a different bacterial test. The genetically changed strain is more sensitive to mutagens that cause DNA lesions than the parent strain [3], [4].

Test for DNA Repair

This experiment, carried out in mammalian cell culture, is intended to find substances harmful to DNA. The test assumes that the damage to the DNA stimulates the mechanism for repair. The increase in 3H-thymidine incorporation into DNA over the control level serves as a marker for DNA repair. Autoradiography or scintillation counting are used to measure radioactivity. Precarcinogens are activated in the cultures by the addition of PMS.The hepatocyte primary culture-DNA repair assay, a variation of this method, employs newly obtained, non-dividing liver cells. As precarcinogens can be activated by hepatocytes, this system does not require PMS. Additionally, there is no background thymidine incorporation in non-dividing cells [5], [6].

Tests for Mammalian Mutagenicity

There are three of these tests in use. Mammalian fibroblasts are used in the first and most popular one. The appearance of colonies that are resistant to the purine analogues 6-thioguanine or 8-azaguanine enables the identification of mutants in this experiment. Hypoxanthine-guanine phosphoribosyltransferase (HGPRT), a "purine salvage" enzyme, is found in most cells and converts these non-cytotoxic analogues into cytotoxic nucleotides. This enzyme uses already produced purines to synthesis nucleic acids. Due to the fact that the majority of cells are able to synthesis purines on their own, it is not necessary for cell viability. In cultures exposed to either 6-thioguanine or 8-azaguanine, normal cells will not proliferate. However, 6-thioguanine-8-aza-guanine-resistant mutants lacking HGPRT emerge

and establish colonies when a mutagen is present. PMS must be added in order to activate precarcinogens. Since HGPRT is not a necessary enzyme and its deletion does not produce lethal mutants, this assay is extremely sensitive. The X (sex) chromosome, which is extremely changeable and has no duplicates, contains the HGPRT region[7], [8].

DISCUSSION

Hepatocytes that have just been created are used as a feeder layer in a modification of this process. Because hepatocytes include xenobiotic-activating enzymes, PMS is not included in this experiment. The thymidine kinase gene, which is necessary for the activation of the antimetabolite iodo-deoxyuridine, is the focus of another mammalian mutagenesis assay. In the presence of the antimetabolite, colonies can only be formed by altered cells that have lost their kinase. Since the kinase is not a necessary enzyme, no deadly mutations are created.For mutant's resistant to the alkaloid ouabain, the third experiment in this class yields positive results. The gene responsible for producing membrane ATP-ase, an enzyme involved in K+-Na+ transport, has mutated, leading to ouabain resistance. By noncompetitively inhibiting this enzyme, ouabain interferes with crucial cell processes. The only mutants that can be scored in this experiment are those in which the ATP-ase has been changed so that it still exhibits enzymatic activity but does not bind ouabain. Inactive ATP-ase mutants are deadly and, as a result, do not establish colonies. The assays previously covered provide results for mutagens and, hence, genotoxic carcinogens. Both genotoxic and epigenetic carcinogens are applicable to the two assay techniques that are provided below[9], [10].

Assay for Sister Chromatid Exchange

The interchange of loci between sister chromatids of different chromosomes is measured by this test (4). For the duration of the two rounds of DNA replication, the cells are cultured in the presence of 5-bromodeoxyuridine (5BrdUR). Thymidine is replaced with 5BrdUR in the newly created DNA strand. One DNA strand of the chromosome's one chromatid carries 5BrdUR after the first replication; after the second replication, both strands of the first chromatid and one strand of the second chromatid carry 5BrdUR. The two chromatids can be separated from one another using fluorescent staining methods. This process makes it possible to observe the chromatid segment exchanges brought on by mutations. Although this assay is exceedingly sensitive, the chemical insults that cause these chromosomal abnormalities have typically not been discovered.

Assay for Cell Transformation

The only test that directly measures malignant transformation rather than mutagenesis, as have the assays previously described, is a cell transformation assay. Both geno-toxic and epigenetic carcinogens are included by this rule. A monolayer of mammalian cells is grown on agar. When confluence is reached, contact inhibition stops the development of healthy cells. The cells that change into cancerous cells continue to divide when a carcinogen is present in the culture. The converted cells pile up on top of one another because there is nowhere for them to multiply in the horizontal plane, making colonies simple to count. Precarcinogens must be activated in the culture by adding PMS. Tumors are created when these multiplying cells are injected into animals. This finding establishes the colonies' identity as malignantly altered cells.Fish are used in a number of carcinogen testing methods. These technologies eliminate the need for labor-intensive cage sterilization and bedding replacement. As a result, a lot more animals may be used for less money. This topic has already been the subject of an extensive review.

Animal Biological Testing

Bioassays, which include testing substances on lab animals, provide accurate information about carcinogenicity. All human cancers can be recreated in animals, and the majority of animals are susceptible to cancer despite species differences in their susceptibility to carcinogens. It is not feasible to test all 50,000 chemicals in widespread use due to the cost of bioassays (EPA estimates range from $390,000 to $980,000 per assay) and the time required (up to 30 months). As a result, a selection procedure has been established for chemical bioassay testing.In the United States, there are now two such testing programs in operation. The EPA Administrator receives chemical recommendations for testing from an eight-member Interagency Testing Committee that is made up of representatives from various federal agencies and departments. The National Cancer Institute (NCI) receives reports from the National Toxicology Program (NTP) Chemical Nomination and Selection Committee. Selection for bioassay is based on evaluation of chemical structures and outcomes of several in vitro tests. Numerous classes of compounds have been the subject of structure-activity relationship (SAR) research, and at least for some of these categories, it is possible to make rather accurate predictions about a compound's potential carcinogenicity.

Guidelines for Carcinogenic Bioassay in Small Rodents, released by the NCI, outlines the minimal specifications for a bioassay's conception and implementation (10). The main points of these recommendations are summarized as follows. Each chemical should be tested on at least two different species, including both sexes (often rats and mice). Each experimental group in a bioassay needs to have at least 50 animals. Chemical exposure should begin at 6 weeks of age (or younger) and continue throughout the majority of the animal's lifespan (for mice and rats, this is typically 24 months). After the last dose has been administered, the observation period must last for another three to six months.

The maximum tolerated dose (MTD), which is the largest dose that can be administered without affecting the animals' normal life span from consequences other than cancer, should be administered to one treatment group. A smaller amount of MTD is administered to the other treatment group. The method of administering a chemical should be the same as, or as similar to, the one used for human exposure. The chemicals can be administered orally (with food, water, or by forcing feeding), topically (by applying to the skin), or by inhalation.In some cases, two-generation bioassays are carried out in which the possible carcinogen is exposed to both generations. This process has the advantage of exposing fetuses and young animals, who are significantly more vulnerable to chemical harm than adults. Tumors are inspected in both the animals that pass away during the experiment and the survivors that are put to death at the end. The statistical evaluation of the results yields a p value of 0.05, which indicates that there is a less than 5% possibility that the outcomes might have been the result of chance. A positive bioassay result suggests, but does not prove, that a substance may cause cancer in humans. 142 chemicals had been experimentally demonstrated to be carcinogenic in animals as of 1982, according to the International Agency for Research on Cancer (IARC). Only 14 of those have been identified as human carcinogenic. Reference 10 provides a thorough discussion of this topic.

Dose-Response Evaluation

To get a quantitative estimate of human risk from dose-response data generated by bioassays, two factors must be taken into account: biological extrapolation and numerical extrapolation.

Extrapolation from Biology

Humans and laboratory animals differ metabolically, and whereas the human population is genetically very varied, laboratory animals are typically extremely inbred. These differences raise the fundamental issue of how to adapt the dose determined by bioassays to the dose received by humans. One or more of the following methods may be taken into consideration: Straight translation from animals to humans of milligrams per kilo-game per day; Straight translation from animals to humans of milligrams per square meter per day; Straight translation from animals to humans of milligrams per kilogram per lifetime; and In cases where the experimental dose is measured as parts per million (ppm) in food, water, or air, human exposure is expressed in the same units.

The incidence of site-specific chemically generated tumours in experimental animals and people was compared in the National Research Council (NRC) study. The evaluation of five substances and cigarette smoking used milligrammes per kilogramme per lifetime as a bioassay for people. The human occurrence of two of these chemicals—N,N-bis(2-chloroethyl)-2-naphthylamine and benzidine—as well as smoking cigarettes happened as predicted by the animal studies. Aflatoxin B1, diethylstilbestrol, and vinyl chloride, on the other hand, had human incidence that was significantly inflated (10, 50, and 500 times, respectively). The Consultative Panel on Health Hazards of Chemicals and Pesticides came to the following conclusion: Although there are significant risks involved, extending findings from animal studies to humans is frequently the only feasible strategy. Despite the unknowns, there is enough information to suggest potential dose and time dependencies and offer ballpark estimates of the incidence of induced cancer in the general population.Another issue is how to interpret the results of the bioassay if the responses of the two tested animal species differ significantly or if only one does. Despite some disagreement over how to interpret these data, U.S. federal agencies generally concur that the extrapolation should be based on data from the more vulnerable species[11], [12].

Calculation Extrapolation

It is required to expose the test animals to relatively high doses of the possible carcinogen in order to acquire meaningful results within bioassay limitations. For high doses, a negative dose-response relationship can be shown. However, compared to the levels utilized in laboratory animals, humans are often exposed to far lower levels of environmental carcinogens. It is anticipated that such modest exposure will result in cancer incidence that is many orders of magnitude lower than that shown in bioassays. For exposures below the lowest detectable bioassay exposure, the dose-response curve's shape can only be conjectured. Because of this uncertainty, a straight line from the lowest observed dose-effect point to the zero dosage is the extrapolation that is most frequently utilized. Other strategies, though, have been put forth.

Models based on the best fit of observable data points into a mathematical equation can yield the infra-linear extrapolation. Unfortunately, there are typically only two or three observable data points available in practice. As a result, numerous models will equally well fit the experimental dose- response curve, rendering the projected section highly speculative.Super-linear extrapolation can generate a number of speculative lines without offering a convincing argument for choosing one over another. The idea behind the super-linear model was inspired by the discovery that in some biological studies, lower doses were more successful at causing tumors than greater levels. The issue with this strategy is that the toxicity of the drug was what caused the comparatively poor effectiveness of the higher doses. Numerous animals

perished at the higher doses before developing tumors. According to the extrapolation model of the dose-response curve, there are significant differences in dose-response assessment. The infra-linear model underestimates and the super-linear model overestimates tumor incidence when compared to straight-line extrapolation. All of these models are predicated on the widely held belief that there is no dose below which tumors do not form. This assertion cannot be supported or refuted; even if tumors cannot be seen below a particular dose, perhaps some tumors would show up if more animals were utilized.

Unfavorable Results

The absence of tumors in a test population of 100 animals does not mean there is no risk. The absence of tumors, according to statistical calculations, only suggests that there is a 95% probability that the true incidence of tumors is no higher than 0.45%. This estimate of tumor incidence that might go undetected indicates the top 95% confidence limit of an experiment involving 100 animals. We must draw the conclusion that it is highly speculative to quantify the quantitative cancer risk of environmental contaminants.

Exposure Evaluation

Who and what are likely to be exposed to the substance in question? are the elements to be taken into account in exposure assessment. How much potential exposure is there? How, for how long, and under what conditions will the exposure take place? Standard parameters of human anatomy and physiology are specified (11) to enable estimations of the total human exposure. Man 70 kg, woman 60 kg, and child 20 kg. 1.8 skin surface area (m2) overall (180 cm tall), 0.3 skin surface area (m2) with short sleeves, and 0.1 skin surface area with long sleeves. Man's resting respiration rate was 7.5, a woman's was 6, and a child's was 4.8. Respiration rate (L/min) during light activity: 20 for men, 19 for women, and 13 for children. Daily air intake (m3): 23 for men, 21 for women, and 15 for children.

Man consumes two liters of fluid per day, a woman consumes one liter per day, and a child consumes one liter per day of food. In addition to the fact that people move around and participate in a range of activities, the exposure assessment is challenging since it must take into account all potential exposure routes. In order to estimate the total human exposure to a carcinogen from contaminated groundwater, for example, it is necessary to calculate the contributions of the following exposure pathways: direct exposure through drinking; indirect exposure through inhalation from showering, bathing, and other water-related activities; indirect exposure through skin contact with the contaminated water; and ingestion of food that has come into contact with the contaminated water.Additionally, the bioavailability of the carcinogen for each route of entry and its metabolism must be taken into account at each level of this analysis. The exposure evaluation has generally come under fire for assessing each carcinogen separately whereas, in reality, people may be exposed to multiple carcinogens simultaneously. An effect of a cumulative exposure could be additive, synergistic, or antagonistic. Additionally, concurrent exposure to agents that stimulate or inhibit xenobiotic-metabolizing enzymes may further muddle the real picture.

CONCLUSION

There are various ways to express the cancer risk. The individual lifetime risk is the most widely used risk indicator. This reflects the likelihood that a person will get cancer at some point in their lifetime as a result of ongoing exposure to a carcinogen, such as 1 in 10,000 or 1 in 100,000 or so. The percentage of cancers per unit of the carcinogen is computed from the straight-line extrapolation of the dose-response curve to zero. "Potency" for carcinogens or

"unit cancer risk" are terms used to describe this. It is possible to calculate the individual lifetime risk by multiplying the potency by the exposure dose.Calculating population or social risk requires multiplying individual risk by the quantity of exposed individuals. It indicates the number of instances that are attributable to a year's worth of exposure to a carcinogen, or alternatively, lifetime exposure. Because the findings will differ significantly depending on whether the computation is done for a year or for a lifetime, the time parameter must be defined

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CHAPTER 8

EXPLORING THE OCCUPATIONAL TOXICOLOGY

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ABSTRACT:
Measures of biological exposure and threshold limit values. The population group most susceptible to chemical harm is made up of industrial workers. The American Conference of Governmental and Industrial Hygienists publishes annual revised threshold limit values (TLVs) (1), which are standards for permissible chemical exposure at work, to safeguard people from harm connected to their occupation. The term TLV refers to the highest airborne material concentrations in parts per million or milligrams per cubic meter to which most employees can be exposed daily without risk. These principles only apply in the workplace. They are not meant to serve as recommendations for population-wide norms for ambient air quality. Obviously, genetic variances and various lifestyles (such as smoking, drinking, using drugs, and using prescription medications) must be taken into account. Even below the TLV limits, exposure to some substances can have negative effects on hypersensitive people.

KEYWORDS:
Blood, Cells, Exposure, Immune, Lungs.

INTRODUCTION

TLVs should therefore only be regarded as recommendations and not as unchanging standards. The ideal outcome is to reduce chemical exposure as much as possible at work. There are three ways to express TLVs:

1.The time-weighted average (TLV-TWA) specifies the average chemical concentration to which employees may be exposed for up to 8 hours per day, five days per week, without risk.

2.The short-term exposure limit (TLV-STEL) specifies that exposures must last no longer than 15 minutes, occur no more frequently than four times a day, and be separated by at least 60 minutes.

3.Concentrations that should never be exceeded are called ceiling concentrations (TLV-C).

The TLVs' level of protection is being questioned. Only a few cases demonstrated no detrimental effects at exposures at or below the TLV, according to the 1990 report that examined the scientific basis for the TLVs. In certain circumstances, all those who were exposed had an impact. However, there was a strong association between the TLVs and the measured workplace exposure. This suggests that the TLVs are not protective limits but rather amounts of pollutants that might be present at work.Another technique to examine chemical exposure is through biological exposure indices (BEIs). This technique is an addition to air monitoring to check for TLV compliance. BEIs are guidelines for the levels of chemicals that are acceptable to be present in exposed employees' blood, urine, or breathed air[1], [2].

These standards are helpful for evaluating the effectiveness of personal protective equipment and figuring out whether a substance has a chance of being absorbed through the skin or the

digestive system. Of course, BEI results need to be carefully interpreted. External factors, like lifestyle and exposure outside of the workplace, may have an impact on the outcomes.

Environmental Toxicology

The most vital of the lungs' many functions is respiration, which involves the exchange of O2 and CO2 with blood. Excreting gaseous metabolites, metabolising, and controlling blood levels of vasoactive hormones such angiotensin, biogenic amines, and prostaglandins are other roles (3). Damage to the lung tissue that performs these regulatory activities may alter blood pressure, which will impact how well the lungs are supplied with blood. Alveolar ventilation1 (5250 mL of air per min) and the amount of blood perfusing the lungs (5000 mL/min) must match for the blood to be properly oxygenated. Any alteration in blood flow will upset the ventilation-perfusion balance and cause the organism to become dysfunctional. Toxins (gases, vapours, or aerosols) can harm respiratory tissue or induce systemic toxicity by permeating the tissue and getting inside the circulatory system. Depending on the substance and level of intoxication, respiratory system injuries can range in severity from irritation to edoema, fibrosis, or neoplasia. The size of aerosol particles or droplets, or the solubility of a gas in water, determine the location of toxicity[3], [4].

Hydrocarbon Gases

Water-soluble gases like ammonia, chlorine, sulphur dioxide, and hydrogen fluoride can harm the upper respiratory system. A gas must permeate the mucous lining in order to reach the tissue. Although the tissue is somewhat protected against extremely small doses of hazardous gases by this barrier, it is not shielded from high concentrations. Irritation is the most common symptom of toxicity to the respiratory tissue in this area. Edoema, though, might develop in more serious situations.Damage to the cell membrane, which alters membrane permeability and results in the discharge of cellular fluid, leads to edoema. Edoema manifests as tissue swelling, narrowing of the airways, breathing difficulties, and increased susceptibility to infection. The process of edoema developing is gradual. The affected person might not be aware of the hazard because it could take many hours for it to fully emerge. People with respiratory conditions like asthma or chronic bronchitis are more severely impacted than healthy people. However, extremely severe exposure to such water-soluble gases may be lethal, even though survivors may recover without suffering long-term effects[5], [6].

Significant Aerosol Particles

Aerosols with particles bigger than 2 mm can harm the upper respiratory system as well. Arsenic oxides, sulphides, and chlorides are employed in a number of industries, including the processing of hides and the production of coloured glass, ceramics, semi-conductors, and fireworks. However, the businesses that process ore and produce pesticides are more likely to expose workers to these substances at an upper respiratory level.

In these situations, arsenic compound particles are typically too big to enter the lung alveoli and instead deposit in the nasopharynx and upper bronchi. Their toxicity is shown by inflammation of the airways, which causes a persistent cough, laryngitis, and symptoms resembling bronchitis. Exposure to arsenic trioxide (As2O3) should be maintained to a minimum as it is thought to be a human carcinogen. Hexavalent chromium compounds, such as chromate (CrO2i) and bichromate (Cr O2i), are used in the production of stainless steel, chrome plating, pigment, and hide processing. The National Toxicology Programme lists and describes substances considered to be carcinogens in their annual report on carcinogens and

in the monographs of the International Agency for Research on Cancer (IARC) induce nose discomfort, symptoms similar to bronchitis, and (with prolonged exposure) lung cancer and tumours. During the processing of nickel ores, exposure to nickel and its byproducts, monoxide (NiO) and subsulfide (Ni2S3), is possible. The nasal mucosa and the big bronchi are the only areas where the ore dust particles' toxicity can spread due to their size. Whether in the form of dust or fumes, nickel subsulfide is a known human nasal cavity carcinogen.

DISCUSSION

Ozone (O3), nitrogen dioxide (NO2), and phosgene (COCl2) are examples of poorly water soluble gases that enter the lungs deeply and harm alveolar tissue. The oxidizing potential of ozone and nitrogen dioxide is connected to how they work. Edema results from the peroxidation of cellular membranes. In addition, NO2 combines with alveolar fluid to produce the corrosive acids HNO2 and HNO3, which further harm the cells. Because ozone is used to bleach oils, waxes, and textiles, exposure to ozone can happen in a number of industrial situations. The manufacture of explosives and the chemical industry both make extensive use of nitrogen dioxide.Pulmonary edoema is a side effect of several metals and their compounds, including beryllium, nickel carbonyl, and cadmium oxide (CdO), among others. Glass, battery electrodes, semiconductors, silver alloys, and cadmium electroplating are among the products made with cadmium oxide. CdO fumes include incredibly small particles that can enter alveoli. Edoema, pneumonitis, and type I pneumocyte growth of the alveolar lining are caused by inhaling such chemicals. Emphysema may develop as a result of repeated exposure. The EPA and the International Agency for Research on Cancer (IARC) both identify CdO as a carcinogen that mostly causes prostate cancer. A highly flammable liquid called nickel carbonyl is utilised in nickel plating and nickel refining. Pulmonary edoema is a result of inhaled vapours. 48 hours of observation are required in the event of exposure[7], [8].

Metallic mercury and its compounds are utilised in a variety of industrial applications, including as fungicides and catalysts. Exposure is particularly harmful since metallic mercury is very volatile and can rapidly enter the bloodstream through the respiratory system. Although mercury vapour inhalation mostly damages the central nervous system, it can also result in interstitial pneumonitis and corrosive bronchitis. The production of ceramics and alloys as well as the extraction of beryllium from its ore may expose workers to beryllium dust. When beryllium dust penetrates alveoli, it results in pulmonary edoema. Granulomatous pulmonary disease, also known as berylliosis, is brought on by exposure and can develop into pulmonary fibrosis. Beryllium has been demonstrated to cause cancer in animals, and it is also thought to cause cancer in humans. The chemical phosphorus, which is used to make a variety of organic chemicals, is also produced as a military gas. Due to its breakdown into CO2 and HCl in the lungs, it is extremely poisonous. The alveolar cells are damaged by the released HCl, which leads to severe edoema. It may take up to 48 hours before the edoema starts to manifest.

Paraquat

The respiratory system is extremely hazardous to the pesticide paraquat. Regardless matter how it enters the body, it produces pulmonary edoema. Paraquat penetrates the alveolar space, whether through ingestion or inhalation, and concentrates in type II pneumocytes. The production of superoxide radicals (O2), which may lead to the peroxidation of cellular membranes, is the likely source of its toxicity. The renal tubules actively secrete paraquat, which is then excreted from the body. It also impairs its own secretion by damaging the

tubules, though. It consequently builds up in the blood and causes lung toxicity. Although similarly harmful to cultivated lung cells as paraquat, diquat, a structural analogue, does not cause pulmonary toxicity in humans. Diquat is not retained in the alveolar cells, which is probably why there is a variation in the activity[9], [10].

Thoracic Fibrosis

Pneumoconiosis, another name for pulmonary fibrosis, is another way the lungs react to respiratory pollutants. Small solid particles or fibres act physically rather than chemically to injure the cells at first. Small (1–10 mm in diameter) islets of collagen are deposited in the pulmonary area in the early stages of the disease. The islets increase in size over time, eventually joining together to form a network of fibres that permeates the entire lung and reduces the lung's flexibility. Alveolar walls are also damaged, and the affected areas' blood arteries shrink, leading to the decompartmentalization of the alveoli and the development of emphysema. It is believed that the damage is caused by the activity of macrophages, which absorb the harmful particles and inflict damage on lysosomal membranes and release lysozymes as a result. The absorbed particles are released by the macrophages once they have been digested by their own enzymes; the process can then be repeated. Consequently, a single particle has a large macrophage killing capacity. The activation of fibroblasts by a substance or factors produced from damaged macrophages is likely what causes collagen to be deposited. A second component, known as the lipid factor, is also released at the same time and stimulates the more macrophages are produced (4). Collagen seems to be deposited in increasing levels as a result of a series of processes.

Silicosis

Silicosis is brought on by long-term exposure to respirable crystalline silica particles; amorphous versions of the substance are not to blame. Animal studies show that breathing in amorphous silica only mildly induces fibrosis. Only a modest amount of silica was retained in the lungs under these circumstances, though. In contrast, amorphous silica was more fibrogenic than crystalline quartz when injected into the peritoneum or the lungs (4). The emergence of tuberculosis frequently makes silicosis more difficult to treat.

Black Lung Illness

Blackened lungs of the deceased victims led to the long-held theory that black lung disease, a prevalent condition of coal miners, was brought on by prolonged exposure to coal dust. It now appears that the condition, which shares all the symptoms of lung fibrosis, is most likely brought on by the silica dust created during the process of mining coal.

Asbestosis

The two main groups of asbestos are the curly "serpentine" and the rodlike "amphibole," which are both hydrated fibrous silicates (5). The most pathogenic amphibole kinds are those whose toxicity is determined by the size of the fibres and maybe by other physical characteristics. 5 mm long and 1 mm wide fibres are the most dangerous. Workers who mine asbestos, build or demolish homes that contain asbestos, or both, are at risk of developing asbestosis. Additionally, cases of asbestosis have been noted among janitors and plumbers employed in educational institutions and commercial buildings. In this instance, the asbestos insulation of steam pipes and boilers is the source of the exposure.

The symptoms of asbestosis also include lung calcification and mesothelialtumour development in addition to fibrosis. Mesothelialtumour growth has an abnormally extended

latency period. Between exposure and the clinical manifestation of neoplasia, up to 30 years may pass. The high incidence of asbestosis, as well as lung and mesothelialtumours that it causes, that was widely reported to have occurred in the 1970s was brought on by American shipyard workers being exposed to asbestos. During World War II, the Navy. Asbestos fibresmay enter the peritoneal cavity and grow there, leading to tumours of the peritoneal mesothelium. Asbestis is amplified by tobacco smoke, which also encourages the growth of lung tumours (6).

Respiratory exposure to polycyclic aromatic hydrocarbons (PAHs) is one of the often occurring causes of occupationally linked lung neoplasia. PAHs are transported into the lungs by tiny particles of soot and fly ash, as will be addressed in the next chapters. Workers who operate in coal tar pitch and coke ovens are most at risk of developing lung cancer from this source. The population exposed to PAHs at work is more at risk for pulmonary neoplasia due to tobacco smoke, which is the primary cause of lung cancer overall. Smoking is still a strongly established habit among blue-collar workers, despite its steady decline in the more educated sections of society. Unfortunately, this group of people is especially susceptible to chemical harm due to the nature of their jobs.

System of Defense

The immune system has two crucial roles: it protects against developing neoplastic cells and offers resistance to infectious pathogens. These tasks are carried out by a variety of highly specialised cells known as leukocytes, or white blood cells as they are more often called. The bone marrow's stem cells are the source of leukocytes. They develop into granulocytes, lymphocytes, and macrophages as they mature. T-lymphocytes, B-lymphocytes, and non-T, non-B lymphocytes are further divided from the lymphocytes. Immune responses have two different mechanisms: The nonspecific immune system lacks antigen specificity and does not require prior exposure to an inciting substance. It consists of two different phagocytic cell types—granulocytes (polymorph nuclear leukocytes, PMNs), macrophages (mononuclear leukocytes, MOs), and two different non-T, non-B lymphocytic killer cell types—natural killer (NK) cells and antibody-dependent killer cells (antibody-dependent cellular cytotoxicity, ADCC) cells. These cells are the organization's main defences. The NK cells spontaneously attack various tumour cells with cytolytic activity. Antibody is necessary for the ADCC killer cells to lyse the target tumour cells.These cells have a one- to three-day lifespan and circulate in the blood. Antigens are necessary for the individual immune system's activation. Specific immunological responses come in two flavours: humoral immunity, which involves B lymphocytes, and cell-mediated immunity, which involves T lymphocytes.

T-lymphocytes work by maturing into killer cells that target a particular antigen and lyse foreign cells that have that antigen on their plasma membrane. In order for these cytolytic T-cells (CTLs) to grow, precursor CTLs, antigen-processing cells (typically macrophages), and phages) and other T-cells referred to as T-helper cells. B-lymphocytes play a role in cellular immunity by producing antibodies following antigen-induced sensitization. Proteins that make up antibodies typically have two light chains and two heavy chains. S-S connections are used to join the chains together (Figure 8.1). "Variable region" and "constant region" are both present in every chain. While the constant sections of heavy chains are in charge of biologically activating ADCC killer cells, granulocytes, and macrophages, the variable area is in charge of interacting with an antigen.

The Mode of Action of the Antibodies

IgM, IgG, IgA, IgD, and IgE are the five main types of antibodies. Ig stands for immunoglobulin. Four routes are involved in their method of action: opsonization, which is the coating-based inactivation of viruses and bacteria; binding to antigens and linking them to ADCC killer cells; complement fixation, which is a series of events involving sequential binding to 20 serum proteins and the production of biological activities capable of cell lysing.

Immune system dysfunction

At toxic agent dosages that are significantly below that at which toxicity becomes apparent, immune system damage might happen. The immune system is extremely sensitive to substances that inhibit cell proliferation because immunocompetent cells need to continuously proliferate and differentiate.

Typical Agents

There are many different substances that can cause an allergic reaction, including metals, dusts, germs, and organic chemicals. Toluene isocyanate, which is used in the production of plastic and resin, formaldehyde, which is widely used in the production of phenolic resins, textile finishes, the processing of hides, and many other industrial processes, and hexachlorophene, which is used in the production of germicidal soaps and cosmetics, are some examples of chemicals that are frequently to blame for allergies related to work. Contact dermatitis can be brought on by some metals like nickel, chromium, and beryllium[11], [12].

CONCLUSION

Increased susceptibility to infections, changes in the peripheral leukocyte count and cell differential count, changes in the histology of lymphoid organs, and decreased cellularity of the lymphoid tissue can all be used to assess immune system damage. Allergies, immunological suppression, unchecked proliferation, and autoimmune disease are immune system dysfunctions that can occur. When the immune system reacts negatively to environmental factors, allergic responses happen. When exposed to certain toxins, the immune system, which is meant to neutralise and get rid of foreign objects, reacts abnormally in some people. Asthma and contact dermatitis are two conditions caused by allergies. Leukaemia and lymphoma are two conditions where proliferative growth is unchecked. Immune suppression may be a hereditary trait, but it can also be brought on by medications, infections, neoplasia (such as leukaemia), radiation exposure, starvation, and exposure to chemical agents in the environment or at work.

The term "autoimmunity" refers to a person's system reacting against its own tissue. It could be genetically determined or brought on by exposure to environmental toxins that bind to tissue or serum products. As a result, these altered "self-antigens" trigger immunological reactions.

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CHAPTER 9

THE DEMERITS OF THE AIR POLLUTION

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ABSTRACT:
The consequences of air, water, and soil pollution are interchangeable, it is somewhat artificial to evaluate each one separately. Pollutants in water and land are the result of chemicals released into the air eventually settling down and combining with rain or snow. On the other hand, air pollutants are created when volatile compounds from the soil or those that enter lakes and rivers evaporate. When pesticides are sprayed on land, the wind carries them away as transient air pollutants, which eventually find a place on land or in water. However, it seems that some systematic categorization is necessary for discussion purposes. Although air pollution issues have long been acknowledged, they were originally thought to be local in nature and limited to industrialized urban areas. Air pollution has become a major issue on a global scale as a result of the recent recognition of the depletion of stratospheric ozone, the greenhouse effect, global deforestation, and the acidification of lakes and coastal waters. All of these sources of pollution, with the exception of trash incineration, rely on fossil fuel, and to a lesser extent, fuel derived from renewable resources like plant matter

KEYWORDS:
Air particles, Carbon, Pollution, Sulphur, Respiratory.

INTRODUCTION

Therefore, even though the amount of each component may vary from source to source, they all create fundamentally the same pollutants. Carbon monoxide (CO), sulphur dioxide (SO2), nitrogen oxides (NOx), a mixture of hydrocarbons known as volatile organic compounds (VOCs), suspended particulate matter (SPM) of various sizes, and metals, mostly bound to particles, are the main pollutants produced by incineration. Additionally, the burning of organic materials containing chlorine results in the formation of certain chlorinated dioxins and furans.

The majority of these air pollutants are caused by atmospheric, biological, and geophysical factors. They provide a sizable global impact to overall air pollution. This reality should not make us lose concern for anthropogenic ally induced air pollution. There is a constant state between the emission and elimination of biogenic contaminants in nature. Earth's life evolved in harmony with these outside factors. Similar to how the climate is changing, the steady state may be gradually altering, but these natural changes take thousands or even millions of years to manifest[1], [2].

However, the current substantial rise in anthropogenic sources' annual pollution emissions has only been existent for about 200 years, which is comparably a very short time.

The disruption of nature's steady state is therefore not shocking. Numerous plant and animal species are in danger of going extinct, the pH of the water and soil is impacted, crops and forests are harmed, etc. Additionally, the sources of anthropogenic pollution are concentrated in a few (mainly populous) regions. They therefore have a bigger influence on health and the environment than the majority of biogenic sources.

CO, or carbon monoxide

The majority of this gas's global emissions (60–90%) come from natural processes like volcanic activity and the breakdown of organic materials (2). The primary cause of the anthropogenic origin is incomplete combustion of fossil fuel, especially in internal combustion engines. Motor vehicles are the primary offenders as a result. Colourless, odourless, and extremely poisonous, carbon monoxide is a gas. Because of its capacity to replace oxygen linked to hemoglobin, it is poisonous. The Haldane equation describes the quantitative relationship between car oxyhemoglobin (Igbo), oxyhemoglobin (HgbO2), and the partial pressures of O2 and CO where PCO and PO2 are the ambient partial pressures of CO and O2, respectively, and K is a constant (245 for human blood at pH 7.4 and body temperature). Hemoglobin takes a long time to acclimatizeto the ambient carbon monoxide. process that takes a long time. The concentration of carbon monoxide, the length of exposure, and, to some extent, the minute volume of breathing all affect the degree of intoxication. Although prompt removal of a drunken person from a poisonous environment completely restores their physiological functions, it takes some time for carbon monoxide to separate from haemoglobin. It takes 320 minutes to remove 50% of the gas at one atmosphere of pressure.At less than 2% carboxyhemoglobin level, no adverse health impacts are observed in people. However, at larger doses, nonsmokers have reported effects on their central nervous systems1. Cardiovascular abnormalities have been seen at 5%. Equation 8.1 predicts that equilibration at 45 ppm ambient CO concentration will result in 5% carboxyhemoglobin content. As a result, those who have heart issues are more at risk from carbon monoxide exposure (3). Headache, nausea, disorientation, and eventually death are symptoms of more severe carbon monoxide overdose. 0.5–1% of nonsmokers have carboxyhemoglobin in their blood, whereas 5–10% of smokers may have it[3], [4].

Only an enclosed environment can produce a deadly CO poisoning. Dispersion lessens the impact of carbon monoxide in open areas. However, in areas of dense urban traffic, carbon monoxide levels inside moving vehicles can be roughly three times higher than those outside (10–40 ppm) (3). Tunnels and underground parking lots have had concentrations as high as 80 ppm. The negative effects of long-term exposure to low levels of carbon monoxide on health are unknown. However, considering that exposure to CO from tobacco smoke is at least one of the risk factors for coronary heart disease in smokers, one may hypothesise that ongoing, low-level exposure to CO could have a cumulative effect.Despite having no direct effects on the environment, carbon monoxide does have an indirect effect on the greenhouse gases and the stratospheric ozone [5], [6].

Oxygenated Sulphur (SO2)

Sulphur dioxide is a colorless gas with a potent stifling odour that is extremely irritating to the upper respiratory system and eyes. Sulphur dioxide emissions from artificial and natural sources are almost equal worldwide. The burning of sulfur-containing coal and the smelting of nonferrous ore are the principal sources of anthropogenic emissions, which predominate over land and in industrialised areas. Volcanoes and organic matter in decay are two sources of sulphur dioxide in nature. In addition, the atmosphere changes dimethyl sulphide, which comes from the oceans, into sulphur dioxide.

Sulphur dioxide causes physiological changes in test animals, including thickening of the mucous layer in the trachea and slowed mucociliary escalator function (3). Sulphur dioxide, a gas that dissolves in water, irritates the upper respiratory system but only barely2 enters the lungs. When present in high concentrations, the majority of it is often held in the upper

respiratory tract and expelled by coughing and sneezing. However, a little amount of systemic absorption happens via the entire respiratory system (3). Sulphur dioxide exposure narrows the bronchial tubes and increases airflow resistance. Therefore, it poses a special risk to those who have respiratory issues. Additionally, sulphur dioxide harms plants by bleaching their leaves.

DISCUSSION

On small particles (by-products of coal combustion, such as charcoal, ferric oxide, and metal salts), sulphur dioxide is easily adsorbed. The particles catalyse the oxidation of SO2 to SO3 in the presence of moisture (such as in clouds or fog droplets), which quickly reacts with water to create sulfuric acid. The concentration of gas in the breathed air is related to the fraction of SO2 that enters the alveolar space. 90% of it is eliminated in the upper respiratory system at high concentrations. The gas enters the lungs in 95% of cases at low concentrations (1 ppm or less). The solid particles that have been covered in sulfuric acid remain suspended in the air after the moisture evaporates. Over 80% of these particles have a diameter of less than 2 mm (4). They enter the alveolar spaces and the tracheobronchial area when inhaled. Sulfuric acid can also be produced from SO_2 in the gas phase, albeit slowly, through interactions with free radicals. Due to the need for sunshine for the production of free radicals from the air's moisture, these reactions are more pronounced in the summer than in the winter. According to animal research, sulfuric acid has an irritant effect on the respiratory system that is 4–20 times more potent than sulphur dioxide. Particulate sulfuric acid that is on the surface is easily dissolved in pulmonary fluid. When present in sufficient amounts, it harms the respiratory tissue will cover the role of atmospheric sulfuric acid in acid deposition [7], [8].

Oxides of Nitrogen (NOx)

Natural phenomena like lightning and microbial decomposition of organic materials produce nitric oxide (NO). Nitrous oxide (N_2O), which is the first byproduct of microbial digestion, is then transformed into NO. When nitrogen in the air and oxygen combine at a high temperature to burn, nitrogen oxides are produced that are caused by human activity. Nitric oxide easily oxidises to NO_2 in the environment, and the resultant combination is known as NOx. The fuel-to-air ratio and combustion temperature both affect the total quantity of NOx produced during combustion as well as the NO/NO_2 ratio.

Nitrogen dioxide is a very poisonous, irritable, and reddish coloured gas. It causes lungs to become inflamed when inhaled, and after a few days, this inflammation may turn into edoema. 100 ppm is harmful for a brief exposure, while 200 ppm is fatal. Nitrogen dioxide may increase susceptibility to bronchoconstrictive substances, such as sulphur dioxide, in normal persons at lower concentrations, such as 5 ppm, and in asthmatic subjects at concentrations as low as 0.1 ppm (189 mg/m3) (3). In contaminated urban air, concentrations of 0.1 ppm or more have been reported. Furthermore, findings from animal studies indicate that exposure to nitrogen dioxide raises susceptibility to respiratory illnesses caused by the influenza virus and bacterial pneumococci (3). In general, stationary sources have better control over NOx emission than moving vehicles do. Additionally, pollution from motor vehicles is produced at the road level, as opposed to industrial pollutants, which are often released through smokestacks and dispersed by the wind. This high-altitude dispersion may lessen the amount of NOx that urban dwellers are exposed to, but it most likely has little impact on ozone and smog formation[9], [10].

Biological Smog

A respiratory poison is ozone. Low water solubility allows it to enter bronchioles and alveoli deeply. Acute exposure to ozone destroys the respiratory tissue and results in edoema, which can be fatal. Ozone is mostly a workplace concern. Sensitivity to infections and Broncho constrictors is increased by sublethal exposure. Bronchitis and emphysema may develop as a result of prolonged exposure to ozone. Additionally, photochemical smog (which includes ozone, Emphysema is a condition marked by decompartmentalization of alveoli, which reduces the surface area accessible for gas exchange and results in breathing problems. PAN and other byproducts) irritate the skin, eyes, and mucous membranes.

The severity of photochemical smog is greatly influenced by topographic and climatic factors. Because they are characterised by bright sunlight and steady descending air that traps pollution near the ground, persistent high-pressure systems have a tendency to exacerbate smog development. The dispersing power of wind is lessened in areas bordered by mountains. The retention of photochemical smog close to the ground is also favoured by atmospheric temperature inversion. When warm air in the upper atmosphere covers colder air close to the ground, an inversion occurs, preventing contaminated air from rising above the inversion boundary.

PAN and ozone are both harmful to plants. While PAN mostly harms herbaceous4 crops, ozone damages all plant tissues and prevents photosynthesis. Additionally, it makes plants more vulnerable to diseases and drought. O_3, NO_2, and SO_2 work together to harm plants in a synergistic manner. The main known risks to the environment and human health associated with NOx emission are photochemical oxidation and smog production. The direct impact of NOx on health, however, is a developing worry. It appears that nitrogen oxides are to blame for a significant increase in respiratory illnesses such bronchitis, pneumonia, and viral infections in highly polluted urban regions. Concern has also been raised concerning their participation in acid deposition; almost one-third of nitric acid has been deposited.

Organic Volatile Compounds

Both artificial and natural sources produce VOCs. The sources are biological decay, forest fires, vegetation, and natural gas. The natural emission of VOCs is thought to be between 30 and 60 million metric tonnes per year, according to an editorial that appeared in Science (7).

The incomplete combustion of fossil fuels and the evaporation of liquid fuels and solvents during storage, refining, and handling are the two main causes of anthropogenic emissions. The type of VOC released in flue gases or from the exhaust of cars varies depending on the fuel used, the type of combustion (external or internal), and whether pollution-abating equipment is present or not. There are lots of low-molecular-weight aliphatic, olefinic, and aromatic chemicals, some of which are created during burning. Olefins and dienes have a tendency to polymerize via free-radical production at 500–800 °C to create polycyclic aromatic hydrocarbons (PAHs) (8). Between the gas phase and solid particles (combustion byproducts as soot and fly ash), airborne PAHs are dispersed. At least 26 airborne PAHs, some of which may be mutagenic and carcinogenic, have been identified.

measured and quantified (8). Benzo[a]-pyrene was the subject of the most thorough study r 5). Benzo[a]pyrene, which has frequently been employed as an indication of the total concentration of PAHs in the atmosphere, has an average concentration of around 10 times greater than the total concentration of PAHs in the air. Regarding this procedure's accuracy, certain concerns have been voiced (8), shows the contributions of various fuels and

combustion processes to the atmospheric emission of benzo[a]pyrene. According to this facts, domestic wood combustion produces the most benzo[a]pyrene per BTU. In fact, as depicted in, wood-burning in fireplaces and stoves was responsible for 85.5% of the 655 metric tonnes of PAHs that were released annually in the US during the 1980s. Agricultural burning was the second-largest source, and forest fires were the third (9).

Particle Size

Although PAHs in the vapour phase may not pose a significant threat to health, those that are attached to respirable particles do. Because only small particles enter the pulmonary system, the health effects of atmospheric carcinogenic PAHs depend on the size of the particles with which they are associated. It is possible for particles with a diameter of 1 mm or less to enter the lungs. The pulmonary P-450 system activates the PAHs there, turning them into carcinogens, or they reach the bloodstream. The alveoli are not reached by the bigger particles (2–5 mm). The mucociliary escalator launches these particles into the oral cavity, where they may be ingested. In this instance, the gastrointestinal tract is the route by which the PAHs reach the bloodstream. Depending on the exposure method (whether through breathing or ingestion with food), the tissue absorption of PAHs and their carcinogenic potential may vary.

Exposure from the Food Chain and at Work

However, some professions carry a higher danger than others, such as those involving coal tar pitch and coke ovens. Their exposure may be 30,000 times or greater than that of the normal population. Additionally, urban-generated particles that are PAH-loaded settle on land or in water, where they are likely to become contaminants and enter the food chain. The sediment in the Charles River in Boston was studied, and the results showed a startling match between the composition of the concentration of PAHs in the air and those in river sediment. It seems that the primary cause of PAH water contamination is the burning of fossil fuels.

Ethylene with Benzene

The hydrocarbons benzene and ethylene are among those of importance. Myelocytic and acute nonlymphocyticleukaemia have been linked to benzene, a human bone marrow toxin and carcinogen. One of the main byproducts of vehicle exhaust is ethylene, though it can also be produced by other combustion processes. It makes a considerable contribution to photochemical oxidants. It regulates plant growth, causes epinasty (the movement of a plant, such as the folding and unfolding of a flower petal), leaf abscission (the falling of leaves), and fruit ripening. Ethylene is a normal component of plants. Therefore, excessive exogenous ethylene is a plant poison. We have spoken about how hydrocarbons contribute to the production of photochemical haze.

Airborne Substances

Suspended specific matter (SPM) is a term used to describe particles. They can be separated into liquid droplets and suspended particles. Their effects on systemic and respiratory toxicity vary. Dust, sea spray, forest fires, and volcanoes are examples of natural sources of airborne particles. Solids with a diameter of 0.01 to 100 mm and minuscule drops of sulfuric, sulphurous, and nitric acids are examples of anthropogenic particles. They are by-products of either industrial processes (such as milling and grinding) or combustion (such as fly ash, soot, and various metals). Continuous contact between different types of particles and between particles and the elements of the gas phase occurs in the atmosphere. The chemical makeup

and particle size are both impacted by this interaction. Large particles (those with a diameter of more than 30 mm) may be an annoyance, but they do not pose a severe threat to health, and they disperse quite fast. The atmospheric residence period of particles with a diameter of 1 to 10 mm is 6 hours to 4 days, and it is significantly longer for particles with a diameter of less than 1 mm. Particles with a diameter of less than 5 mm reach the tracheobronchial and pulmonary regions, irritating the respiratory system and exacerbating pre-existing respiratory conditions. We've already talked about their function as carriers of PAHs, sulphate, and sulfite ions into the lungs. Numerous cities' epidemiological investigations found a link between daily variations in SPM levels in the ambient air and daily mortality counts. These observations, however, did not identify whether SPM in and of themselves had harmful effects on health or whether they merely acted as carriers of other dangerous pollutants.

Metal contaminants

Due to their toxicity, lead, mercury, and beryllium are of particular importance among the metal contaminants. Leaded petrol was gradually phased out, which significantly reduced the amount of lead in the air. In the United States, lead emissions decreased from 144,000 tonnes in 1975 to 17,900 tonnes in 1985 (14); 69% of these emissions came from using leaded petrol. Municipal waste incinerators started to play a bigger role in lead contamination at the same time. Most of the mercury and beryllium in the world comes from burning coal. Lead and mercury are both fundamentally water and land contaminants, regardless of where they came from. Beryllium emissions into the atmosphere are expected to be 1134 metric tonnes per year (15). Pneumonitis, a condition marked by lung inflammation, and berylliosis, a persistent lung condition, are two of beryllium's main harmful consequences. According to epidemiological research, it may possibly be carcinogenic. It is uncertain whether the concentration of beryllium in urban air is high enough to pose a risk to the general public's health. In any event, beryllium poses a risk to those who work with it throughout production, processing, and use. **Metal-free**

Pollutants

Both asbestos and fluorides are nonmetal contaminants. A byproduct of burning coal is fluorine. It is emitted in rather significant amounts, exclusively in the gas phase. Because it is a reactive element, fluorine easily joins with other atoms and molecules to generate fluorides, which are irritating to the respiratory system. They are also phytotoxins, and plants are the primary target of their environmental effects. Fluorides harm leaves and eventually lead to defoliation. Industrial use and the destruction of ancient structures containing asbestos are the main sources of airborne asbestos. The majority of those who are affected by its health consequences are asbestos workers and employees who unintentionally come into contact with asbestos while performing their jobs. As a result, asbestos exposure is regarded as a work-related risk. Chapter 8 discusses how this exposure will affect your health.

Trends and Current Air Quality Status

The National Ambient Air Quality Standards (NAAQS) and World Health Organisation (WHO) recommendations for the main urban air contaminants are included in Table 9.2. The trends in sulphur dioxide levels in the air of a few U.S. cities and other cities worldwide from 1976–1978 to 1990–1995 are depicted in data. The results show that between 1976 and 1995, industrialised countries made good progress towards reducing sulphur dioxide emissions. It is crucial to remember that the figures shown which represent the average values for the suburban, commercial, industrial, and residential regions. A city's self-evaluation may have

revealed that some sections have exceeded expectations. For instance, the mean daily SO2 concentrations in the residential area of New York's city centre were, for three monitoring periods (72 mg/m3 in 1976–78, 74 mg/m3 in 1979–81, and 65 mg/m3 in 1982–85), above the WHO limits (2). Milan stood out among industrialised cities as having extraordinarily high SO2 pollution levels between 1976 and 1978, much above WHO limits. However, by 1990 to 1995, the levels of sulphur dioxide had significantly dropped, falling well below WHO recommendations. Cities in underdeveloped countries have not made much progress in reducing sulphur dioxide pollution. Some of them had significant increases in pollution throughout the monitoring period, including Teheran, Calcutta, and Beijing. This was most likely the outcome of an industrialization endeavour with insufficient investment in contemporary technologies[11], [12].

CONCLUSION

In order to find an answer to this question, Dr. Morton Lipp**m**an and his team most recently conducted research in the Detroit, Michigan, area. The findings showed that the addition of other pollutants (O_3, NO_x, SO_2, and CO) had no effect on the toxicity of SPM, at least in a two component model. Additionally, the size of the particles in the PM10 and PM2.5 ranges (i.e., those smaller than 10 mm and 2.5 mm, respectively), did not have an impact on the toxicity. A study on animals found that when exposed to a high concentration of SPM, dogs with induced coronary blockage displayed one of the key ECG indicators of myocardial ischemia in humans. A high concentration of SPM also caused cardiac abnormalities in healthy dogs, including alterations in heart rate variability, average heart rate, and certain ECG anomalies. We should wait for more research before determining whether or not this mechanism of harm may be generalized to people. SPM has an effect on the environment as well. Due to their ability to scatter light, tiny sulphate particles are what cause haze to appear. This effect could last for up to a week and is even stronger by high humidity levels. Haze development is further aided by soot particles' capacity to absorb light. SPM buildup on leaves prevents the absorption of carbon dioxide, obstructs sunlight required for photosynthesis, and covers stomata (tiny orifices on the surface of the leaf for water evaporation).

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CHAPTER 10

ATMOSPHERICPOLLUTION

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ABSTRACT:
In terms of volume, the earth's atmosphere is made up of 78% N2, 21% O2, 0.033% CO2, traces of the noble gases NOx and CH3, and varying amounts of water vapor. At sea level, the concentration of water vapor can range from more than 20 g per kg in the tropics to less than 0.5 g per kg in polar-regions.The term "standard lapse rate" refers to the rate at which temperature decreases with altitude (6.49 8C per km). The real lapse rate fluctuates depending on the weather, hence this rate is only a theoretical average value. The air density changes at the same rate as pressure because it is inversely proportional to temperature and inversely proportional to pressure. Of all environmental problems, air pollution is typically the one that receives the least attention. The reasons are that it doesn't directly or immediately effect us. However, this may be the most important issue endangering the sustainability of our society after overcrowding.Consider the size of the earth's atmosphere in relation to the size of the entire planet to understand how delicate it is. Consider a globe that is 1 m in diameter (the equatorial diameter of the planet is 6378 km). The stratosphere's outer margins would rise to a height of 7.8 to 8.5 mm, the mesosphere's outer borders to a height of 12.5 to 14.0 mm, and the troposphere would be between 1.3 and 3.0 mm thick

KEYWORDS:
Atmosphere, Carbon, Chlorofluorocarbons, Ozone, Temperature

INTRODUCTION

Calculations of atmospheric changes brought on by the weather are based on a theoretical collection of data known as the standard atmosphere. The figures are estimated for conditions at sea level and represent 760 mm of mercury (92.29 in., 1013.25 mbar), 1.22 kg/m3 of air density, and 15 8°C (59°F). The lowest layer of the atmosphere, the troposphere, has little effect on the composition of the air; but, as altitude increases, so do pressure and temperature[1], [2].

Ozone in the Stratosphere: Its Creation and Maintenance

The oxygen molecules in the middle stratosphere are divided into single atoms by the solar radiation that enters the higher, highly rarefied atmosphere of the earth. At an altitude of 30 to 40 km, the atomic oxygen concentration is maximum. Ozone is created when the molecular oxygen reacts with the highly reactive atomic oxygen. So, within seasonal and latitudinal changes, the stratospheric ozone concentration is essentially constant in an unpolluted environment. Although there are only a few parts per million (ppm) of ozone in the stratosphere, this is enough to filter some of the sun's ultraviolet radiation, lowering the amount of radiation that reaches the earth's surface.1 This is why the stratospheric ozone is often referred to as a protective ozone layer. Because the cause-and-effect relationship is reversed, this moniker may be deceptive. The term "protective layer" suggests that the ozone is present to safeguard both us and other species. In actuality, the characteristics of life on

earth result from how it evolved in response to environmental constraints. Only aquatic life below the ocean's surface, shielded from radiation that could be fatal by a layer of water, would probably be able to survive in the absence of the ozone layer. Therefore, it is reasonable to assume that any alteration to these circumstances will have an impact on living thing [3], [4].

Chlorofluorocarbons

The idea that chlorine from a group of substances known as chlorofluorocarbons (CFCs) could contribute to the stratospheric ozone hole was first put forth by Molina and Rowland in 1974. When CFCs were first developed in the 1930s, they were used in a wide range of industrial products, including aerosol propellants, plastic foam blowing agents, refrigeration and air conditioning fluids, cleaning solutions for electronic devices, and fire extinguisher fluids. They have the advantage of being nontoxic, nonflammable, and chemically stable. The manufacturing and consumption of CFCs increased continuously from the time they were first introduced to commerce until the 1970s. Their production then decreased as a result of the bans on their usage as aerosol propellants in some industrialized nations due to concerns over their propensity to damage the ozone layer. The demand for foam insulation and cleaning agents in the electronic equipment and semiconductor industries, however, rose after 1982, which led to a rise in CFC output.

The environmental impact of CFCs' chemical stability in the troposphere is negative. $CFCl_3$ (CFC-11) and $CF2Cl_2$ (CFC-12), the two most harmful CFCs, have atmospheric lives of 75 and 111 years, respectively. The polar vortex disappears as the day grows longer, bringing fresh air to the area. This air contains nitrogen oxides, which when combined to generate $ClNO_3$render the active chlorine inactive. When arctic winter arrives, the process will be repeated once more. PSCs will catalyze chlorine nitrate's breakdown and release active chlorine. Ozone depletion was first noticed over Antarctica in the austral spring, when the continent awakens from the winter's darkness, and it looks to be progressively spreading to other latitudes. Since 1979, ozone levels at all latitudes south of 60 8S have decreased by 5% or more.

Impacts on Biology and Economy

Both the intensity and the wavelength composition of UV-B radiation that reaches the planet are impacted by stratospheric ozone loss; more energy is shifted towards the shorter, more harmful wavelengths. A theoretical calculation of the possibility for damaging the species' DNA is used to estimate the risks that UV-B radiation poses to human health and the survival of other species. In accordance with these standards, the International Panel on Substances that Deplete the Ozone Layer calculated that the annual DNA damage dose increased since 1979 by 5% per decade at latitudes 308 N and 308 S, 10% per decade in the arctic, 15% per decade at latitude 558 S, and 40% per decade at latitude 858 S. The equatorial region did not experience any appreciable growth. Because clouds, suspended particles, and tropospheric ozone reduce the amount of UV-B radiation that reaches the earth's surface, people living in heavily industrialized areas are somewhat insulated from its detrimental effects[5], [6].

It is challenging to predict how ozone depletion may affect terrestrial plants in the future since a variety of other factors, such as climate changes brought on by the greenhouse effect, may mitigate or exacerbate the impacts of increasing UV radiation. The way different plant species respond to UV light varies greatly. Numerous lab-tested plants showed signs of decreased growth, flowering, and photosynthetic activity in response to UV light. There is

some ambiguity on the potential severity of the harm to aquatic plants. It is known that UV-B radiation significantly harms aquatic phytoplankton by destroying their DNA, motility mechanism, and photosynthetic system. Fish, crustacean, and marine mammal species may go extinct as a result of the decline in marine plant development. Such modifications might affect the entire marine ecology and further diminish the availability of food for humans. Furthermore, since marine phytoplankton fix more carbon dioxide than any other source on the planet, interfering with this process could increase the greenhouse effect. The EPA predicts that a 10% reduction in stratospheric ozone will result in $2 billion in material damage, in addition to the biological effects of increased UV radiation on the durability of materials like wood, paints, and plastics.

DISCUSSION

The United Nations Environment Program (UNEP) organized the First International Conference on Substances that Deplete the Ozone Layer, which took place in Montreal in October 1987. A conference agreement asked CFC manufacturers to maintain current production levels and cut it in half by 1998. 36 countries had ratified this pact by the middle of 1989. The Montreal Convention's approved measures were quickly deemed to be woefully insufficient. There are already enough CFCs in the stratosphere to continue destroying ozone for another 100 years, even if CFC manufacture were to be completely stopped. Even though the Montreal convention's outcomes were modest, their importance shouldn't be underestimated. It heralds the start of worldwide cooperation on issues pertaining to environmental conservation[7], [8].

Another meeting with a more regional focus was held in Colorado in May 1988. The National Oceanic and Atmospheric Administration (NOAA), the National Science Foundation (NSF), the Chemical Manufacturers Association, the World Meteorological Association, and UNEP all collaborated to jointly fund this conference. The conference's goal was to review the findings of the 1987 Airborne Antarctic Ozone Expedition, a venture between NASA and Harvard University. This trip discovered that "the ozone hole was larger than ever in 1987." Nearly all of the ozone in some areas of the stratosphere perished, and more than half of the ozone column was destroyed. Additionally, the hole lingered longer than it ever had, finally closing at the end of November.

NASA planned an aerial excursion to the arctic region since there were some signs of disturbed atmospheric chemistry there. In response to shifting lighting conditions, certain phytoplankton can change where they are in the water column. 1989, in January and February. Despite the fact that the concentration of over the Arctic was almost as high as that over Antarctica, subsequent satellite observations showed that there was no significant ozone depletion. The polar vortex in the arctic region swiftly collapsed after emerging from the polar night, which was the explanation for this phenomena.

Exiting Fluorocarbons Gradually

Diplomats, environmentalists, and CFC producers from the 36 countries that had signed the Montreal agreement met in Helsinki, Finland, in May 1989 to prepare for the Second International Conference on Substances that Deplete the Ozone Layer, which was going to be held in London in 1990. They created the following plan for a potential complete phase-out of CFCs and other ozone-depleting substances:

1. To eliminate CFC manufacturing and use by the year 2000

2. To eliminate halons, carbon tetrachloride, and methyl chloroform from manufacturing and use as soon as is practical, must pledge their dedication to the swift creation of environmentally friendly alternatives, to provide Third World nations with all necessary knowledge, tools, and training.

The terms of this agreement permitted the production and use of ozone-depleting compounds after the year 2000 in some circumstances, provided that output did not exceed 15% of production in 1986. During the 1990 London Convention, this proposal was approved and signed by the participating countries as an addendum to the Montreal Protocol. The largest CFC producer in the world, DuPont, announcing that it will phase down CFC production by the year 2000 was a significant advance in this sector. CFC-141b ($C_2H_3Cl_2F$), HCFC-123 ($C_2HCl_2F_3$), HCFC-22 ($CHClF_2$), and HFC-134a are examples of CFC replacements. In order to substitute fully halogenated CFCs, (CH_2FCH) were created.Before they reach the stratospheric ozone layer, hydrogen-carrying fluorocarbons (HCFCs) degrade significantly their lifespan in the atmosphere and capacity to deplete the ozone. The discovery of HCFCs is encouraging, but the EPA warns that a careful evaluation of their toxicity and the toxicity of their breakdown products is required before their true utility can be determined. HCFCs carry some chlorine into the stratosphere despite being less harmful to stratospheric ozone than CFCs. Because of this, the EPA claims that they ought to be regarded as transitional drugs, to be used until better alternatives are created. Concern over the use of HCFCs and HFCs is another issue.

Focuses on their characteristics as potent GHGs

The development of foam-blowing processes without the use of CFCs, HCFCs, or HFCs is another trend. Dimethyl esters will be utilized by DuPont to replace CFCs in the propellants (16) for aerosols that are still in use in Europe. A foam-blowing procedure that completely forgoes the use of CFCs was introduced by the BASF Corporation. Over populous parts of North America, northern Europe, and northern Asia, an alarming discovery of abnormally severe ozone depletion in the northern hemisphere was reported in 1992. The atmospheric scientists hypothesized that the conversion of the inactive chlorine species to active chlorine may have been catalyzed by suspended sulphate particles because there are no PSCs at these latitudes. Although some sulphate particles naturally occur in the stratosphere, Mount Pinatubo's eruption in the Philippines in June 1991 was blamed for their extremely high concentration in 1992. 15 to 30 tons of sulphur dioxide were released into the atmosphere during this eruption. Sulphur dioxide was quickly transformed to sulfuric acid, which then combined with metal salt particles in the stratosphere to create sulphate aerosol [9], [10].

The United States unilaterally chose to push back the deadline for the total eradication of ozone-depleting chemicals to the end of 1995 in response to these worrying developments. The signatories of the Montreal Convention subsequently convened in Copenhagen. They adopted 1996 as the timetable for the global phaseout of ozone-depleting chemicals, following the lead of the United States. They also imposed limitations on the use of HCFCs, mandating a stop to their manufacturing by 1996 and their total elimination by 2030. At the moment, emissions of chlorine-containing substances like CFCs, carbon tetra-chloride, and others are the principal cause of stratospheric ozone loss. However, a widespread use of supersonic travel could prove to be even more harmful to the ozone layer than are CFCs. Nitrogen oxide (NO_x) generation is related to fuel combustion. Nitric oxide (NO) has a strong potential to destroy ozone, especially when it is released in the middle of the ozone layer where supersonic aircraft fly (19). Nitrogen dioxide (NO2) protects ozone by binding the

active chlorine molecules. It is already possible to see the results of the Montreal protocol's limitations on the use of substances that deplete the ozone layer. The pace of growth in the main CFC concentration in the atmosphere is slowing down. One must keep in mind, though, that even complete elimination of all ozone-depleting compounds would leave the atmosphere with enough chlorine radicals for ozone breakdown to continue for another century, albeit at a slowly slowing rate.

Climate Change Models and CO_2 Emission

A fixed supply of fundamental elements and chemicals, including carbon, nitrogen, oxygen, and water, is necessary for life to exist on earth. They must be continually recycled because their supply is fixed. Biogeochemical cycle is the term used to describe this process. The biogeochemical cycling equilibrium is currently being severely disturbed by human activity. The carbon cycle involves the exchange of carbon between the atmosphere, the biosphere (i.e., living plants and soil), and the seas, primarily in the form of carbon dioxide. The latter are where the most dissolved carbon dioxide is found. About 2000 and 700 billion tons of carbon are held in the biosphere and atmosphere, respectively (20). About 14 times as much is contained in the oceans as in the biosphere and atmosphere combined. Additionally, a significant portion of carbon is stored as fossil fuels (oil, coal, and gas) and a smaller portion as sediment in the oceans, all of which are nonexchangeable forms of carbon. The primary source of life support on Earth is atmospheric carbon dioxide, which is absorbed by green plants and then transformed into essential nutrients. Additionally, O2 is released throughout the absorption process to maintain the oxygen stores in the environment.

Earth's temperature

The earth's temperature is kept stable at a level that supports life as we know it by carbon dioxide and water vapor. The planet absorbs around half of the total solar energy that it receives. The atmosphere either reflects or absorbs the remaining energy. 10% of the thermal energy is used to directly heat the atmosphere, and the remaining 50% is used to evaporate water from the oceans, rivers, lakes, and land. Long-wave radiation is released as the remaining 40%. The atmosphere bounces 88% of carbon dioxide, water vapor, and minor amounts of other gases. The natural greenhouse effect is the process through which heat from the atmosphere is directed towards the ground, warming the planet's surface.3 As a result, there is a relationship between the amount of carbon dioxide in the atmosphere and the earth's temperature. Radiative forcing, or the amount of heat (in watts) per square meter of the earth's surface, is a way to measure the size of the greenhouse effect.

The history of this association goes back 160,000 years. The hydrogen-deuterium ratio in ice of the appropriate age was calculated after the carbon dioxide content of air bubbles trapped in the glacial ice core from Antarctica was examined. Rain and snow contain more deuterium as the temperature rises. A separate layer of ice is formed from the annual snowfall in regions where ice is permanent. Thus, by counting the ice layers, the age of the ice samples under analysis may be ascertained. According to a study done by a French-Soviet team at Vostro, Antarctica, the plot of atmospheric carbon dioxide concentration and the Antarctic air temperature. These findings suggest that the maximum temperature, 2.5 8C above the current temperature, occurred around 135,000 years ago when atmospheric CO2 content peaked at 300 ppm. Nearly 108C below what it is today, the lowest temperature of the time period happened 20,000 years ago at a CO2 concentration of 185-195 ppm and again about 150,000 years ago.

The findings of 20 years of meteorological, hydrologic, and biological records in the Experimental Lakes Area of northwest Ontario were published in 1990 by a study team from the Freshwater Institute in Manitoba (23). This data shows that the area's air and lake temperatures have risen by 2 8C, and the usual amount of time the lakes are covered in ice has dropped by 3 weeks. Similar findings include that the ice cover on Mount Kenya shrank by 40% from 1963 and that alpine glaciers are melting ten times more quickly than they did at the end of the previous ice age. In contrast to Antarctic ice shelves, which lost over 3000 km2 (1/8 of their total size) in just one year, the Ok glacier in western Iceland declined from 6 square miles in 1910 to 1 square mile in 1993, according to a study. Actual measurements of the radiative forcing showed a rise from 1 to 2.5 W/m2 between the late nineteenth century and the present, which is consistent with our findings. This modification results in a 1% improvement in solar output. Despite variations in solar output being noted during the previous 100 years, they did not differ by more than 0.5%.

Natural nitrification by bacteria results in the production of nitrous oxide. The amount of N2O in the atmosphere is rising as nitrogen-containing fertilizers are used more frequently. Future projections suggest that by 2030, methane may contribute 20–40% and nitrous oxide may contribute 10–20%, respectively, to the greenhouse impact (28). Deforestation results in higher GHG emissions and lower atmospheric carbon dioxide removal because trees absorb atmospheric carbon dioxide. Despite not being a GHG in and of itself, carbon monoxide eliminates hydroxyl radicals that are responsible for GHG oxidation. As a result, the release of carbon monoxide contributes to the rise in GHG concentration.

Climatic Change Models

There is no question that GHGs and atmospheric temperature are related. However, it is unclear how the rise in GHGs will impact the climate. The intermediate scenario assumes a moderate degree of climate sensitivity and matches the current trend in GHG emission. (A degree of the earth's temperature change with a doubling of the CO2 concentration is known as climate sensitivity (t2x). The range of t2x estimates is 1.5 to 4.5 8C.) This scenario predicts that by 2100, the average earth temperature will have increased by 3.3 8C. High climate sensitivity and rapid GHG emissions are reflected in the high scenario. The low scenario predicts dramatic reductions in GHG emissions and little sensitivity to climate change. The models also anticipate that for every degree of global warming, the mean rate of evaporation and precipitation will rise by 2% to 3%. Regional climatic changes can be challenging to anticipate, and different models may produce different outcomes. The primary issue is that the greenhouse effect is susceptible to feedback mechanisms, of which we are mostly ignorant. The greenhouse effect may be increased by the feedback mechanisms (a positive feedback) or decreased by them (a negative feedback).

Result on the Vegetation

A shift in agricultural areas may result from regional warming and altered precipitation patterns, making some now fruitful places unfit and opening up other areas for agriculture. Similar to how the changed conditions will necessitate rapid tree species adaption to the new environment. Some plant species might become extinct if they don't adapt in the little amount of time they have. In the central latitudes, an increase in average (winter-summer) temperature of 3.3–4.0 °C would necessitate a 200–375 mile northward migration of forests. Only 12.5 miles can be covered by some trees, like beech, over a century. The fastest migrating species, the spruce, can only cover 125 miles in a century [11], [12].

CONCLUSION

Throughout its history, the planet has seen periodic climatic shifts, but they typically happened at a rate of a few degrees per tens of thousands of years. The greenhouse effect, on the other hand, is anticipated to take place over one or two centuries. Economic catastrophe may result from the relocation of agricultural regions and the extinction of tree species. It might cause some places to become desert, which would lead to a shortage of food and increased prices. Result for Oceans is an additional worry about global warming is that more frequent and more deadly hurricanes and typhoons would result from warmer water temperatures in the tropics. Three scenarios for how ocean levels might alter in response to the anticipated rise in temperature. The expected melting of the polar ice cap and the thermal expansion of water are reflected in the rise in ocean levels predicted for the middle and high scenarios. The low scenario's expectation of lower ocean levels is based on a forecast for higher snowfall, which would result in more Antarctic ice mass. Due to the higher ice mass's chilling impact, there should be a loss of water from the oceans as a result of this increased ice mass. This cooling would then encourage the creation of more ice

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CHAPTER 11

WATER AND LAND POLLUTION

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ABSTRACT:
Freshwater, which is essential for maintaining plant and animal life, makes up only 3% of this. The hydrological cycle ensures a steady supply of fresh water. This cycle includes precipitation, infiltration into the soil, transpiration by plants, evaporation from oceans and inland waters, and runoff of surface water into lakes and rivers. The water that has been absorbed is used for plant development and to replenish groundwater supplies. Although there is enough freshwater available on a global scale to support life, it is not distributed equally. There are some places where the supply is constrained by the climate or unable to keep up with the needs of a dense population. While freshwater is plentiful in some locations, the water is unfit for human consumption due to industrial chemical contamination. In addition, aquatic life in chemically tainted water becomes unfit for human consumption, including fish. Thus, water pollution deprives other animals and humanity of two need for survival: food and water.

In an urban setting, impervious areas (such streets, parking lots, and retail malls) replace previous ones. These changes result in a significant decrease in groundwater replenishment and a significant rise in runoff. As a result, urbanization not only increases water pollution but also the likelihood of flooding.

KEYWORDS:
Lead, Organic, Pesticides,Soil,Water.

INTRODUCTION

An essential component for maintaining life is nitrogen. However, it must be transformed into an assimilative form, such as an oxide or ammonia, in order to be integrated into living matter. The majority of atmospheric nitrogen was transformed into assimilative form by soil microbes and lightning up to the turn of the twentieth century. The denitrifying bacteria broke down nitrogen molecules that weren't used by living things into elemental nitrogen, which was subsequently released back into the atmosphere, preventing them from accumulating. The nitrogen cycle was finished in this manner.

The production of nitrogen oxides significantly increased as humankind's reliance on fossil fuels and fertilizers containing nitrogen increased. As a result of the denitrifying micro-organisms' inability to handle the overload, the inorganic nitrogen compounds started to build up in the soil. The groundwater becomes tainted by the nitrates and nitrites that are dumped on the land and seep through the soil. Additionally, they are flushed into rivers, lakes, and estuaries with agricultural runoff, which encourages an excessive development of algae and other aquatic plants. The oxygen dissolved in the water is used by microorganisms to grow and by bacteria to breakdown decaying plants, a process known as eutrophication. Since aquatic organisms need 5–6 ppm of dissolved oxygen to survive, excessive growth results in oxygen depletion, which suffocates fish and kills them[1], [2].

Pollutants in Water are transported

There are three ways that contaminants might enter water: through point sources with clearly defined sources, such the discharge from a factory or a city sewer pipe, through nonpoint sources, which are those that don't have a clear point of origin, including runoff from fields or streets, through the air, with the wind or air currents. Even while all forms of pollution are a major problem, point sources can, in theory, be managed. Nonpoint sources are challenging to manage, whereas airborne transmission cannot be managed at all and can only be avoided by ceasing to use harmful compounds. Waters that are moderately or severely contaminated so that their intended usage is hampered are considered impacted.

Pollutants in Cities

Municipal sewage, runoff from city streets and landfills, and industrial effluents are the main sources of urban pollution.

Local Wastewater

Municipal sewage is primarily composed of human and animal waste, making it rich in organic substances that contain nitrogen. Additionally, it has roughness, sus-detergents, phosphates, metals, pended soil, and other chemicals. Eutrophication is caused by the overgrowth of aquatic bacteria, algae, and other plants that is sparked by raw sewage entering streams and lakes.

Organic Matter that is Metabolisable

The biological oxygen demand (BOD) test can be used to determine the level of pollution caused by metabolizable organic materials. This calculates how much oxygen aquatic bacteria require over the course of five days to break down organic materials. So-called BOD pollutants are organic pollutants that can be metabolized. A well operating wastewater treatment facility may rather simply remove BOD pollutants, grit, soil, detergents1, and metals. However, many plants lack an advanced treatment stage, which is necessary for the removal of phosphates and nitrates. Such plants could be a significant source of nutrients contaminating the water. Since the Clean Water Act was passed in 1972, the percentage of the between 1970 and 1985, the percentage of the US population served by wastewater treatment facilities increased from 40% to 72% (3). Rural and suburban populations that use septic tanks for waste disposal make up the remaining 28% of the population that is not connected to sewage-treatment facilities. Although they do not pose a significant threat to surface water, septic tanks frequently cause groundwater contamination[3], [4].

Organic synthetic chemicals

Some synthetic organic compounds' removal from wastewater could be problematic. Municipal wastewater contains synthetic chemicals that come from both industrial and domestic use. In an industrialised culture, common household products like cleaning solutions, medicines, cosmetics, and paints consume significant amounts of organic compounds. These pollutants could wind up in small amounts in the sewer system. Hospitals, colleges, dry cleaners, garages, and other small businesses are prohibited from disposing of their chemical waste in the sewer system. It is therefore the duty of municipal authorities, who are in charge of wastewater treatment, to keep an eye out for unlawful disposal. Obviously, illegal dumping may occur.

When industrial plants enter into a contract with the city to dispose of their liquid waste through the municipal sewage system, a problem may arise. Although industrial companies must prepurify their effluent before releasing it into municipal sewers, the Clean Water Act (CWA) of 1972 still leaves room for the possibility of contamination with harmful substances that are not well understood. Such chemicals may be difficult to remove from effluent and may also be expensive. Additionally, the majority of municipal sewage-purification facilities are not prepared for this problem. Sewage containing toxic compounds can endanger aquatic life and prevent the biological decomposition of pollutants. Additionally, they increase the poisonous nature of sewage sludge, which must be dumped in landfills[5], [6].

DISCUSSION

Another issue is storm water runoff from towns and cities. As best from car brakes, rubber from tyres, hydrocarbons from motor vehicle exhaust condensates, oil, grease, soil and inorganic nutrients from construction sites, metals, street litter, animal waste, food waste, residue from sulfuric and nitric acid atmospheric deposition, and a variety of other chemicals are all present in this runoff. Some communities have a sanitary and storm sewer system integrated. In these circumstances, the storm sewage is purified. But a dramatic downturn in pour could go above the wastewater treatment facility's capability. The receiving waters may then receive rough sewage. Storm runoff is a nonpoint source of pollution when there isn't a combined system in place. It is therefore challenging to regulate. After a significant downpour, runoff from city streets, building sites, and landfill leachates may introduce a sizable amount of contaminants into streams and lakes. Urban nonpoint pollution has a significant negative impact on the quality of freshwater, according to research. In densely populated places, its effects might even outweigh those of rural pollution.

Lead Contamination

Although it mostly affects cities, lead pollution also regularly affects agricultural areas, lakes, and rivers. Lead has a wide range of harmful effects, such as the suppression of red blood cell production, renal damage, and nervous system damage.

Sources

Leaded petrol, paint made with lead and garbage disposal are the main causes of lead pollution. The United States has essentially stopped using lead petrol, with the exception of a few rural vehicles, therefore the amount of airborne lead is negligible. But decades of burning petrol with lead have resulted in significant amounts of lead building up in the soil. Estimates from the Environmental Protection Agency (EPA) indicate that the soil beside intensively trafficked roadways may have 10,000 ppm or more lead. Agricultural land is contaminated by farm vehicles using leaded fuel, which is still permitted by law. Surface and groundwater become contaminated as a result of runoff and seepage from lead-contaminated soil. For many years, lead-based paint was primarily thought to be a hazard in old, run-down tenements where young children might accidentally eat crumbling wall paint. The hypothesis that the main exposure pathway is inhalation and inadvertent ingestion of home dust resulting from lead-based paint was nevertheless widely accepted until quite recently, despite the fact that this idea was altered by subsequent studies [7], [8].

As a result, the majority of preventative strategies concentrated on getting rid of lead-based paint from older homes. In more recent years, research on the amount of lead in urban and suburban soil was carried out in a number of major cities, including Baltimore, Maryland; Minneapolis-Saint Paul, Minnesota; and New Orleans, Louisiana, as well as numerous

smaller towns in Louisiana and Minnesota. The findings suggested a relationship between city location and soil contamination. Regardless of the age of the structures, it was discovered that soil contamination was highest in the city centre and decreased exponentially towards the periphery (7). Additionally, pollution levels were significantly greater in the big cities than they little ones. This pattern of contamination suggests that industrial activities, waste incineration, and decades of burning lead petrol are the most significant sources of lead in the soil (7). The idea that lead-based paint is not the primary cause of lead intoxication is further supported by the fact that the lead-loading in the soil between streets and buildings is on the order of 106 times higher than that in interior dust. Concerns over lead in drinking water have recently grown significantly. Lead from lead pipes or pipe solders may contaminate drinking water even if the water source is clean. Old water fountains in offices and schools have been found to contain significant quantities of lead. Even while children are not the only ones who are exposed to this source of lead, it is particularly concerning. The EPA has changed the standards for lead in drinking water from 50 to 10 ppb in light of the risk of chronic lead exposure.

Symptoms of Toxins in Children

Children are especially vulnerable to subclinical toxicity, a form of encephalopathy caused by low-level lead intoxication. There are no overt signs of intoxication present. The child's neurophysiological behaviour, such as hyperactivity, misbehaviour, and a low IQ, is what causes the brain damage. According to a 1986 EPA report, blood levels of 10-15 mg/dL are sufficient to produce neurological deficiency.

Earth Erosion

The pace of soil erosion, a natural occurrence brought on by water and wind, is influenced by the amount of grass or trees covering the ground, the amount and timing of rainfall, and the slope of the land. This natural occurrence is accelerated by agricultural practises that remove plant coverage from the soil. Currently, soil erosion is one of the most harmful parts of agriculture because it contaminates surface water with nutrients and pesticides, causes lakes and rivers to silt up, and reduces soil fertility. Sediment makes up 22% of all lake pollutants and 47% of all nonpoint river pollutants in the United States (see Table 11.2). Although urban areas may occasionally contribute significantly, the majority of the silt comes from rural areas.

Leaving sediment from the runoff of dirt from cities and topsoil from fields is a serious ecological and monetary challenge. It stifles the habitat by lowering the survival of eggs and young, it helps to move nutrients and hazardous contaminants, and it generates water turbidity that lowers light penetration, restricting plant development and diversity. By clogging them up with silt, it also hastens the demise of lakes, streams, reservoirs, harbours, and irrigation canals. The rate of soil erosion could become alarming involves subpar agricultural management, the use of land not meant for farming, excessive grazing, and deforestation. The issue is getting worse, particularly in emerging nations where more land is being cleared for agriculture and more forests are being cut down. For instance, between 1960 and 1980, deforestation reduced the forest cover in Central America from 60% to 40%. There, soil erosion has become such an issue that siltation has obstructed coastal harbours, irrigation canals, and hydropower reservoirs. In the Philippines, for instance, deforestation of the yearly sedimentation rate in two significant reservoirs increased by 121% and 105%, respectively, between 1967 and 1980, in direct proportion to the unsuitable agricultural practises that affected 1.4 million hectares of an upland watershed [9], [10]

Pollutant Binding

Pollutants' chemical and physical characteristics, as well as the composition of the soil, all influence the ability of soil to bind and transport them. In addition to organic chemicals derived from plant and animal matter, soil also contains inorganic elements. The soil's inorganic components are categorized as follows: sand, 0.02-2 mm; silt, 0.002-0.02 mm; and clay, less than 0.002 mm. Organic substances are classified as either non-humic substances (if only partially decomposed) or humic substances (if entirely decomposed and chemically altered). Only 10% to 15% of soil organic matter is made up of non-humic materials. Although organic matter makes up between 0.1% and 10% of the soil overall, it can coat inorganic components and prevent them from absorbing water.

Nonionic and hydrophobic chemicals are bound by soil organic matter. The inorganic substance interacts with polar and ionic molecules, and it also has the ability to exchange cations. It matters how big the dirt particles are. Compared to the surface area of large particles, the huge surface area associated with very small particles offers a greater number of binding sites. Another characteristic of a contaminant that influences how it interacts with the soil is its water solubility. The presence of other organic molecules, temperature, pH, salt concentration, and temperature all have an impact on water solubility.

Fertility of Croplands

Due to its impact on farmland fertility and role in water contamination, soil erosion is a significant problem. When paired with overgrazing and the cultivation of agriculturally marginal land, this issue becomes urgent. According to a 1982 estimate, soil erosion in the United States occurs at a rate of 18 metric tonnes per hectare each year. In certain poor nations, it is significantly greater. For example, it reaches 42 (1986 estimate) metric tonnes per hectare per year in Ethiopia and 72–138 (1980 estimate) metric tonnes per hectare per year in Kenya . The results of such a swift topsoil loss on the capacity of developing nations to produce adequate food for their constantly expanding populations might be disastrous.

Although the loss of topsoil is the main consequence of erosion, in some extreme cases the ground is twisted by the formation of gullies, making it nearly hard to recover the affected area. Other factors that contribute to land degradation include nutrient depletion, soil compaction from heavy machinery or animals, waterlogging, salinization, and acidification. Despite the other causes, soil erosion continues to be the main factor in soil degradation. It is to blame for 84 percent of all agricultural land losses worldwide.

Salinization

The fertility of the land decreases as a result of too much salt building up in the soil's higher layers or on the surface. In extreme circumstances, some areas might get sterile. Salinization can be caused by salt concentration or salt loading. When fields with too much salt are watered and adequately drained, salt loading occurs. The salt may wash into the irrigation water's source streams. Each farmer after that utilises water with a higher salinity than the neighbour upstream. High salt loads eventually cause the stream to become contaminated. Both the land and aquatic organisms are harmed by this condition. On the other side, salt concentration happens when there is waterlogging in places where a lot of water is evaporated. When field drainage is compromised or the groundwater table is too near the surface, waterlogging may happen. Salt is released from the ground by standing water. The salt concentration increases close to or on top of the land when the water evaporates.

Pesticides and nutrients

Nutrients from fertilisers, such as nitrates and phos- phates, as well as animal waste from feedlots pollute the environment when runoff from farms occurs. Animal faeces as well as fertilisers are responsible for the eutrophication of lakes and streams.

Nutrients

Because of their potential toxicity, nitrates are particularly concerning. Because they are very soluble in water, they rapidly leak from the soil and contaminate both surface and groundwater. They may be reduced to nitrites in the soil (and the mouth; see Chapter 3). Nitrites can be consumed through drinking water may lead to hypertension and methemoglobinemia2 in youngsters. Some pesticides' chemical reactions with nitrites can produce nitrosamines, which are known mutagens and carcinogens. Nitrites exposure can result in foetal abnormalities and gastrointestinal cancer in humans.

Phosphates, as opposed to nitrates, are predominantly carried by the soil when it erodes. Even when used as a soluble orthophosphate in the field, it quickly transforms into an insoluble form that is easily absorbed by soil particles. Phosphate accumulates in the sediment as a result. There might, however, be exceptions to this behaviour in certain situations. According to a study on the contamination of U.S. coastal estuaries, the majority of phosphate exists in solution rather than bonded to the sediment in an estuary's brackish waters at least (12). If applied to the fields in moderation, manure makes an excellent fertiliser.

The danger of groundwater and surface water pollution is brought on by the large amounts of manure that build up in cow feedlots, producing leachate rich in organic nutrients as well as phosphates, nitrates, and ammonia. The Dutch pork sector is one illustration of how excessive manure accumulation poses a serious ecological risk. More manure than the nation can use for its agriculture has been created by the 14 million animals in the south of the country. As a result, phosphate and nitrate levels in the soil's surface layers are extremely high and water is highly polluted in many regions (13). The piled manure releases nitrous oxide into the air, which is created in the soil when bacteria oxidise ammonia to create nitrous oxide. About 20% of the acid deposition in the Netherlands is caused by the conversion of N2O to nitric acid in the air (14). Similar circumstances have lately arisen in the US state of North Carolina, where corporate hog farms' leachates have contaminated streams and groundwater.

Pesticides

Although pesticides make up a very minor portion of all water contaminants, their usage should not be taken lightly. By virtue of their very nature and intended use, pesticides are poisons, whether they are insecticides, herbicides, or fungicides. Even though they are much less prevalent than silt, their effects on the environment could be significant. In the United States, pesticide usage has more than doubled since 1962. In most states, it currently puts the quality of the groundwater in peril.

The EPA has published regulations to protect groundwater from pesticides. These regulations impose limitations on the use of pesticides where their content in drinking water is getting close to the Safe Drinking Water Act's upper limit. The use of pesticides is forbidden in cases of extreme pollution. Pesticides' properties, such as selective toxicity, environmental permanence, biface- mulat*i*on potential, and mobility, are a major source of concern. The most important aspect in determining if something is acceptable is likely its persistence in the environment. Thus, they are separated into three categories: persistent, which degrade by 75–

100% in 2–5 years; moderately persistent, which decomposes in 1–18 months; and no persistent, which decomposes in 1–12 weeks.

In addition to photochemical and chemical processes, bacterial digestion is another method of pesticide decomposition. Frequently, metals, elements of the soil, or organic substances catalyse it. The reactions include hydrolyses, oxidations, reductions, interactions with free radicals, and water-based nucleophilic replacements. A pesticide's "decomposition" (i.e., loss of the intended activity) does not necessarily imply that it turns into a harmless compound. Food Chain Bioaccumulation is dependent on a substance's lipid-water partition coefficient and susceptibility to biotransformation and degradation[11], [12].

CONCLUSION

Lipid solubility rises along with bioaccumulation potential. In general, aquatic creatures bio-accumulate more than terrestrial ones. The degree of bio-magnification in the food chain depends on the length of the food chain and the amount of pesticides that have accumulated in a terrestrial or aquatic organism. The silt at the bottom of lakes or rivers may include pesticides that have adsorb onto soil particles. They might ingest phytoplankton; which higher organisms then eat. Then, even higher species consume these higher organisms, and so forth. The substance's concentration rises with each additional consumption step. Despite not being a pesticide, PCB shares several physicochemical traits with chlorinated hydrocarbon pesticides. The lack of specificity in pesticides is another issue. Although pesticides are made to be more hazardous to insects than to birds or mammals, they frequently do not differentiate between various insect species. As a result, they eliminate not just the pest they were intended to control but also any additional insects that would act as natural predators of the pest or as food for fish and birds. Additionally, fish may suffer if chemicals reach a watershed in large quantities. Spectacular fish deaths brought on by aerial spraying or the dumping of insecticides into waterways were described by Rachel Carson.

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CHAPTER 12

THE BENEFITS OF THE POLLUTION CONTROL

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ABSTRACT:

Coal is used in the generation of around 28% of commercial energy worldwide. It is approximately 31% in the United States, whereas the percentages are 73%, 56%, 95%, and 86%, respectively, in China, Germany, Poland, and the Czech Republic—all of which are coal-rich but oil-poor nations. Because there is a plentiful supply of coal accessible, there will likely be a long period of heavy dependency on coal as an energy source. The most polluting fuel, however, is coal, which mostly emits sulphur dioxide and suspended particulate matter (SPM). Depending on where it came from, coal has a sulphur content of at least 1.5% and up to 2.5%. Pyrite (FeS2), organically bonded sulphur, and a very small amount of sulphates are the three main forms of this sulphur. 15% of the total sulphur is retained in the ashes after combustion. The remaining portion is released as flue gases, primarily as SO2 but also, to a lesser amount, as SO3. The name SOx is widely used to describe this mixture. The three main methods for reducing SOx emissions are pre-purification of coal before burning, sulphur removal during combustion, and flue gas purification.

KEYWORDS:
Carbon, Coal, Combustion, Fuel, Petrol

INTRODUCTION

The first method, known as a benefication process, is based on the fact that pyrite has a specific gravity of 1, while coal has a specific gravity of 1.2-1.5. Despite the fact that the technical setups could differ, the procedure includes floating the crushed coal in a liquid with between pure coal's and pyrite's specific gravities. While pyrite and other minerals sink to the bottom, coal is taken from the surface. Sulphur content can be reduced by around 40% using coal benefication. Even though the sole method used right now is gravity separation, research on microbial coal purification has already begun. The Institute of Gas Technology carried out a study with American financing. Department of Energy, intended to create microbes that could remove organic sulphur from coal through genetic engineering. The naturally occurring microorganisms Thiobacillusferrooxidans, Thiobacillusthiooxidans, and Sulfolobusacidocaldarius can all extract inorganic sulphur[1], [2].

Clean Burning

Coal gasification combined cycle (GCC) and fluidized-bed combustion are the two processes for the clean burning of coal, respectively. GCC includes using the following procedure (4) to convert coal to methane. Methane, one of coal's volatile components, is removed by preheating coal to 500–800 °C. Steam is used to treat the leftover char at temperatures above 900 °C, creating water gas (a combination of CO and H2). The following equations then translate the water gas into methane and carbon dioxide. Fluidized-Bed Combustion Pulverised coal is combined with limestone (CaCO3) in the fluidized-bed combustion process. A stream of hot air from below ignites and maintains the suspension of this combination. The combination of heat generated and air velocity gives the impression that a fluid is on the verge of boiling. Limestone and sulphur react to generate CaSO4. Given that

the boiler tubes are submerged directly in the fluidized bed, this procedure also has the added benefit of having a very efficient heat transmission. The combustion temperature is then able to stay relatively low (730–1010 °C as opposed to 1510–1815 °C for traditional units burning pulverised coal). NOx production is decreased at low combustion temperatures.

Cleaning of Flue Gases

Scrubber use for desulfurization De-sulfurization can be accomplished by using scrubbers. Scrubbers come in two varieties: non-regenerative and regenerative. Scrubber use consumes 5- 15% of the plant's energy output and raises electricity costs by around 20–30% (2). No regenerative Scrubbers Flue gases are passed through a slurry of limestone in no regenerative scrubbers, where SOx interacts with CaCO3 to create CaSO3 and CaSO4.

The disadvantage of the limestone scrubbers is that a lot of sludge builds up. It is necessary to dispose of this sludge on land, typically in lagoons. Groundwater contamination is a risk due to leaching from these lagoons. Additionally, the scrubbers may briefly stop working due to sporadic functioning issues. Regenerative Scrubbers Regenerative scrubbers reuse the SO2-trapping agent and create sulfur-based goods with a marketable value. Sodium sulfite, which is used in the Wellman-Lord method, combines with SO2 to create sodium bisulfite[3], [4].

By treating the sodium bisulfite with steam and alkali to create sodium sulfite and SO2, the process is reversed. Elemental sulphur, liquid SO2, and sulfuric acid (2) can all be made from this sulphur dioxide. Removal of particle matter from flue gases is another issue, known as suspended particulate matter (SPM). The fly ash, soot, and smoke particles released during the combustion of coal are the three main types. In contrast to soot, which is made up of tiny, unburned carbon particles, fly ash mostly consists of mineral stuff found in coal that has been changed by high temperatures. In reality, the amount of admixed soot particles in fly ash can vary depending on how completely the combustion process was completed. Condensed tar vapours and soot combine to form smoke. Because incomplete combustion produces smoke, the combustion process is crucial in the elimination of smoke. Using finely ground coal and a smoke and soot are eliminated by thorough mixing of fuel with an abundance of air, as in modern boilers.

The size of the particles affects how fly ash behaves. Small particles are driven by the gases, whereas large particles precipitate upon impact with one another and any obstructions present.

The extremely tiny particles, which are on the scale of molecules, behave like gas particles, moving like molecules and colliding regularly. Because they are the most hazardous to human health, small and very small particles (less than 1 mm in diameter) must be removed. Filtration, centrifugal separation, the use of wet collectors, and electrostatic precipitation are the four methods for removing particles from flue gases.

Bags, mats, or columns are used in the process of filtering. For particles of all sizes, these devices have an efficiency of roughly 99%. However, they gradually require higher gas pressures as they get partially clogged over time, which uses energy. Additionally, they are susceptible to corrosion and high temperatures. Centrifugal separators are very effective and reasonably priced.

The gas is driven into a revolving motion when it enters a conical vessel from the top. Centrifugal force causes particles to fly against the walls and slide into a collecting section. Wet collectors use a variety of setups to wash the particles out of the gas as it passes through

a water spray. Wet collectors produce a lot of sludge and lower the flue gas temperature, despite the fact that they are quite effective, particularly for the removal of tiny particles. The removal of 0.05- to 200-m particles with electrostatic precipitators is very effective m of particles. Although they are expensive to install, they have low operational costs. They work by passing a gas through an electric field, causing the particles to charge up and move towards collecting electrodes[5], [6].

DISCUSSION

The cutting-edge technologies, fluidized-bed combustion and GCC, outperform flue purification techniques. Additionally, compared to flue gas purification systems, GCC and fluidized-bed combustion are more affordable to operate. They get rid of issues like sludge and solid waste accumulation and malfunctions brought on by clogged filters. But neither of these clean-coal innovations reduces CO2 emissions.

Limiting Mobile Source Emissions

Exhaust emission, volatile organic compound (VOC) emission, rubber and asbestos emission from brakes and tyres, respectively, and VOC emission are just a few of the factors that need to be controlled in order to reduce pollution from mobile sources (such as cars, trucks, and buses).

Emissions of carbon dioxide from motor vehicles are also a cause for concern. Despite the fact that burning petrol produces less carbon dioxide per unit of heat than burning coal does, 19 lb of carbon dioxide, or 5.3 lb of carbon, are still released for every gallon of petrol used. Motor vehicles account for 25% of the nation's national carbon dioxide emissions in the United States and 14% of the total carbon dioxide discharged into the atmosphere globally [5], [6].

Exhaust Gases

Lead, nitrogen oxides (NOx), hydrocarbons (also known as VOCs), carbon monoxide (CO), and nitrogen dioxide (NOx) are the principal exhaust contaminants. Fuel combustion that isn't complete produces both CO and hydrocarbons. By using catalytic converters and strictly adjusting the circumstances of combustion, this issue can be remedied. Since NOx mostly comes from the combustion of nitrogen from the air and not from fuel, it is the pollutant that is hardest to regulate. Technology for NOx control will be covered later.Control Systems Catalytic converters, which are made of an alumina substrate and a platinum or platinum-palladium catalyst, help to oxidise CO and unburned hydrocarbons. Catalysts are vulnerable to lead inactivation. In order for catalytic converters to function properly, unleaded petrol (0.05 g of Pb per gallon as opposed to 2 g of Pb per gallon in leaded petrol) must be used. As an added bonus, lead contamination is significantly reduced.A computer-controlled electronic system that monitors the composition of exhaust gases helps to further reduce pollution. To reduce pollution, the same mechanism modifies the fuel-air ratio and spark advance as necessary[7], [8].

Alternative Fuels

The use of alternative, less-polluting fuels is now being discussed in the US. This adjustment would lessen reliance on imported oil while also reducing emissions. Considered are the following possibilities:

The use of compressed or liquefied natural gas in place of petrol

The use of alcohols, methanol, or ethanol in place of petrol

Adding oxygen-containing chemicals to petrol (called oxygenates), which promote more efficient combustion

Petrol reformulation to reduce the evaporation of VOCs while re-fuelling

A mix of some of the aforementioned options

Of all fossil fuels, natural gas burns cleanly and emits the least amount of carbon dioxide per energy unit. The disadvantages of using it for motor vehicle propulsion include the need to modify the fuel system of the vehicle and create a new fuel delivery network. The known global natural gas reserves are thought to last for roughly 60 years at the current global production rate of 70,770 petajoules (PJ) per year. In North America (the United States and Canada), 21,482 PJ/year of oil are used as fuel for automobiles. The production rate would need to increase by that much, to a total of 92,252 PJ/year, should it all be replaced by natural gas. The world's natural gas reserves would still be sufficient to endure for around 45 years in such a scenario, but the United States would need to import more than 90% of it. Additionally, this ignores the fleet's anticipated expansion and the possibility that other countries may have similar plans. The calculations above were constructed using information [9], [10].

Methanol is an additional fuel option. Methanol is a highly effective fuel that is frequently utilised in racing vehicles. Methanol burning emits fewer volatile organic compounds (VOCs) and carbon dioxide than petrol. However, nitrogen oxide emissions and emissions of the carcinogen formaldehyde cancel out these environmental advantages. The raw material used to make methanol is an essential consideration. Because carbon dioxide emissions occur during the process of preparing methanol from coal, it is not practical to use coal.

The carbon dioxide emissions from methanol combustion and methane synthesis combined would raise those from petrol burning by 80%. Natural gas is the most cost-effective raw material for the production of methanol; however, it is more practical and economically sound to transform natural gas into methanol rather than using it as is. One might doubt the fuel. Wood and agricultural waste are some more feedstocks to take into account.

Ethanol can be used as a fuel on its own or in a 10% petrol blend with regular petrol. Fuels that burn cleaner than petrol include pure ethanol and petrol. However, there are disadvantages to using 100% corn ethanol: There isn't even enough corn in the globe to feed the world's hungry people while also providing the United States with the fuel it needs for its cars.

The energy balance is unfavorable, which means that the energy required to develop the soil, harvest the grain, and distil the ethanol is almost equal to the energy generated by ethanol combustion (12). Although the carbon dioxide assimilated by maize during growth balances the quantity of carbon dioxide released during ethanol burning, the overall carbon dioxide balance is unfavourable.

The potential of the growing maize to absorb the amount of carbon dioxide released during the production of feedstock and product distillation (13), however, is greatly outweighed. Other feedstock, such plant matter or municipal trash, may offer more advantageous possibilities for the generation of ethanol (14).

To make petrol burn cleaner, oxygenates are petrol fuels combined with additives that include oxygen. Methyl tert-butyl ether (MTBE) is the additive that is used the most frequently. Ethanol is another option.

The drawback of ethanol is that it makes petrol more volatile, which increases VOC emissions when you refuel, defeating the aim of reformulated petrol. Large cities that fall short of the NAAQS ozone limitations must use petrol that has been reformulated to satisfy low-volatility criteria, according to the Clean Air Amendments of 1990. The utility of ethanol as an addition to reformulated petrol is severely constrained by this criterion (15).

Due to the discovery that MTBE, which only a few years ago seemed to be a useful petrol additive, easily pollutes groundwater, a source of drinking water for many towns, it is now likely to be phased out of use. MTBE causes water to taste and smell unpleasant even at very low concentrations, and the EPA has classified it as a potential human carcinogen.

The Department of Energy has a new advisory group called the Alternative Fuel Council. This group is carefully examining the arguments in favour of and against alternative motor fuels, taking into account not only current fossil fuels but also future fuels like hydrogen and solar energy.

Organic Volatile Compounds

Fuel evaporation through the fuel tank and carburetor vents, crankcase gas escape, and fuel evaporation while refueling are the three sources of VOC emission aside from exhaust emission. Controls in the Vehicle The gasoline tank and carburetor are connected to a container of activated charcoal to prevent fuel evaporation through their vents. When the car is at rest, the charcoal captures the gasoline vapours, and when the engine is running, it releases them into the induction system. Some petrol vapours escape from the engine's compression stroke through the crankcase's piston ring gaps, and subsequently through the breather tube into the atmosphere.

The breather is linked to the intake manifold to avoid this. In order to sweep the gases into the intake manifold, a portion of the air drawn into the air cleaner is utilised to purge the crankcase. PCV, short for positive crankcase ventilation, is the name of this system.

Controls at the Gas Tank When gasoline is put into a gas tank that isn't completely full, the vapours inside the tank are driven out and into the atmosphere. In the United States alone, refuelling is predicted to release 1.27 billion pounds of VOCs into the environment per year (16).The installation of a stage II vapour recovery equipment at the petrol pump can lower this emission level. The vapour balance system is the most basic installation and consists of a rubber boot on the filler nozzle connected to the underground tank by a hose.

The vapours that have been dispersed are pushed into the subsurface tank when the boot is tightly closed over the car's filler neck. A vacuum-assisted system is a modification of the vapour balance system; in this method, vapours from the vehicle tank are drawn into the underground tank by a pump, thus there is no need for airtight contact between the boot and the filler neck. With this configuration, more air and vapours are sucked into the subsurface tank than fuel is provided to the vehicle.

As a result, the subsurface tank needs to be vented, which necessitates the attachment of a vapor-trapping mechanism near the vent. Theventure effect of a gasoline side stream creates a little amount of vacuum that is used by a hybrid system. In the vacuum-assisted system, the vacuum is not as strong as the one produced by a pump. A balance between the volume of

fuel delivered and the amount of vapour expelled is preserved since little extra air is sucked into the subsurface tank. Most states have not yet adopted the usage of stage II vapour recovery.

Limitation of nitrous oxides

Because NOx comes from the air, it is challenging to reduce NOx emissions. Thus, regardless of the fuel utilised, it is a byproduct of all combustion processes. Mobile and stationary sources both contribute to NOx pollution, although their effects on the environment are considerably different. Urban pollution is generally caused by mobile sources, whereas acid and nutrient precipitation is primarily caused by stationary sources. Because hydrocarbons of natural origin are abundant in the ambient air and hence the anthropogenic contribution is less significant, the successful control of NOx emission depends more on this than on that of hydrocarbons (17).

Conditions for Combustion

The correct adjustment of the combustion conditions is necessary to control NOx emissions from stationary sources. Therefore, management strategies require a low flame temperature and slow cooling of the flue gases because NOx is only generated in considerable proportions at temperatures over 1400-1500 8C and it decomposes slowly with cooling. It helps to reduce NOx generation to reduce extra air in combustion gases.

The partial recirculation of flue gases back into the combustion chamber, the addition of moisture to the combustion air in the form of steam or water spray, and a two-stage combustion process in which the fuel is burned initially with insufficient air are all practical ways to lower the combustion temperature. In the second step, complete combustion is accomplished by combining the resultant gases—CO and hydrocarbons—with more air.

Control Mechanisms

NO_x cannot be removed from flue gases using current procedures. Because NO_x is very weakly soluble in water, wet scrubbers are ineffective. Selective catalytic reduction (SCR), a novel technique that may decrease NO_x to N2 and H2O by 85–90%, has been developed and is currently popular in Europe and Japan. The procedure entails adding ammonia to an exhaust stream that contains nitrogen oxides and then passing the resulting combination over a catalyst. Platinum, vanadium pent-oxide on a titanium dioxide support, and zeolite catalyst are the three types of catalysts now in use (18). Three-way catalytic converters are used to reduce NO_x emissions from cars and trucks. These converters have a rhodium catalyst that converts NO_x to N2, in addition to a platinum-palladium catalyst that oxidizes CO and hydrocarbons. As previously established, careful regulation of combustion conditions is necessary for catalytic converters to function well; Proper maintenance is crucial to provide this control.

Energy efficiency

Energy conservation is a potentially important approach of reducing air pollution. Increased vehicle fuel efficiency and strict adherence to speed limits may result in significant energy savings depicts the connection between vehicle speed and fuel usage. By lowering air pollution and CO2 emissions, energy conservation has a favorable effect on the environment, human health, and the economy. Energy conservation and the consequent reduction of pollution from stationary sources are made possible by thermally insulated homes, energy-efficient electrical appliances, and lighting. Energy production and consumption both have an

effect on the environment. Energy conservation can lessen the environmental risks brought on by practices like offshore oil drilling and ship-borne oil transportation.

The LRVs, also known as hybrid vehicles, combine an electric propulsion system with a small internal combustion engine to power the vehicle. The gas engine powers a generator, which in turn charges batteries and generates electricity for the electric motor. This design has the benefit of ensuring that the petrol engine operates as efficiently as possible at all times, including in stop-and-go metropolitan traffic.

The electricity for the electric ZEVs comes from batteries. They have a limited operating range, and the batteries need to be recharged, which raises the demand for electricity. However, not only is this method more environmentally friendly than using individual automobiles, but pollution can also be better managed at the power plant. The other category of ZEVs consists of fuel cell-powered electric vehicles. Water electrophoresis is reversed in a fuel cell. Under carefully controlled circumstances, hydrogen and oxygen combine to produce an electric current. Because there are now no economically viable methods of manufacturing hydrogen and insufficient infrastructure, these are the automobiles of the future.

The LEVs and ZEVs will contribute to maintaining clean urban air, but they cannot stop water pollution from street runoff or reverse environmental degradation brought on by questionable land use. Regardless of the means of propulsion, highways and parking lots are necessary for motor vehicles to function. As the number of motor vehicles and miles travelled continue to rise, more and more paving the land will be necessary to handle the rising traffic. Thus, the creation of public transit in our cities is the most pressing requirement if we are to reduce our reliance on automobiles.

Treatment of Wastewater

The four levels of wastewater treatment are primary, secondary, tertiary, and advanced. Not every plant incorporates all four phases due to the expense. But all American communities are compelled by law to receive both primary and secondary treatments. Sewage typically goes through grit chambers, where large nonputrescible materials (such grit, stones, and bits of lumber) are filtered out by sedimentation and screening via grills before entering the primary stage.

Bacteria that are still suspended in the now-purified water leaving secondary treatment tanks are to be eliminated by tertiary treatment. This removal can be done using a mixture of sand filtration, long-term retention in shallow oxidation ponds (where aeration is achieved by growing algae or by mechanical means), or by using both techniques simultaneously. Advanced treatment is used to remove salts and certain compounds that may be found in the wastewater of some locations, as well as nutrients (such as phosphates, nitrates, and ammonia). While nitrates and ammonia can be reduced to elemental nitrogen by anaerobic or aerobic bacteria, respectively, phosphates are best eliminated by precipitation with lime. Other procedures are occasionally applied, including chlorination and filtration (using activated charcoal or ion exchangers).

At the pump station, bar screens filter out large particles from the sewage, and hammer mills grind it down to a size that the 600-hp pumps can handle. Since these pumps raise the sewage to a higher level, gravity may now be used in the majority of the remaining operations. (2) Sand and gravel that are heavier (mostly inert) materials sink to the bottom in the grit chamber and are then removed for disposal. The "balancing reservoir" is the equalization

tanks. They take excess flows and ensure that only flows with a composition and volume that are suitably uniform enter the secondary process downstream. Microorganisms devour organic matter and stabilize nitrogen in the sewage in the oxygen-transfer basins. The on-site cryogenic oxygen-supply system provides pure oxygen, which is what is needed for the microorganisms to breathe. Sludge, which primarily contains microorganisms, is number five[11], [12].

CONCLUSION

Sewage is initially treated by being held in settling tanks with surface skimmers for one to three hours. The large, solid particles sink to the bottom, and the lighter ones are skimmed off. During this process, 25–40% of the BOD pollutants are eliminated. The sludge from primary treatment is broken down by anaerobic bacteria.

The leftover material, which has almost no (or none) Putrescible materials are dumped in landfills. Putrescible matter is present in solution or colloidal suspension in the water that has undergone initial treatment. The putrescible components are broken down by aerobic bacteria during subsequent treatment.

The wastewater is vigorously aerated or oxygenated to aid in aerobic digestion. In this stage, 85–99% of the BOD contaminants are eliminated. Sludge is created when the bacterial mass collects at the bottom. Sludge from secondary treatment facilities is nutrient-rich and was once dried and sold as fertiliser. Because heavy metals, which are present in sewage at low amounts, are concentrated in the sludge and make its use as fertiliser risky, this practice has mostly been abandoned.3 Sludge from secondary treatment was afterwards dumped in landfills. The tendency was again reversed, nonetheless, as a result of the scarcity of landfill locations and rising costs of solid waste disposal. If the sludge meets the Environmental Protection Agency's (EPA) regulations for metal and polychlorinated biphenyl concentration, it can now be sold for use as fertiliser.

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