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Impact of Pesticides on Human Life and Health

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ABSTRACT:

India spreads out nearly 90,000 tons of pesticides within the fields and have become one among the very best users within the world. The chemical war isn't won and everyone life is caught in its brutal crossfire. In our everyday food may have around 1000 milligrams of pesticides. Pesticides are the natural or synthetic agents, and it is used to kill all types of pests. Pesticides are used in fields like agriculture, forestry, aquaculture, food industry etc. Due to its comprehensive use these pesticides threaten public health and ecosystem. This review has organized to present a comprehensive review on pesticides with respect to their definition, classifications, routes of exposure, and health impacts. We have reviewed the most common diseases including cancer which are associated Pesticides have shown to be involved in the Childhood cancers, Prostate cancer, Breast cancer, Colorectal cancer, Non-Hodgkin lymphoma (NHL), Leukaemia, Birth defects, Cognitive effects, Genetic damages, Endocrine disruptors, Epigenetic effects pathogenesis of Parkinson's and Alzheimer's diseases as well as various disorders of the respiratory and reproductive tracts. Oxidative stress caused by pesticides is a crucial mechanism through which many of the pesticides are affecting the human health. Those effects are very harmful to health as well as for the environment therefore control of their used in a proper way is necessary. By proper training of the farmers and other people regarding their effect and process of screening may lessen these pesticide problems.

KEY WORDS: Pesticides, Classification of pesticides, Route of exposure, Human health

1 INTRODUCTION

A pesticide is defined as a single substance or a mixture of chemicals used for preventing, destroying, repelling, and mitigating pests such as nematodes, rats, mites, insects, weeds, and fungi [2]. Pesticides are toxic chemical substance or mixture of substance or biological agent that are deliberately released into the environment in order to kill, prevent, deters, control, destroy, repel or mitigate population of insect, weeds, rodents, fungi, or other harmful pest in agricultural, domestic and industrial setting [3]. Pesticides are, in practice, collected of many subgroups that are generally divided based on their target pests. The primary classes include Pesticides targeting insects (insecticides), Weeds (herbicides), Fungi and molds (fungicides), Rodents (rodenticides) [4]. Pesticides are chemicals that are applied to private gardens, agricultural land, and other public areas to eliminate unpleasant organisms. Pesticides in aquatic resources adversely impact on both the ecosystems and humans health [5]. Pesticides are important to local farmers for the control of plant pests and diseases, as well as for the control of malaria vectors and related purposes in developing countries [6]. Basically, the input of pesticides in Indian agriculture increases after the announcement of Green Revolution which in turn helps our country to fight the major problem of food crises [7]. They may also be dangerous to people who are exposed to pesticides through occupational (or home) use, eating foods or liquids containing pesticide residue, or inhalation (or contact) of pesticide-contaminated air. Even very low levels of exposure may have adverse health effects at early development [8].One of the most rapidly growing sectors in the food industry is organic agriculture. Its growth primarily

based on the conviction that organic foodstuffs are healthier and safer than their conventional counter parts (Figure 1) [9].

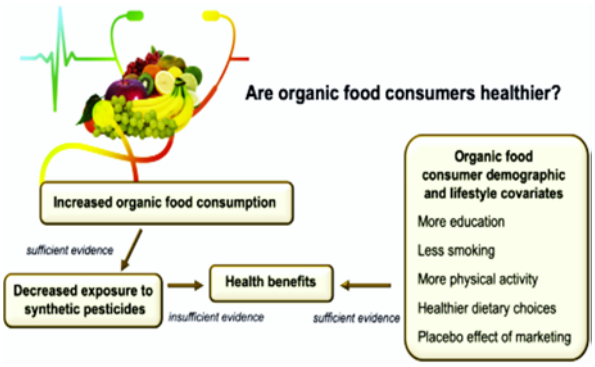


Figure 1 Insufficient evidence supports health benefits from a decreased exposure to pesticides through organic food consumption.

The claim that organic foodstuffs are safer than nonorganic food obtain from synthetic chemical-based agriculture is in part based on the fact that a move towards an organic diet significantly reduce the consumer's dietary exposure to synthetic pesticides sprayed during crop cultivation and storage [9].

2 CLASSIFICATION OF PESTICIDES: [1, 8, 10, 11]

Pesticides can be classified by various criteria such as
1. Toxicity, 2. Target molecules, 3. Mode of formulation, 4. Chemical structure, 5. Based on origin, 6. Based on function, 7. Mode of entry, 8. Mode of action, 9. Type of Pesticide Formulations

Without the above factors' pesticides can be broadly classified as 1. Organochlorine pesticides, 2. Organophosphorus pesticides, 3. Carbamates pesticides, 4. Pyrethroids pesticides, 5. Biorational pesticides, 6. Microbial pesticide, 7. Growth regulators, 8. Neonicotinoids.

CLASSIFICATION OF PESTICIDES BASED ON DIFFERENT CRITERIA.

2.1 TOXICITY :-

Table 2.1: Based on toxicity criteria [1]

WHO class Toxicity level		LD50* for the rat (mg/kg body weight)		Example in terms of active ingredients
		Oral	Dermal	
Ia	Extremely hazardous	< 5	< 50	Aldicarb, parathion, mercuric chloride
Ib	Highly hazardous	5–50	50–200	Acrolein, Cadusafos, Ca-arsenate
II	Moderately hazardous	50–2000	200–2000	Alachlor, Bentazone, Copper, sulfate
III	Slightly hazardous	Over 2000	Over 2000	Hexaconazole, Atrazine, Butachlor
U	Unlikely to present acute hazard	5000 or higher		Mancozeb, Captan, Bifenox

*LD50 is the amount of the substance required to kill 50% of the test population.

2.2 TARGET MOLECULES:-

Table 2.2: Based on target pest [8, 1]

Pesticide Type	pest	Example
Acaridae	Mites	Bifonazole
Bactericide	Bacteria	Copper complexes
Fungicide	Fungi	Azoxystrobin
Herbicide	weeds	Atrazine
Insecticide	Insect	Aldicarb
Larvicides	Larvae	Methoprene
Nematicide	Nmatodes	Aldicarb
Piscicide	Fish	Rotenone
Repellents	Insects	Methiocarb
Termiticides	Kills termites	Fipronil

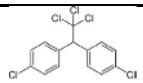
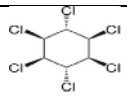
2.3 MODE OF FORMULATION

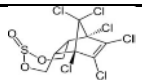
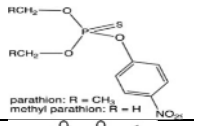
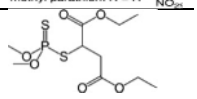
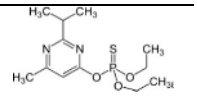
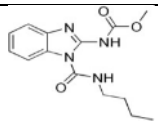
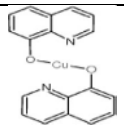
Table 2.3: Based on the mode of formulation [8]

Physical state	Characteristics
Emulsifiable concentrates	Do not require constant agitation prior to each application.
Wettable powders	Require constant agitation prior to each application.
Granules	Obtained by mixing the active ingredient with clay
Baits	Obtained by mixing with active ingredients with food
Dusts	Dust cannot be mixed with water and they must be applied dry

2.4 CHEMICAL STRUCTURE

Table 2.4: classification of pesticide based on chemical structure [8].

Type	Example	Structure	Effect of pest
Organo-chlorides (five or more chloride atoms)	DDT		Nervous system disruptors leading to convulsion and paralysis of the insect
	Lindane		

	Endosulfan		and its eventual death.
Organo-phosphorus	Parathion		Nervous impulses fail to move across the synapse causing a rapid twitching of voluntary muscles and hence paralysis and death.
	Malathion		
	Diaznon		
Inorganic	Benomyl		Predominantly stomach poisoning
	Oxine copper		

2.5 BASED ON ORIGIN :-

Table 2.4: classification of pesticide based on origin.

Based on origin	Source and Examples
Organic sources	Natural-plant phytochemical (essential oil, plant extracts, leftover oilseed cakes), synthetic-product by chemical synthesis e.g., pyrethroids, organophosphates, carbamates, organochlorine
Inorganic sources	Inorganic-mixture of inorganic salts, Bordeaux mixture $Cu(OH)_2.CaSO_4$, Malachite $Cu(OH)_2.CuCO$ and sulfur
Biological	Biological: microbial pesticides (bacteria, virus and fungi)

2.6 BASED ON FUNCTION :-

Table 2.5: classification of pesticides based on function.

Action	Function	Example
Feeding deterrents	Prevent an insect or other pest from feeding	(Azadirachta indica A. Juss)
Ovipositor deterrent	Prevent egg laying by graving female	Azadirachta indica
Repellents	Deters pest from approaching toward crops	Plant essential oil
Attractants	A chemical that lures pests	Gossyplure
Fumigants	Kills the target pests by producing vapor	Phosphine
Insect growth regulator	A substance that works by disrupting the growth or development of an insect	Diflubenzuron
Synergist	A chemical that enhance the toxicity of a pesticide but not by itself toxic to pest	Piperonyl butoxide

2.6 MODE OF ENTRY :-

Table 2.6: Classification of pesticides on the basis of mode of entry [11].

SN	Types of pesticide	Description	Examples
1	Systemic pesticides	These are pesticides which are absorbed by plants or animals and transfer to untreated tissue	2,4-D glyphosate
2	Contact pesticides	It acts on target pests when they come in contact	Paraquat, diquat
3	Stomach poisons	It enters the pest's body through their mouth and digestive system	Malathion
4	Fumigants	Pesticides which acts or may kill the target pests by producing vapour and enter pest's body through tracheal system.	phosphine
5	Repellents	Repellents do not kill but distasteful enough to keep pests away from treated area. They also interfere with pest's ability to locate crop.	Methiocarb

2.7 MODE OF ACTION :-

Table: 2.7: classification according to mode of action [11].

S.N.	Type of pesticide	Mode of action	Example
1	Physical poison	pesticides bring about killing of one insect by exerting a physical effect	Activated clay
2	Protoplasmic poison	Pesticides are responsible for precipitation of protein.	Arsenicals
3	Nerve poison	Chemicals inhibit impulse conduction	Malathion
4	Chitin inhibition	Chemicals inhibits the chitin synthesis in pests.	Diflubenzuron
5	Respiratory poison	Chemicals which inactivate respiratory enzymes	Hydrogen cyanide

2.8 TYPE OF PESTICIDE FORMULATIONS :-

Table 2.8: Types of pesticide formulations [11]

S.N.	Type of pesticides formulation	Description	Typical uses	Examples
solids				
1	Bait	Mixture of active ingredient and food that attracts pests in the form of meal, pellets.	For insects, rodents, birds or slugs.	Maxforce FC, Niban, Amdro etc.
2	Dry flowable (DF) or water dispersible granules (WDG)	Mixture of active ingredient and inert material made into small pellets, granules. Forms a suspension in water.	Sprays for insect's disease and weed control.	
3	Dust (D)	Finely ground inert particles i.e., talc, clay and volcanic ash.	Spot treatment, animal powder, seed treatment.	Deltadust, Ficam D, Drione, Sevin D, Malathion D.
4	Ear tag/ vapour strips	Solid material with volatile or solid active ingredient slowly release vapour.	Animal ear tag, Fly control.	
5	Granules (G or GR)	Dry inert materials (i.e., clay, walnut shell, corn cob)	Sol treatment for insect or weed control	Dursban G, Talstar G
6	Pellets	Inert material containing active ingredient like granules, but has more uniform shape and weight.	For control rodents, slugs	
7	Soluble powder (SP)	Dry powder or granules which dissolves in water to spray solution.	Mostly sprays for insects and weed control.	
8	Wettable powder (WP or W)	Finely ground inert ingredients with active ingredients forms a suspension in water	Sprays for insect, disease and weed control.	Demon WP, tempo WP
liquids				
9	Aerosols (A)	Usually contain small amount of active ingredients and a petroleum solvent. Two main types: 1. Ready to-use small pressurized containers. 1. Fog generators are not under pressure; equipment breaks the liquid into fine mist or fog.	Spray cans used for home/ garden insecticides used in greenhouses or mosquito control.	Wasp freeze, ULD- BP_50, Ultracide, Ultraguardian.
10	Emulsifiable Concentrate (EC)	Contains active ingredient, petroleum solvent and emulsifiers. Pesticide is suspended in spray which is milky coloured.	Sprays for insect, disease and weed control.	Chlorpyrifos EC, cypermethrin EC
11	Flowable (F)	Finely ground particles suspended in an insert liquid carrier. Forms suspension in spray mix like WP.s		
12	Gel	Semi liquid Emulsifiable concentrate	Herbicides and insecticides	
13	Micro-encapsulated materials	Consists of pesticide surrounded by aplastic coating. Mixed with water and sprayed.	Insecticide and pheromone sprays	Demand ES
14	Solution (SN)	Active ingredient dissolved in liquid. Forms a solution in spray mix.	Spays for weed control.	Premise SC, Termidor SC, bora-care
15	Ultra-low volume concentrate (ULV)	Liquid with very high concentration of active ingredient designed to be used as is or slightly diluted in ULV equipment.	Insecticide sprays inside greenhouse or for forestry.	
Gases				
16	Fumigants	Volatile liquids or solids packaged to release toxic gas.	Greenhouses. Mushroom houses, graineries. Pre plant soil treatment for soil borne pests.	Phosphine, Phostoxin.
Packaging				
17	Water-soluble packets	Pre-weighed amount of WP or SP formulation in a special plastic bag which dissolves in spray tank and releases contents.		Demon WP

Table 2.9: The toxicity rate between pesticides and beneficial organisms is shown according to the IOBC.

No.	Categories of chemicals	Kill beneficial species of insects (%)
1	Harmless	<25%
2	Slightly harmful	25-50 %
3	Moderately harmful	50-75 %
4	Harmful	4 > 75%

The WHO categorized a globally harmonizes system for chemical classification. The substances are classified into 5 classes. This information is presented in Table 2.10 [1].

Table 2.10: The WHO classified a globally harmonized system and labeling of chemicals class Intensity.

class	intensity	Signal words	Hazard symbols	Color
Ia	Extremely hazardous	very toxic		PMS[1] Red 199 C[2]
Ib	Highly hazardous	Toxic		PMS Red 199 C
II	Moderately hazardous	Harmful		PMS Yellow C
III	Slightly hazardous	Caution	No symbol	PMS Blue 293 C
U	Unlikely to present acute hazard in normal use	No signal word	No symbol	PMS Green 347 C

1: PMS= Pantone Matching System. It is a system that is used for color accuracy and consistency.

2: C= Coated. (C, U, and M indicate the type of color in Pantone Matching System).

3 THE MOST COMMONLY USED PESTICIDES[5]:

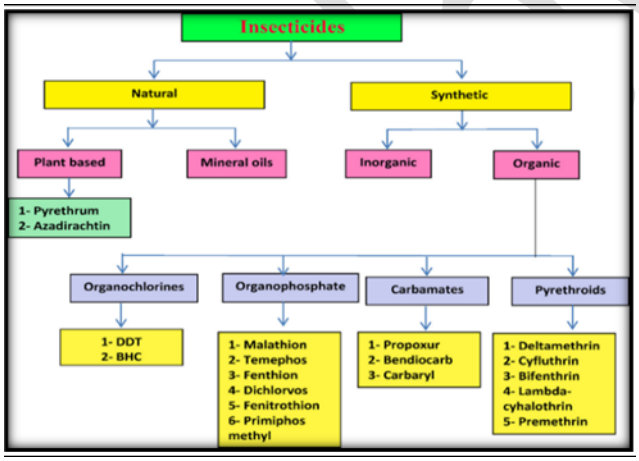


Figure 2 Pesticides Classification

3.1 ORGANOCHLORINE PESTICIDES (OCPs) :-

Organochloride are stable chemical that are very persistent in the environment and have the potential to accumulate in adipose tissue. In humans, these compounds or their metabolites mostly work at the level of the central nervous system modify enzymatic nerve membranes and electrophysiological properties, which leads to switch in the kinetics of the flow of K+ and Na+ through the nerve cell membrane and may cause symptoms such as acute poisoning death and seizures from apnea. Structurally, organochlorines fall into five classes:

1. Dichlorodiphenylethanes e.g. dicofol (kelthane), dichlorodiphenyltrichloroethane (DDT), dichlorodiphenyldichloroethylene (DDE), dichlorodiphenyldichloroethane (DDD), methlochlor, and perthane [12], 2. Chlorinated benzenes and cyclohexanes e.g. Hexachlorocyclohexane (HCH), Hexachlorobenzene/Benzene hexachloride (HCB/BHC) [12], 3. Chlorinated cyclodienes e.g. aldrin, dieldrin, endrin, chlordane, endosulfan and heptachlor [12], 4. Toxaphene, 4. Mirex and chlordecone.

3.2 ORGANOPHOSPHATE PESTICIDES :-

Some esters acquire from phosphoric acid are known as organophosphate pesticides. These esters form are active in humans on the central nervous system by blocking the enzyme acetylcholine. This enzyme manages the amount and levels of the neurotransmitter acetyl cholinesterase, which disarrange the nerve impulse by the serene phosphorylation of the OH group in the active site of the enzyme. Insobriety symptoms are coma, dizziness, nausea, headache, cramps, convulsions, loss of reactions, and even

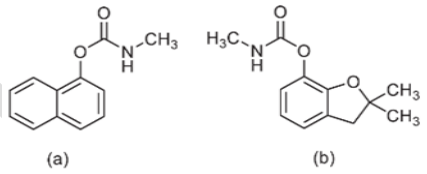


Figure 3 Chemical structure (a) Carbaryl (b) Carbofuran.

death. The ultimate treatment for organophosphate poisoning is atropine, which competes with acetylcholine at the muscarinic receptors. [5].

3.3 CARBAMATE PESTICIDES

Some organic ester compounds derived from dimethyl N-methyl carbamic acid are used as herbicides, insecticides, nematicides and fungicides, and named as carbamates (Fig. 4.4). Carbamates such as thiobencarb, propoxur, molinate, disulfiram, pyridostigmine, methiocarb and carbaryl are mainly used in both cats and dogs.

The carbamate compounds toxicity differ according the molecular structure, but in general they have shorter duration than that of organophosphates and organochlorines, and the latter inhibits acetyl cholinesterase. The treatment of acute carbamate toxicity is also alike to that of organophosphates. These poisoning symptoms seem in different organs and can be listed as follows:

1. Bronchial tree (wheezing, dyspnea, increased secretions, muscarinic (parasympathetic), cough, pulmonary edema, cyanosis, and bronchoconstriction), 2.

Glandular stimulation (increased salivation, lacrimation, and sweating), 3. Cardiovascular effects (bradycardia, and hypotension), 4. Eye (miosis, and blurred vision), 5. Bladder dysfunction (incontinence, and frequency), 6. Gastrointestinal manifestations (nausea, vomiting, abdominal cramps, diarrhea, and incontinence), 7. Nicotinic receptors stimulation (including sympathetic and motor neurons), 8. Motor activity compromised (muscle twitching, depression of respiratory and circulatory, fasciculation, cramps, and weakness), 9. Sympathetic dysfunction (tachycardia, hypertension, and pallor), 10. Central nervous system effects (restlessness, emotional lability, confusion, drowsiness, Cheyne Stokes respiration, slurred speech, tremor, ataxia, generalized weakness, coma, areflexia, convulsion, and hypothermia) [5].

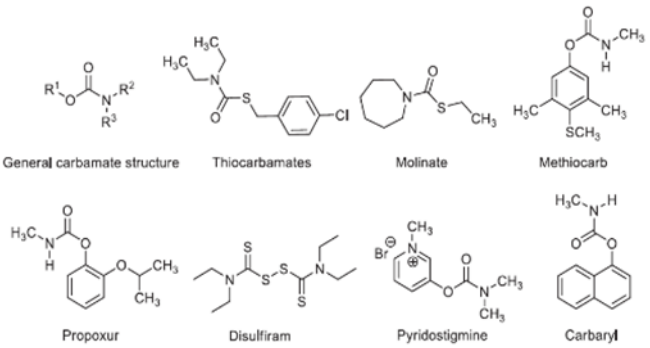


Figure 4 Chemical structure of some carbamate and thiocarbamates pesticides

3.4 PYRETHROID PESTICIDES:-

Pyrethroids are natural insecticides obtain from the pyrethrum extracts of chrysanthemum flowers known as pyrethrin found in Kenya. It works on the central nervous system, which causes alteration in the dynamics of sodium cation channels in the membrane of the nerve cell, which leads to a rise in the time of gap of the sodium channels. The sodium cation stream expand across the membrane in both vertebrates and insects. A neuronal hyperexcitation can be a result of these activity. Due to the severe need for large amount of these pesticides and due to the growing shortage of essential oils necessary for the manufacture of natural organic pyrethrum, Scientists have turned to the production of synthetic pyrethroids. Most pyrethroid insecticides (Fig. 3.4) share several characteristics such as low toxicity to birds and mammals; high toxicity to arthropods since it requires very low doses to kill insects; highly toxic to fish if applied directly to water.

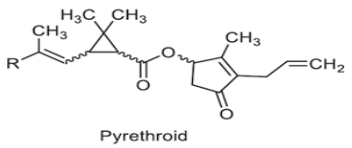


Figure 5 General structure of pyrethroids pesticides.

Although many pyrethroid insecticides can be absorbed by insect pests when they walk on dry residues, they are not successful in penetrating the soil to kill underground pests because they adhere tightly to soil and organic matter. In addition, they are poorly soluble in water [5].

4 ROUTES OF PESTICIDE EXPOSURE TO HUMAN

Exposure to pesticides can occur directly from occupational, agricultural, and household use, while they can also be transferred incidentally through diet. The most routes of human exposure to pesticides are through the food chain, air, water, soil, foliage, and animals. Pesticides are distributed throughout the human body through the bloodstream but can be eliminate through urine, skin, and exhaled air [8].

There are four common ways pesticides can enter the human body:

1. Dermal, 2. Oral, 3. Respiratory pathways, 4.Eye

4.1 DERMAL EXPOSURE: -

Dermal exposure is one of the most common and effectual routes through which pesticide applicators are exposed to pesticides. Dermal absorption may arise as a result of a splash, spill, or spray drift, when mixing, loading, disposing, and cleaning of pesticides. Absorption may also result from exposure to large quantity of residue. Pesticide formulations vary broadly in physicochemical properties and in their capacity to be absorbed through the skin, which can be affect by the amount and duration of exposure, the appearance of other materials on the skin, temperature and humidity, and the use of personal protective equipment. In general, solid forms of pesticides (e.g., powders, dusts, etc.) are not as readily absorbed through the skin and other body tissues as liquid formulations. The hazard from skin absorption increases when workers are handling concentrated pesticides. Certain areas of the body are more susceptible to pesticide absorption than other areas of the body. As such, the rate at which dermal absorption proceeds differs for every a part of the body (Fig. 5) [8].

4.2 ORAL EXPOSURE:-

The most severe poisoning may result when a pesticide is enter through oral exposure. Oral exposure of a pesticide usually arises by accidentally thanks to carelessness. The most frequent cases of coincidental oral exposure were reported to occur when pesticides were transferred from their original labeled container to an unlabeled bottle or food container. There are many cases in which people have been poisoned by drinking pesticides kept in soft drink bottles or after drinking water stored in pesticide- polluted bottles. Workers handling pesticides or equipment for their

application can also consume pesticides if they do not wash their hands foregoing to eating or smoking. Consequently, applicators should be carefully instructed on the handling of pesticides such as not to clear a spray line or nozzle by blowing through their mouth [8].

4.3 RESPIRATORY EXPOSURE:-

Due to the presence of volatile components of pesticides, their potential for respiratory exposure is large. Inhalation of sufficient quantities of pesticides may cause serious damage to nose, throat, and lung tissues. However, the probability of pesticide exposure is in general approximately low when pesticides are sprayed in large droplets with conventional application equipment. If low-volume equipment is used to apply a strenuous material, the potential for respiratory exposure is increased due to the production of smaller droplets. It is recognized that respiratory exposure to pesticides can be significant if applied in limited spaces. Thus, it is recommended that pesticides should not be applied at air temperatures more than 30 °C. Moreover, pesticides with high vapor hazards should be applied with sufficient equipment for respiratory protection [8].

4.4 EYE EXPOSURE:-

The possibility for chemical injury is high for tissues of the eye. Some pesticides were reported to be absorbed by the eyes in adequate quantities to cause serious or maybe fatal illness. Granular pesticides create a particular hazard to the eyes depending on the size and weight of individual particles. If pesticides are applied with power equipment, the pellets may bounce off vegetation or other surfaces at high velocity to cause significant eye damage. Eye protection is also require when measuring or mixing concentrated or highly toxic pesticides. Protective face shields or goggles should be worn whenever spraying pesticides or to prevent eye contact with dusts [8].

5 IMPACTS OF PESTICIDE USE ON HUMAN HEALTH

Studies suggest that pesticides may be related to many diseases including cancers, leukemia, and asthma. The likelihood of health hazards thanks to pesticide exposure depends not only on how toxic the ingredients are but also on the extent of exposure. Additionally, certain people like children, pregnant women, or aging people could also be more sensitive to the consequences of pesticides than others [8].

Effect of pesticide on health: Human beings are highly vulnerable to deleterious effect of pesticide due to nonspecific nature, haphazard application or misuse of pesticide. The pesticide enters human body through ingestion, inhalation, penetration but majority of people get affected via intake by pesticide contaminated food. Pesticide shows acute as well as chronic effects which are [9].

5.1 CANCERS :-

Various studies have analyzed the impacts of pesticide exposure on the danger of cancer. The main reports on the relationship of pesticides with disease were introduced around 50 years previous in regards to higher predominance of lung and skin cancer in the farmers due to the largest usage of pesticide sprays as a part of grape fields. Scientist have been found with: leukemia, lymphoma, breast, brain, kidney, liver, lung, prostate, pancreas and skin cancers (Figure 7).

A mother's exposure to pesticides in the middle of pregnancy is connected with expansions in her child's chance of leukemia and brain cancer. The other exposure to pesticide sprays inside the home and herbicides outside is connected with blood tumors in kids [13].

Figure 6 Strength of dermal exposure to pesticide on different parts of the body.

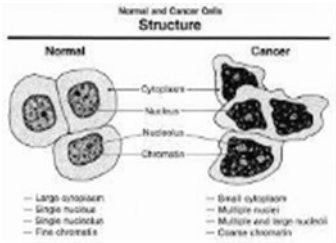


Figure 7 Structure of normal and cancer cells.

5.1.1 Childhood cancers:-

Many childhood cancers are found to be related with pesticide exposure. Compared to other cancer types, more persuasive evidence was presented in a population-based case-control study of acute myelocytic leukemia (AML). A comparison of 491 cases between an age group of 0-9 years was done for polymorphisms in CYP1A1, CYP2D6, GSTT1, and GSTM1 genes responsible to encode enzymes responsible to metabolize carcinogenic substances. Enzymes of Cytochrome P-450 family are involved in the transformation of pro-carcinogenic compounds to reactive species which have genotoxic and cytotoxic effects [14].

5.1.2. Prostate cancer :-

Environmental endocrine disrupting chemicals (EDCs) such as various industrial chemicals and pesticides are released into our environment and pose major health problems. Increase incidence of hormone dependent cancers such as breast, testis, and prostate of the male reproductive system have been associated with the hormone disrupters. 2, 4-dichlorophenol (DCP) a metabolite of 2, 4-dichlorophenoyacetic acid are extensively used in agriculture settings to control weeds. These chemicals also increased the localization of androgen receptor in the nucleus from the cytosol, suggesting DCP may act as a tumor promoter. A significant association between prostate cancer risk and use of simazine, lindane and DDT for high exposure was found, additionally the study also reported significant excess risk for several constituents like malathion, endosulfan, dichlone, carbaryl, 2,4-D and 2,4-DB. Interestingly, that chlorinated pesticides and methyl bromide were associated with increased risk of prostate cancer, but for other pesticides, greater risk was observed for people with a family history of prostate cancer [14].

5.1.3 Breast cancer :-

Exposure to persistent organic pollutant's which includes o,p'-dichlorodiphenyltrichloroethane (o,p'-DDT), and its metabolites p,p' dichlorodiphenyldichloroethylene (p,p'-DDE), and p,p'-dichlorodiphenyldichloroethane (p,p'-DDD) and other related pesticides are common due to the increased load of chemical pollutants in the environment. POPs are known endocrine disruptors in humans. Another herbicide atrazine has been estimated for its carcinogenic effect on breast cancer. Epidemiological studies do not support any cancer-causing role between atrazine and breast cancer [14].

5.1.4 Colorectal cancer

Colorectal cancer (CRC) is that the second leading explanation cancer-related deaths within the US men and ladies combined. In an Agriculture Health Study (AHS), an investigation was done to elucidate the connection between pesticides and colorectal cancer. Most of the pesticides were not found to have an association with colorectal cancer. For rectal cancer, chlorpyrifos has shown a significant exposure response pattern that was increased by 2.7 fold. Aldicarb was found to be significantly related to carcinoma and highest exposure increased the danger by 4.1 fold. However, strong evidences are lacking to prove a close association between these pesticides and colorectal cancers which requires further studies with detailed mechanisms [14].

5.1.5 Non-Hodgkin lymphoma (NHL)

Non-Hodgkin lymphoma is a various group of malignancies which affects lymph and immune system; it consists of more than 20 different malignancies. Phenoxyacetic acid herbicides, in particular, 2, 4-dichlorophenoxyacetic acid is used in agricultural settings and are found to be associated with 2-8-fold increase of NHL in studies conducted in Sweden, Kansas and Nebraska. Growing evidence specify that exposure to organochlorine pesticides (OCPs) increases the risk of growing NHL. In a meta-analysis, the probability to pesticide exposure for NHL was studied, positive associations for dichlorodiphenyldichloroethylene, hexachlorocyclohexane, chlordane, and hexachlorobenzene were reported. Similarly, a positive association was found in another meta-analysis performed with organophosphate pesticides (OPs) [14].

5.2 ENDOCRINE DISRUPTORS:-

Another potential reaction of pesticide is endocrine inconveniences, specially blocked male hormones that may impact human generation [2]. Pesticide act as endocrine disruptors as it is interfere with endocrine system by blocking/mimicking, displaying, and the hormone in living organism. Mainly they confirmed estrogenic action as affect the reproductive system such as still birth, miscarriages, and abortion infertility etc. endocrine receptor also mimic insulin thereby block the insulin receptor site and cause diabetes mellitus [9]. Vegetable pesticides are connected to blocking testosterone and different androgens, which are crucial for sound male conceptive frameworks. The major part of these endocrine disruptors is fungicides and pesticides that are sprayed to fruits and vegetables which will remain in the food products [13].

5.3 INFERTILITY AND STERILITY:-

Pesticides have been connected to female infertility and male sterility. Extreme exposure to pesticides through food and environment could be the rationale for low sperm levels. Studies shown that there's more chances for having infertility and sterility diseases farmers and people who are more exposed to different pesticides. Sperm count has been declining worldwide and might be the after effect of eating foods which are highly sprayed by different kinds of pesticides [13].

5.4 RESPIRATORY DISORDERS:-

Another concerning symptom of introduction to or ingestion of pesticides are respiratory disarranges, including wheezing, interminable bronchitis, asthma and agriculturist's lung (Figure 6). Standard presentation to pesticides expands your danger for creating respiratory

issues, yet can be decreased with legitimate respiratory assurance and day by day precaution measures [13].In the 1700s, Bernardino Ramazzini was one of the first researchers who informed the probability of respiratory disorders are greater in farmers.

In developing countries like India, most of the pesticide applicators do not use Personal Protective Equipments (PPE) which brings them into direct contact and large doses of pesticide exposure. As most of the pesticides are sprayed in the fields, it generates aerosols that can directly enter into the respiratory system of these agricultural workers. [14]

5.4.1. Asthma

Several clinical and epidemiological studies have reported an alliance between pesticide exposure and symptoms of bronchial hyper-reactivity and asthma. Pesticide exposure may contribute to the exacerbation of asthma by irritation, inflammation, immunosuppression, or endocrine disruption also investigated the relationship between early life exposure to OPs and respiratory outcomes among 359 mothers and children in USA. They concluded that such exposure could lead on to respiratory symptoms according to childhood asthma. In a cross-sectional study covering female farm workers in Africa, the prevalence of ocular-nasal symptoms was positively associated with entering a pesticide-sprayed field. However, most pesticides are weakly immunogenic such their potential to sensitize airways in exposed populations is restricted, while just some pesticides are potent enough to wreck the bronchial mucosa [8].

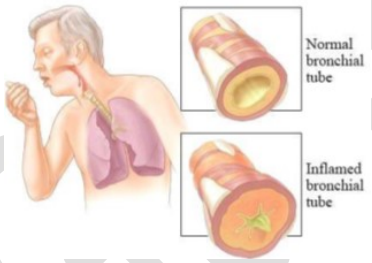


Figure 8 : Respiratory Disorders like Acute Bronchitis, Emphysema, and Coronary Heart Disease

5.5 DIABETES:-

Emerging scientific evidence recommend that diabetes should be affected by exposure to environmental pollutants. Exposure to pesticides, particularly organochlorines and metabolites, is suspected to impart a bigger risk of developing type 2 diabetes and its comorbidities. A systematic review of the literature indicated a positive association between diabetes and serum concentrations of several pollutants (such as polychlorinated dibenzodioxins and dibenzofurans, PCBs, and several organochlorine pesticides. A meta-analysis of 23 suitable articles concluded that exposure to organochlorine pollutants is associated with an increased incidence risk of type 2 diabetes (T2DM), such as polychlorinated biphenyls (PCBs) and p,p'-DDE [8].

5.6 PARKINSON'S DISEASE:-

Etiology of Parkinson's disease (PD) is actually unknown. PD is an idiopathic disease and its pathological feature is loss of pigmented neurons in substantia nigra of the brain. Rotenone a broad spectrum herbicide could also be a known inhibitor of mitochondrial complex I. it had been found that chronic, systemic inhibition of this complex by rotenone causes selective nigrostriatal dopaminergic degeneration, which is said to partial or complete loss of muscle movement because of disruption within the basal ganglia. During a case-control study, 36 frequently used pesticides were studied. The study included 357 occurrences of PD cases and 752 population controls living within the central valley of California. Results showed a strong relationship between these pesticides and etiology of idiopathic PD. during an identical case control study, contribution of gas synthase gene and organophosphate to PD risk was investigated. NOS enzyme produces gas, a pro-oxidant which can damage neurons, is taken under consideration as a candidate for PD. For this stud, 357 PD incident cases and 495 population controls were taken into consideration. With the help of worldwide information system, the household and ambient agricultural OP exposure were accessed. Eight NOS SNPs from the blood and saliva samples of the beyond population were investigated. Their findings indicated that the OP pesticides were more strongly associated with PD among the participants having variant genotype of NOS1 [14].

5.7 REPRODUCTIVE DISORDERS:-

Exposure to certain pesticides in sufficient doses may increase the danger of sperm abnormalities, decreased fertility aberrant abortions, defects in birth and fetal growth retardation. Carbosulfan, a carbamate pesticide has shown a rise in chromosomal aberrations (CA), bone marrow micronucleus formation (MN), and sperm abnormality in mice. in the least three acute doses utilized in the study (1.25, 2.5 and 5 mg/kg) there was a concentration-dependent increase within the CA, micronucleated polychromatic erythrocytes (PCEs) and sperm head abnormalities, but didn't affect the entire sperm count. These findings indicate carbosulfan as a potent genotoxic agent and will also act as a potent reproductive cell mutagen. Cypermethrin, a pyrethroids insecticide was evaluated for its toxic potentials on reproductive and fertility parameters within the man

Sprague-Dawley rats. These animals were exposed to water containing different doses of cypermethrin in ppm concentrations for 12 weeks. A big decrease in fertility was recorded in male rats, which ingested cypermethrin at a degree of 13.15 and 18.93 mg/per day. a big reduction within the number of viable fetuses has occurred in females impregnated by the treated male rats. A weight gain in testis and seminal vesicles and reduce in epididymal and testicular sperm counts was also observed within the treated animals. To review the underlying molecular mechanism, expression of androgen receptor and levels of testosterone were analyzed and both were significantly reduced in rats fed with cypermethrin. Thus cypermethrin has potential to induce impairments of the structure of seminiferous tubules and spermatogenesis in male rats. Another extensively used, non-selective herbicide paraquat, has also shown to cause genotoxicity in mouse somatic and germ cells. The mouse were exposed singly or multiple times. Single time exposure didn't cause any chromosomal anomaly (CA), but with multiple exposures there was a rise in CA. The sperm shape abnormality was also increased when animals were treated at three stages of cell development: spermatozoa, spermatid and preleptotene spermatogonial cells [14].

5.8 LEUKEMIA:-

Exposure to pesticides is one among the foremost important causes of leukemia. In some previous studies, the effect of pesticide exposure on childhood leukemia was investigated. From 12 case–control studies of childhood leukemia, reported that ORs for acute lymphocytic leukemia (ALL) for 3 sorts of pesticide exposure, shortly before conception, during pregnancy, and after birth, were 1.39, 1.43, and 1.36, respectively. During a case–control study in Iran, an occupational farmer was at significantly increased risk of developing leukemia as compared to other jobs, especially for his or her children thanks to exposure to pesticides. Meta-analysis of the 40 studies in France showed that the danger of lymphoma and leukemia increased significantly in children when their mother was exposed during the prenatal period. Exposures during pregnancy to unspecified residential pesticides, insecticides, and herbicides were positively related to childhood leukemia. Found that such exposures during pregnancy were positively related to childhood leukemia in their systematic review supported meta-analysis of previous observational epidemiologic studies [8].

5.9 BIRTH DEFECTS:-

Birth imperfections from pesticide usage are another pathetic situation for subsequent generation. There are many evidence for the pesticide exposure to birth defects, fetal death and altered fetal growth. The connection amongst pesticides and birth deformities has been fixing to utilization of pesticides which won't to kill and control garden insects, ants, mosquitoes and insects. These powerful chemicals are wont to control these insects, but indirectly it's affecting fetus and results in increase the danger for oral clefts, ectoderm defects, heart defects and limb defects. Presentation to pesticides and bug sprays need to be maintained a strategic distance from regardless of what amid pregnancy [13].

5.10 ALZHEIMER'S DISEASE:-

High exposure to pesticide causes neuroinflammation and neuropathology in human bearings and results in Alzheimer's disease (Figure 6.3). The progression of AD takes place over 1-3 decades and thus the calculable time between triggering events and onset of the illness ranges from a few years to several decades, creating it tough to pinpoint explicit causal factors. The usage of synthetic pesticide, DDT caused many sorts of side effects in human bearings, especially Alzheimer's disease. DDT residues can remain within the environment for many years within the sort of DDE, weakened of DDT. Studies and researches proven that the patients with Alzheimer's disease had DDE in their bodies. But thus far it's not proven that DDT exposure causes Alzheimer's disease. Most of the pesticides are strongly associated with neurotoxicity, neurodegenerative disease and other brain disorders, like Parkinson's disease. The author's note that additional analysis should be done to understand prove the link between pesticides and Alzheimer's [13].

Figure 9 Cross sections of the brain show atrophy, or shrinking, of brain tissue caused by Alzheimer's disease

5.11 COGNITIVE EFFECTS:-

Despite growing evidence associated with to pesticide exposure to neurological diseases, epidemiological data on neurobehavioral consequence of chronic pesticide exposure are limited. Plasma concentrations of three OC pesticides (p, p'-DDE, trans-nonachlor, and hexachlorobenzene) were measured among 989 men and ladies aged 70 years within the Prospective Investigation of the Vasculature in Uppsala Seniors (PIVUS), Sweden. The results showed that individuals with high levels of OC had about 3 time's higher future risk of cognitive impairment than those with low levels of OC [8].

5.12 GENETIC DAMAGES:-

Genetic damages caused by pesticides are often broadly classified into three major classes namely

1. Pre-mutagenic damages like DNA strand breaks, DNA adducts, 2. Gene mutations like insertions, deletions, inversions and translocation, 3. Chromosomal aberrations, including loss or gain of whole chromosome, deletion or breaks, and chromosomal segments or rearrangements.

It is widely established incontrovertible fact that ROS production is related to DNA damage, lipid peroxidation and alter in mitochondrial membrane potential. Enzymes involved in pesticide detoxification produces electrophilic compounds which are carcinogenic epoxides, these events can also render the repair machinery less efficient leading to premature aging and apoptosis. ROS imbalances can also recruit aberrant proteins which can leads to imbalance of the signaling pathway resulting in tumorigenic processes [14].

5.13 OXIDATIVE STRESS:-

Living in an oxygenated environment is extremely challenging, it took many years for the living organisms to evolve effective strategies to detect and neutralize metabolites of molecular oxygen, which are referred to as ROS. Oxidative stress may be a condition when there's an imbalance between pro-oxidant and antioxidant homeostasis that leads to the formation of toxic reactive oxygen species. These ROS (Reactive Oxygen Species) can cause damages to lipids, proteins and DNA. ROS are very unstable with very high reactivity thanks to unpaired electrons, to realize electrons; they attack nearby molecules which ends up in their damage. All the nearby biomolecules are susceptible for his or her attack, but lipids get severely affected. Generation of ROS is related to the danger of cancer. ROS can influence the expression of the many genes involved in inflammation; cell transformation; and tumor necrobiosis or survival, proliferation, invasion, angiogenesis, and metastasis. Oxidative stress is additionally found to be closely related to the pathogenesis of the many neurodegenerative diseases like Parkinson's disease (PD) and Alzheimer's disease (AD). ROS is additionally found to be related to ageing, chronic inflammation and cancer. One among the modes for the toxicity of organophosphate pesticides is that the formation of ROS [14].

5.14 EPIGENETIC EFFECTS:-

Epigenetics is that the study of heritable changes in organic phenomenon that happens with none change within the DNA sequence. Environmentally induced changes in gene regulatory mechanisms correspond with many diseases including cancer. Epigenetics majorly contains changes within the DNA methylation patterns, histone modifications and differential expression of non-coding RNAs, which causes variations in organic phenomenon. Research during this area has revealed many important relations between epigenetic changes and pathogenicity of several diseases including cancer. Environmental factors are found to be related to epigenetics. Evidence from animal studies supports the role of environmental epigenetics in disease vulnerability. Pesticides are environmental contaminants and now these chemicals are found to be related to epigenetic modifications thus pertaining effects on human health [14].

6 DIFFERENT CLASSES OF PESTICIDE AND ITS IMPACT IN HUMAN HEALTH EFFECT AND THEIR TREATMENT [3].

Table 6.1: Different classes of pesticide and its health effect

Pesticides	Exposition	Sign and symptom	Treatment
Organo-phosphorus	Skin, conjunctiva, gastrointestinal tract and lungs.	Muscarinic syndrome and nicotine syndrome, resulting of excess	Maintenance of vital function and cholinesterase levels. Avoid the use of partasympathomimetric agents.
Carbamets	Lungs, gastrointestinal tract and skin	Miosis, salivation, sweating, tearing, behavioral change	Maintance of vital function and cholinesterase levels. Avoid the use of partasympathomimetric agents.
Organochlorine	Lungs, gastrointestinal tract and skin	Dizziness, headache, nausea, vomiting, diarrhea, muscle weakness, mental confusion, anxiety	Maintance of vital function and administer diazepam and phenobarbital to control seizures.
Pyrethrine and pyrethroids	Lungs, gastrointestinal tract and skin	In coordination prostration, drooling irregular movement of limbs and hypersensitivity to stimuli	Decontamination of the skin and eyes, besides basic maintenance of vital functions.
Triaznes	Skin, eye, nose and gastrointestinal tract		
Phenoxy derivative	Lungs, gastrointestinal tract		
Glycine derivatives	Gastrointestinal tract and skin		

7 CONCLUSION

Currently, thanks to the need for large-scale cultivation, the pesticides are an integral a neighborhood of our life. It's difficult to eliminate them from agriculture within the near future, but they need to be used with care and caution. Pesticides are utilized in agriculture to protect plants from pests; therefore, agricultural products are increased via the usage of these chemicals. Although their application plays an important role in crop productivity.

Although pesticides are developed to prevent, remove, or control harmful pests, concerns of the hazards of pesticides towards the environment and human health are raised by many studies. There are indeed many inherent problems in conducting large-scale experiments to directly assess the causation of the human health problems related to the use of pesticides. However, the statistical associations between exposure to certain pesticides and thus the incidence of some diseases are compelling and can't be ignored. It is often observed that the farmers don't follow appropriate safety precautions with regard to pesticide application, large amounts of pesticides are inappropriately employed by these farmers, leading to several human health disease. To safeguard human life and environment from the toxic effects of pesticides, adequate steps need to be taken. Now it is a well-established undeniable fact that there is the foremost need to breakthrough towards our mother earth by nurturing it by going for the organic farming system. A solution to the present havoc is that the organic farming, an environmental friendly agricultural approach which ultimately results in proper human health. Though the govt of India has been making concerted efforts to encourage farmers and other people regarding organic produce and merchandise, but it is not resulted in bridging the gap between the demands and provide of organic product within the market. It's been administered that organic food consumption is increasing in India and this is often evident from the particular incontrovertible fact that plenty of organic food stores are prompt up in India.

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