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Review Article

AGRO-PESTICIDES AND ANDROLOGY

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ABSTRACT

The extensive use of pesticides in agricultural practices has resulted in contamination of food and food resources. A number of animal species including humans have accumulated traces of pesticides through food chain. These toxic chemicals influence the physiology of numerous non-target species including man. The effects of many pesticides have been analyzed using *in vivo* and *in vitro* techniques and degenerative changes induced by the toxic chemicals have been reported even at nanomolar concentrations. The adverse effects on the male reproductive system include direct damage of the cells or disruption of the developmental pathways directly or through endocrine modifications. Toxic pesticides are known to cause Germ cells disintegration, loss of Leydig cells, atresia in Sertoli cell, degeneration of seminiferous tubules, alternation in spermatogenesis, depletion in semen quality, teratospermia and endocrine disruption. For ensuring pesticide free food and food supplements it is recommended that biological alternative should be explored to safeguard good health of plants, animals and humans.

Keywords: Testis, Germ Cells, Leydig Cells, Seminiferous Tubule, Pesticides, Endocrine Disruptors, Semen.

INTRODUCTION

The increased use of pesticides since the Green Revolution of the 1960s has introduced new hazards to human being and animals [1]. A broad spectrum of pesticides are extensively being used in agriculture to enhance production [2], minimize losses, protect food grains from fungal contamination, repel ecto-parasites, control vector borne diseases, repel household pests and as anti-helminthes [3] with limited guidelines and restrictions. The extensive use of pesticides in agricultural practices has resulted in contamination of food and food resources. These toxic chemicals influence the physiology of the numerous non-target species including man (Figure 1). A number of animal species included humans have accumulated traces of pesticides through food chainor by occupational exposure [4].

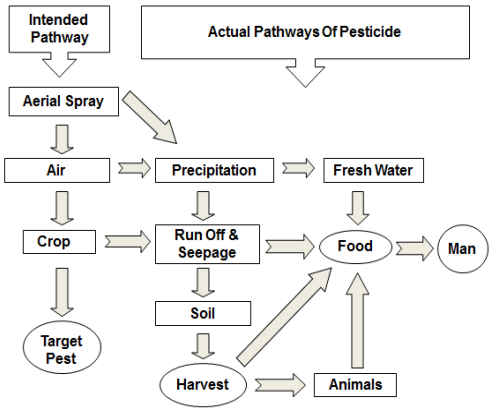

Fig. 1: Flow diagram depicting the intended and actual pathway of the route of exposure of pesticides to target and non-target species (Sharma and Goyal unpublished work).

The reproduction is must to ensure continuity of species on the earth. The testes accomplished two essential functions of reproduction, the spermatogenesis or gamete production in the seminiferous tubules and synthesis and secretion of sex hormones by the interstitium. These two testicular compartments work in collaboration with hypothalamus-pituitary-gonadal axis for normal spermatogenesis to occur [5]. Any alteration in the complex regulation of hormone production and spermatogenesis can result in impairment or cessation of spermatogenesis leading to infertility (Figure 2).

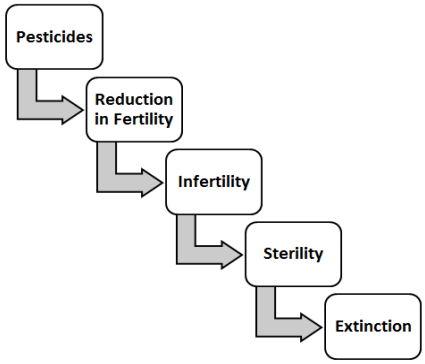

Fig. 2: Flow diagram depicting cascade start by pesticides leading to infertility and extinction (Sharma and Goyal unpublished work).

The pesticides affect the male reproductive processes by inducing direct damage to the cells or through interfering with developmental pathways. .Fecundity of a species is an index of its success in habitat in the specific set of environmental conditions. Pesticides have exerted extra-ordinary pressures on the physical environment and natural resources leading to decline in fertility and increase in neonatal malformation which have to threaten the very existence of human race [6].

The long-term hazard of pesticides on reproduction of animals cannot be ignored and it is therefore in recent years, there has been growing concern about the toxicity of a number of pesticides on the male reproductive system. This review is based primarily on the recent toxicological studies conducted in laboratory conditions using *in vitro* and *in vivo* techniques, and studies in occupational settings in order to explore the relationship between exposures to pesticides agents and the possible effects on Andrology.

Pesticides and their toxicity

Pesticidesare natural or synthetic agents intended for preventing, attracting repelling or controlling any pest including unwanted species of animals, plants or microbes during production, storage,

transport, distribution and processing of food, agricultural commodities and animal feeds. Pesticides also include chemicals which may be administered in animals to control of ectoparasites in festation [7]. The earliest pesticides were salts, sulfurous rock, and extracts of tobacco, red pepper etc. Upto 1940s. Petroleum oils, heavy metals, and arsenic were used liberally to control unwanted pests and weeds subsequently organic synthetic pesticides, the most famous of which was DD Temployed on large scale [8]. The measurement of pesticide toxicity with greater accuracy is crucial to ensure how chemicals can be safely introduced.

Classification of pesticides by the target pest is most familiar. For example, insecticides are pesticides that target insects, and herbicides target plants, fungicides kill fungi, rodenticides are used to control rodent infestation and fumigants used as repellents. More advance method for classification of pesticides is to classify them according to their chemical properties. This includes Organophosphates and Carbamates (inhibit cholinesterase enzyme), Pyrethroids and Chlorinated Hydrocarbons (Destabilize nerve cell membrane), Macrocyclic Lactone (affect GABA dependent chloride ion channels and inhibits nerve transmission), insect growth regulators (Chitin synthesis inhibitors or juvenile hormone mimics), Soaps and Oils (damage the waxy layer of the exoskeleton and cover breathing pores) and Chloronicotinyls (inhibit reception of nerve impulse) [8].

Most recently, the pesticides are classified on the basis of toxicity. Toxicity is the inherent poisonous nature or how dangerous a pesticide is under experimental conditions. Toxicity is commonly expressed as LD_{50}, the dose required to kill 50% of a pest population. Units used are mg/kg, milligrams of toxicant (active ingredient) per kilogram of body weight. This can be measured as either acute or chronic toxicity. Acute toxicity refers to immediate effects of a single, short-term exposure to a pesticide whereas chronic toxicity is repeated exposure to a pesticide. In addition, LD_{50} may be determined based on how a pesticide enters the body, such as orally (ingestion), dermally (skin), or by inhalation (breathing) (Figure 3). This information is then extrapolated to humans. The lower the LD_{50} value, the more toxic is the pesticide [9]. Based on physical and chemical properties of pesticide include Molecular Weight, Color, Form, and Odor, Water Solubility, Partition Coefficient (Kow), Soil Sorption Coefficient (Koc), Vapor Pressure and LD_{50},the pesticides are classified into four generations [9]:

1st Generation Pesticides (Highly toxic)

The chemical packets/containers are labeled as 'Danger/Poison'. In addition, a skull and cross-bones symbol is required on labels for all pesticides of this category, which is described as highly toxic. These pesticides have an acute oral LD_{50} range of 0 to 50 mg/ kg. It primarily includes the inorganic compounds like lead, Mercury and Arsenic etc. They have high accumulation potential.

2nd Generation Pesticides (Moderately toxic)

Pesticides in this category are labeled 'warning' and described as moderately toxic having acute oral LD_{50} range of 50 to 500 mg/kg. It primarily includes the synthetic compounds like DDT. Currently there are thousands of synthetic pesticide products made up of more than 1,000 different chemicals and combinations. They have comparatively less accumulation potential for inorganic compounds.

3rd Generation Pesticides (Slightly toxic)

These are slightly toxic pesticides labeled as 'caution' and have acute oral LD_{50} range of 500 to 5000 mg/kg. It includes insect pheromones and insect growth regulators which disrupt the normal activity of the endocrine or hormone system of insects and other pests, affecting the development, reproduction, or metamorphosis of the target insect. Some compounds are chitin synthesis inhibitors which target exoskeleton.

4th Generation Pesticides (Practically non-toxic)

These are very low toxicity pesticides labeled as 'Caution' and have acute oral LD_{50} greater than 5000 mg/kg. These are mainly product of herbal origin and act as the natural control mechanism.

The non-target mammals including human exposed to pesticides by ingestion of contaminated food product, inhalation of toxic chemical at occupational places and via skin absorption during working with them.

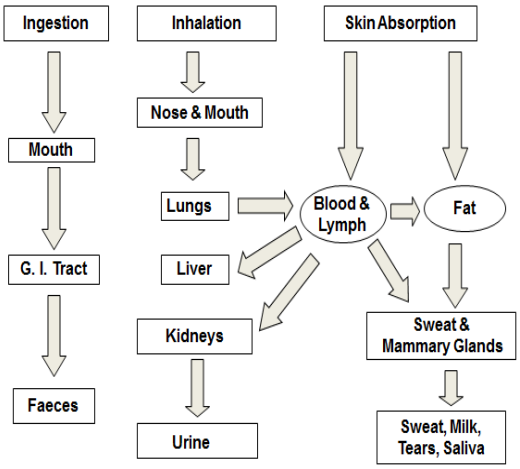

Fig. 3: Various modes of exposure of pesticides and their metabolic route through different organs of the body till their excretion (Sharma and Goyal unpublished work).

Any stage of reproductive cycle including gametogenesis copulation, fertilization, pre-implantation, implantation, embryonic period, foetal period, maternal-placental-foetal relationship, parturition, suckling and post-natal development to puberty may be vulnerable to toxic agents. Pesticides toxicity manifestation may occur in form of the interference with libido, estrous, oogenesis, spermatogenesis, abnormal mating behavior, embryocidal effect, still births, teratogenicity and other birth defectsdepending on the toxicity dose, exposure duration and metabolic rates of animals (Figure 4)[10]. The pesticides affect the male reproduction by interfering with normal physiology of reproductive system. The pesticides are known to cause adverse effect on male reproduction by affecting normal physiology of various parts of the reproductive system. .A number of commercial chemical agents, including many pesticides and combustion products from plastics, can have pronounced estrogenic effects on animals [11-12]. Human fertility seems to be waning in recent years. Although undescended testes can be moved to their correct location in the scrotum by surgical means, boys with this condition at birth often suffer fertility difficulties later in life. Across human populations, sperm counts appear to be declining. In 1940 the average human density of sperm was 113 million per millimeter of semen; in 1990 this figure had dropped to 66 million sperm per millimeter of semen. Researchers also estimate that the volume of semen produced by men has dropped about 20%during the past 50 years, reducing sperm count per ejaculation even further [13-14].

Germ cells

The germ cells determine the fertility potential of an individual because they form the spermatozoa. Failure of the germ cell to survive during the development may lead defective or no gamete production and hence can lead to infertility [15].

The pycnotic nuclei, chromolysis, vacuoles of various shapes and sizes were observed in the cytoplasm of germ cells and somatic cells on exposure of Endosulphan [16]. Chlorpyrifos cause accumulation of exfoliated germ cells within the affected tubules and appearance of cytoplasmic vacuolation [17]. The Methyl parathion also caused a pronounced cytoplasmic vacuolization and pycnosis in germ cells [18].

Deformed and disordered arrangement of germ cells was observed after exposure of Cypermethrin [19], Diazinon [20] and Malathion [21]. Sloughing off germ cells was recorded in many experiments after exposure of different pesticides (Figure 5) [22-24].

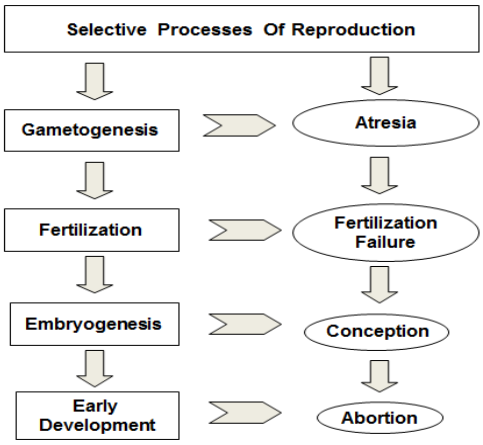

Fig. 4: Figurative representation of various events of reproduction and screening of defective/altered and damaged cells at each step, making this phenomenon a most sensitive index of toxic insult (Sharma and Goyal unpublished work).

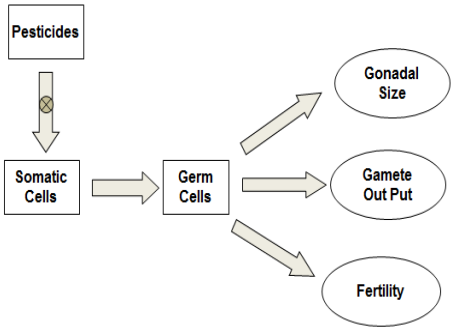

Fig. 5: Diagram representing how pesticide affects the gonadal size, gamete output and fertility via disturbing the germ cells and somatic cells function (Sharma and Goyal unpublished work).

The exposure of Endosulphan [25], Atrazine [26], Methyl Parathion [18, 27], Octylphenol [28], Diazinon [20], Carbaryl [29], Cyhalothrin [30], Malathion [31] and Cypermethrin [19]resulted in the decrease in the numbers of germ cells in testicular tissue.

Seminiferous tubules

The seminiferous tubules fulfill essential functions of spermatogenesis to producing male gametes [5]. .The process of spermatogenesis is started with the proliferation and mitosis of spermatogonia to form primary spermatocytes in mammals which after this undergo meiosis to form round spermatids and get differentiated into mature sperms [15]. The degeneration in seminiferous tubule is marked by decreased tubule diameter, increased lumen diameter and sloughing of cells inside tubule. Any factor which causes degeneration in seminiferous tubule leads to loss of fertility potential in males [5].

The exposure of Atrazine [32] Dieldrin [33], Methyl Parathion [18, 27], Endosulphan [3, 25],Octylphenol [28], Malathion [34], Permethrin, Pirimiphos Methyl, Bendiocarb [35], Cyhalothrin [30] and Profenofos [36] leads to reduction in the diameter of seminiferous tubule. The lumen diameter of seminiferous tubule increased after exposure of Methyl Parathion [18], Profenofos [36] Imidacloprid [37] and Dimethoate [38]. Permethrin [39] and Cyfluthrin [40] also caused the reduction in seminiferous tubule lumen diameter in adult male Wistar rats on exposure at a dose level of 500 mg/kg body weight. The disorganization of seminiferous tubule structure and vacuolization was observed after exposure of Endosulphan [4, 16], Malathion [23], Cypermethrin [19],Dimethoate [38], Chlorpyrifos [41], Imidacloprid [37] and Methyl Parathion [18].

The Carbaryl exposure distorted the shape of seminiferous tubules, disturbed the spermatogenesis, leads to accumulation of cellular mass in the lumen of tubules, oedema of the interstitial spaces, loss of sperms of varying degreesand detachment of germ cells from the basement membrane of seminiferous tubules of testis [42-43]. Dimethoate caused dose related testicular damage characterized by moderate to severe seminiferous tubule degeneration, sloughing, atrophy, germ cell degeneration and partial arrest of spermatogenesis in rats [44].

Deltamethrin were found to cause defects included severe destruction of seminiferous tubule with multiple rupture of the germinal epithelial layersand complete spermatogenic cells degeneration, presence of edema, hyalinizationand necrotic cells inside the degenerative tubule, increase in apical sloughing and vacuolated degeneration of the spermatogenic cells, and exfoliation of spermatocytes in the lumen of some tubule [45].

Spermatogenesis

Spermatogenesis is the process by which mature spermatozoa is develop from germ cell inside seminiferous tubule. Damage to the spermatozoa or their precursors can result in reversible or irreversible impaired spermatogenesis, depending on the stage of differentiation affected by the chemical. Damage to spermatogonia causes impaired sperm production and decreased fertility because of changes in the cell number, structure, motility, or viability of spermatozoa [46].

Exposure of Dimethyl Methylphosphonate leads to lack of spermatogenesis due to degeneration, vacuolization and necrosis of cells in the spermatogenic tubules [47]. Sumithio NP 25/2.5 EC induced damage to the seminiferous tubules by causing separation of spermatogenic cells from the germinal epithelial membrane and leads to hypospermatogenesis due to decreasing number of the spermatogenic cells [48].

The effect of Atrazine on spermiogenesis observed by the Sharma *et al.* (2012) and reveled that at Golgi phase, degenerated nuclear membrane occurred in spermatid. In cap phase disruption of nuclear membrane, abnormal vesicles and small clumps of chromatin material were also observed in spermatid [49]. Imidacloprid [37] exposure caused swollen nucleus, increased perinuclear space, varied size and shape of mitochondria, degeneration of spermatids, margination of chromatin material and apoptotic nucleus.

Masouleh *et al.* (2011) have been observed that exposure of Diazinon induced decline in number of spermatocytes and spermatids [50]. Sperm production was decreased significantly on exposure of Cypermethrin at dose level 30 mg/kg body weight [19] and Dicofolat dose level 4.19 mg/kg body weight in male rats [51]. Exposure of Monocrotophos at a dose level of 1.5mg/kg [52] causes losing in arrangement of spermatogenic cells, sloughed spermatids and decrease in number of spermatids in male rats.

Extensive sloughing, vacuolization in the cytoplasm and condensed and pycnotic nuclei, Chromolysis and hyalinization with nuclear fragmentation was observed in spermatogenic cells on exposure of Endosulphan [25] and Atrazine [53].

Semen quality

The Semen quality is determined by the semen volume, sperm motility and by numberof normal sperm. The good quality semen enhances the chances of fertilization and semen with depleted quality are generally fail to cause the fertilization [54].

Sharma *et al.* (2008) observed that the ejaculate volume was reduced drastically, liquification time increased, total sperm count and sperm motility decreased in pesticide exposed workers [55] and in spray paint exposed workers [6]. The atrazine [56] and Fenvalerate [57] were found to decrease the sperm number, motility and overall semen quality in exposed workers. The semen volume, sperm concentration, total sperm count, motility, vitality and morphology decreased in rice farmersspraying pesticides without personal protective equipment and training [58]. The molecular mechanism involved in this impairment needs to be explored further.

Ethylene dibromide (EDB) decreases the sperm count, viable and motile spermatozoa, increases in semen pH and morphological abnormalities among workers of papaya fumigation industry [59-60]. Decreased sperm motion, sperm progression and beat cross frequency; and increased abnormality rate of viscidity and coagulation was observed in fenvalerate exposed occupational workers [61]. Studies of the semen sample of Carbaryl manufacturing factory workers have shown the reduced quantity and quality of sperm [62]. .Whether this decline is due to reduction in antioxidant or generation of free radicals needs to be studied further.

Sperm morphology is one of important parameter for evaluation of male fertility status. .Spermatozoon is considered normal when there is no visible defect head, acrosome, neck, midpiece and tail. The sperm with abnormal morphology (Teratozoospermia) is not able to made fertilization because they fail to reach female reproductive tract, to capacitate or to penetrate the zona pellucida [54].

Occupational exposure to spray paints [6] and pesticides [55] induce abnormalities in sperm morphology including oligospermia, aflagellate, biflagellate, pin head, fused head, swollen head, pointed head, micro headed, distorted middle piece, bent head, coiled tailed, round headed and amorphous headed sperms [6]. Endosulphan exposure at a dose level of 3 mg/Kg body weight impart abnormalities in male albino rats sperms like abnormal flagellar bending at mid piece, thickening of mid piece region, loss of acrosome from the head region, coiled and bent tail [63]. .The Permethrin, Pirimiphos Methyl, Bendiocarb [35] and Malathion [21, 64, 31] found to affect the sperm tail but defect in head morphology was not observed. The altered physiological components need to be studied at molecular level so as the treat such cases.

A single dose of Atrazine imparted the morphological alterations in spermatids by causing pycnosis, chromatolysis, hyalinization, dislodging, condensation, vacuolization and fragmentation [49]. Decreased sperm motility, reduced epididymal sperm count along with increased morphological abnormalities in head, neck and tail regions of spermatozoa were observed on exposure of Carbofuran [65], Monocrotophos [52] and Endosulphan [66-67]. Similar set of pathological effects of pesticides on the reproductive system of experimental animals had been recorded in many experiments [68-71].

Oligozoospermia and azoospermia in workers of a DBCP (dibromochloropropane)-producing factory was observed by Whorton *et al.* (1977) [72]. Semen samples of Chlordecone (Kepone) producing chemical plant workers revealed oligozoospermia with predominating abnormal and nonmotile spermatozoa [73].

The sperm count, viability, motility and density were reduced by the exposure of Dimethoate [44], Methyl Parathion [74], Lindane [75], Chlorpyrifos [76, 41, 57], Dichlorvos [29], Acephate [77],Diazinon, Profenofos [76] and Dimethoate [61]. Exposure to Dieldrin [33] at a dose level of at 3 mg/kg body weight induced a dose-dependent decrease in the number and the mobility of epididymal spermatozoa.

Sertoli cell

The main function of Sertoli cells is to create a favorable environment for germ cell proliferation and maturation. FSH controls spermatogenesis via direct stimulation of Sertoli cells. It also stimulates inhibin B synthesis in the Sertoli cells. Both testosterone and inhibin B regulate GnRH and LH or FSH secretion through a negative feedback loop [5].

The functional impairment, damage, or destruction of Sertoli cells is also very detrimental to spermatogenesis because these cells are essential for the proliferation and differentiation of all spermatogenic cells. Because Sertoli cells do not regenerate after puberty, extensive damage can lead to irreversible impairment of spermatogenesis [78].

Benomyl affects the microtubules and intermediate filaments of the Sertoli celland causes sloughing of germ cellswhich lead to abnormal elongated development of the spermatids head [79].

Atrazine [26], Endosulphan [4, 16, 25], Dimethoate [38], Carbofuran [65], Malathion [21, 31], Cypermethrin [19], Permethrin, Pirimiphos Methyl and Bendiocarb [35], Chlorpyrifos [17], Methoxychlor [80] and Endosulphan [25]exposure decreased the Sertoli cells number.

Leydig cells

The Leydig cell performed the synthesis and secretion of sexual hormones in the interstitium. LH and FSH are produced by the pituitary gland under the influence of pulsatile secretions of GnRH released by the hypothalamus. LH stimulates Leydig cells in the testes to produce testosterone, which is an important hormone for spermatogenesis through the stimulation of Sertoli cells in the seminiferous tubules [5]. The function of Leydig cells can be impaired by pesticide exposure, the result being decreased testosterone concentrations in serum and testicular tissue [81].

The elongation of Leydig cells indicative of hyper-activity was recorded on the exposure of Profenofos [76]. Permethrin, Pirimiphos Methyl and Bendiocarb [35] exposure caused swelled interstitial matrix and aggregation of Leydig cells. Leydig cells became loose and hyaline in natureand, number of pycnotic and condensed nuclei enhanced on exposure of Endosulphan [25]. Deformed nucleus was noted in Leydig cells after the exposure of Cypermethrin [19].

Declining in number of Leydig cells occurred after exposure of Diazinon [22], Atrazine [24], Endosulphan [82], Profenofos [36], Octylphenol [28], Dicofol [51], Nonylphenol [83], Cyhalothrin [30], Imidacloprid [37], Malathion [31] and Cypermethrin [19].

Diazinon at a dose level of 10mg/kg body weight disturbs the Leydig cell steroidogenesis and hence synthesis oftestosterone in male albino rats [84]. The decrease of plasma testosterone levels on exposure of Malathion suggested that Malathion affected the Leydig cells [21, 85]. Other organophosphoric compounds had been reported to inhibit the non-specific esterase activity in Leydig cells, decreasing testosterone production [86].

Endocrine disruption

An endocrine-disrupting chemical is defined as an exogenous agent that interferes with the synthesis, storage and release, transport, metabolism, binding, action, or elimination of natural blood-borne hormones that are responsible for the maintenance of homeostasis and the regulation of developmental processes in the body [87-88]. Endocrine disruptors can exert their effects in many ways. They can either bind to the hormone's receptor and mimic the hormone, or block the action of the hormone.

Alternatively, they can stimulate or inhibit the enzymes responsible for the synthesis or clearance of a hormone, and thereby give rise to an increased or decreased action of the hormone (Figure 6)[89]. Human exposure to endocrine-disrupting chemicals occurs through multiple pathways with diet, drinking water, air, and skin as the most common routes of uptake of these chemicals into the body [90]. Chronic administration of Lindane results in endocrine disruption in birds as well as in mammals [91].

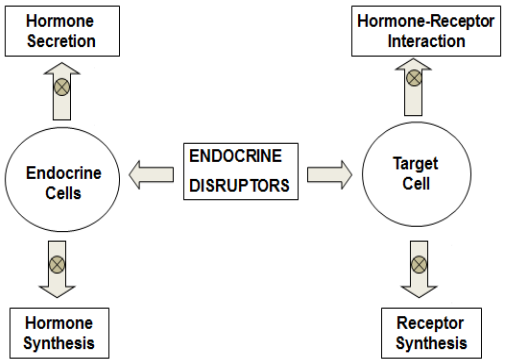

Fig. 6: Diagram showing endocrine disruption by pesticides via blocking various endocrine pathways (Sharma and Goyal unpublished work).

Sex hormone disruptors

Many pesticides have now been found to have estrogenic or anti-androgenic activity, and some bind to the androgen or estrogen receptors. Those which have been found to bind to the estrogen receptor include: Orthophenylphenol, DDT, Methoxychlor, Chlordecone, Dieldrin, Endosulphan, Hydroxychlordene and Toxaphene. Methoxychlor and DDT were found to cause accelerated puberty and accelerated loss of fertility [89]. Anti-androgenic pesticides that bind to the androgen receptor include the Dicarboximide, Vinclozolin, Procymidone, DDE, and Linuron. TheProcymidone caused intersex characteristics and Linuron was found to reduce seminal vesicle weights and delayed puberty [89].

Hormone transport and clearance

DDT [92], Endosulphan and Mirex [93] are potent chemicals which degrade endogenous androgens and results in suppressed androgen- receptor-mediated activity [5]. .Similarly, Lindane has been reported to increase the clearance of estrogens [94].

Hormone receptor recognition and binding

The pesticides can interact with the nuclear estrogen receptors and androgen receptors and disrupt the natural ligand-receptor binding by acting as agonists to the natural ligand [95]. Examples of pesticides acting as estrogen agonists are Endosulphan, toxaphene, Dieldrin, DDT, HCH, methoxychlor, Chlordecone, and Dimethoate [96-100]. Endocrine-disrupting chemicals that may have anti-androgenic activity are, Vinclozolin, DDE and DDT [101-104].

Procymidone possesses weak anti-androgenic activity and may induce hypergonadotropism [105]. Long-term exposure of Procymidone is suggested to inhibit the negative feedback exerted by androgens on the hypothalamus and/or the pituitary, thereby causing hypergonadotropism [106]. Linuron known to binds with human AR (hAR) and inhibits DHT-induced gene expression [107]. Vinclozolin have anti-androgenic properties and it compete for androgen binding to AR and inhibits DHT-induced transcriptional activation by blocking AR binding to androgen response elements in DNA [108].

Star protein expression impairment

The Dimethoate, Roundup, Lindane [109] and Methoxychlor [110] reduce the expression of steroidogenic acute regulatory (StAR) protein. This particular protein mediates the transfer of cholesterol from the outer to the inner mitochondrial membrane, which is the rate-limiting and acutely regulating step in steroidogenesis. By blocking the expression of this protein, Leydig cells produce less testosterone *in vitro* [5, 111-112]. .Chlorpyrifos showed marked reduction in epididymal and testicular sperm counts in exposed male rats and a decrease in serum testosterone concentration [113].

Exposure of Malathion [21, 114-118], Endosulphan [63, 66, 82], Dieldrin [33],Acephate [77, 28], Monocrotophos [52], Dicofol [51], Methoxychlor [119], Methyl Parathion [27], Chlorpyrifos [41,17], Carbaryl [29], Nonylphenol [83], Carbofuran [120], Imidacloprid [37], Carbendazim [121] and Cypermethrin [19] also suppressed the level of testosterone. .The agro-pesticides exposed farmers had significantly lower serum testosterone and higher androstenedion

P450scc enzyme impairment

P450scc is an enzyme that catalyzes the first reaction in the testosterone biosynthesis pathway: the conversion of cholesterol to pregnenolone. The Dimethoate, Roundup, 2, 2-bis (p-hydroxyphenyl) - 1, 1, 1-trichloroethane, Methoxychlor, and Ketoconazolereduce the P450 cholesterol side-chain cleavage enzyme (P450scc) activity [5, 122-123]. A recent study suggests that Endosulphan exposure may delay sexual maturity and interfere with hormone synthesis in male children [124].

Other enzymes impairment

The imidazole fungicide ketoconazole and Methoxychlor has been shown to reduce multiple enzyme activities in testosterone biosynthesis, such as 17, 20-desmolase, 17α-hydroxylase, and 17β hydroxysteroid dehydrogenase, the result being a decrease in testosterone concentrations [110, 125-127]. Mancozeb exposure leads to increased serum cholesterol level [128]. Ketoconazole, TBT and Fenarimol had been found to block steroid synthesis by inhibiting aromatase activity [89].

CONCLUSION

Pesticides are extensively being used to boost agriculture production. Apart from affecting target species, these toxic chemicals also influence physiology of numerous non-target species including man directly or through the food chain. The effect of various pesticideslike Endosulphan, Chlorpyrifos, Methyl parathion, Cypermethrin, Diazinon, Malathion, Atrazine, Octylphenol, Carbaryl, Cyhalothrin, Dieldrin, Permethrin, Pirimiphos Methyl, Bendiocarb, Profenofos, Imidacloprid, Dimethoate. Cyfluthrin, Chlorpyrifos, Deltamethrin, Dimethyl Methylphosphonate, Monocrotophos, Fenvalerate, Lindane, Dichlorvos, Acephate, Dicofol, Nonylphenol, Roundup, Methoxychlor, Ketoconazole, Mancozeb, DBCP, Chlordecone, Ethylene dibromide, Carbofuran and Acephate on reproductive system was observed even at Nano molar concentrations.

They adversely affect the male reproductive system by causing germ cells disintegration, loss of Leydig cells, atresia in Sertoli cell,degeneration of seminiferous tubules, the alternation in spermatogenesis, depletion in semen quality, teratospermia and endocrine disruption. It is therefore recommended that biological alternative should be explored as an alternative to these toxic agents. It is the time to devise and develop environmental friendly technology and switch over to our culturally rich practices for better tomorrow.

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