We are IntechOpen, the world's leading publisher of Open Access books
Built by scientists, for scientists

6,900
Open access books available

185,000
International authors and editors

200M
Downloads

154
Countries delivered to

Our authors are among the

TOP 1%
most cited scientists

12.2%
Contributors from top 500 universities

CLARIVATE ANALYTICS
BOOK CITATION INDEX
INDEXED

WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com

Reproductive and Developmental Toxicity of Insecticides

Ferdinand Ngoula[1], Omer Bébé Ngouateu[2], Jean Raphaël Kana[1],
Henry Fualefac Defang[1], Pierre Watcho[3],
Pierre Kamtchouing[2] and Joseph Tchoumboué[1]
*[1]Department of Animal Sciences, Faculty of Agronomy
and Agricultural Sciences, University of Dschang
[2]Department of Animal Biology and Physiology, Faculty of Sciences,
University of Yaoundé I
[3]Department of Animal Biology, Faculty of Sciences,
University of Dschang
Cameroon*

1. Introduction

Under the pretext of demographic growth with all its consequences, agricultural production resorts to the use of a varied and a large quantity of insecticides to improve the production and preservation of foodstuffs. Thus, the use of insecticides has increased rapidly and is now widespread to the lowest level of agricultural production.

Insecticides are products of chemical or biological origin that control insects (Ware and Whitacre, 2004). They include ovicides and larvicides used against the eggs and larvae of insects respectively and are used in agriculture, medicine, industry and the household. Insecticides are believed to be the major factors behind the increase in agricultural productivity in the 20th century (van Emden and Pealall, 1996). Control insects may result from killing the insect or otherwise preventing it from engaging in behaviors deemed destructive. Insecticides may be natural or manmade and are applied to target pests in a myriad of formulations and delivery systems (sprays, baits, slow-release diffusion, etc.). Biotechnology has, in recent years, even incorporated bacterial genes coding for insecticidal proteins into various crops to kill pests that feed on them (Ware and Whitacre, 2004). Obviously, this abundant and diversified use of insecticides constitutes a danger not only for aquatic and terrestrial biodiversity, but also for humans because of their presence in food chains.

The World Health Organization (WHO) estimates at 20,000 the number of deaths caused by pesticides each year worldwide with a substantial proportion due to insecticides (Darren et al., 2003). These incidents are particularly common in developing countries; where the marketing of pesticides do not respect international quality standards. Moreover, many studies conducted all over the world report undeniable links between insecticides and serious health consequences including endocrine disruption and fertility problems (Colborn et al., 1993; Colborn et al. 1996, Andersen et al., 2000), cancers (Ben Rouma et al. 2001;

Cabello et al., 2001, Clark et al., 2002; Darren et al., 2003), depression of the immune system, genotoxicity, aplasic anemia. (Pesticide Action Network Belgium, 1999)

Exposure to insecticide has been associated in animals and humans with occurrence of spontaneous abortion, low birth weight, birth defects, change in male: female sex ratio of offspring, inhibition of spermatogenesis and ovogenesis, destruction of seminiferous epithelium, hydrocels resulting to reduction in fertility (Ngoula et al., 2007[a]; Ngoula et al., 2007[b]; Farag et al., 2000; Farag et al., 2010; Shalaby et al., 2010; Chung et al., 2002; Moline et al., 2000; Sobrazo and Bustos-Obregòn, 2000[a]; Delemarre-van de Waal, 1993; Villeneuve, 1972; Vartiainen et al., 1999; Lenselink et al., 1993; Talens and Wooley, 1973; Vogin et al., 1971).

Of Hundreds of insecticides available in the market, few were studied for their impact on reproduction and development. On the other hand, information related to this domain is not only scanty, but also very scattered. The objective of this chapter is to review the reproductive and developmental toxicity of insecticides after an overview of animal reproduction and development. Finally, recommendations for insecticides users and researchers will be proposed.

2. Animal reproduction and development

Reproduction can be defined as the process by which an organism continues its species. In simple terms, it is the process by which organisms create descendants (Wikibooks, 2007).

2.1 Male reproductive system

The reproductive role of the male is to produce and deliver sperm to impregnate the female. To carry out these functions, a male has internal and external sexual organs. These structures include the testes, several tubules that carry sperm out of the testes, various glands, and the penis. In most mammalian species, including human, the male's external reproductive organs are the scrotum and penis. The internal reproductive organs consist of gonads that produce gametes (sperm cells) and hormones, accessory glands that secrete products essential to sperm movement, and ducts that carry out the sperm and glandular secretions (Campbell and Reece, 2005). Inside the testis is a network of fine-diameter tubes called seminiferous tubules. Sertoli cells, nourish, support, and protect developing germ cells, which undergo cell division by meiosis to form spermatozoa (immature sperm). Prostate secretions are rich in zinc, citric acid, antibiotic like molecules, and enzymes important for sperm function. During sexual excitation, the bulbourethral glands produce a droplet of alkaline fluid that neutralizes residual urine in the urethra, protecting the sperm from its acidity (Robinson, 2001). Table 1 summarizes the function of the male reproductive system.

2.2 Female reproductive system

The primary function of the female reproductive system is to produce gametes, the specialized cells that contribute half of the total genetic material of a new individual. The female reproductive system has several additional functions: to be the location for fertilization, to protect and nourish the new individual during the gestation period, and to nourish the newborn postpartum, through lactation and nursing (Weck, 2002).

The female's external reproductive structures include: the clitoris and two sets of labia which surround the clitoris and vaginal opening. The internal organs are a pair of gonads

ORGANS	FUNCTION
Testis with seminiferous tubules	Sperm and testosterone production
Collecting ducts	Transport and storage
Epididymis	Transport, maturation and ejaculation
Vas deferens	Transport and ejaculation
Seminal vesicles	Secretion of thick liquid to transport sperm
Prostate gland	Secretion of alkaline solution to neutralize the urine and female system
Cowper's gland	Secretions may lubricate, flush out urine or form a gelatinous plug
Urethra	Passage for urine and sperm
Penis	Copulation

Table 1. Function of male reproductive system.

(ovaries) and a system of ducts and chambers that carry gametes and house the embryo and fetus (Campbell and Reece, 2005). The functions of the female reproductive organs are summarized in Table 2.

ORGANS	FUNCTION
Ovaries	Production of germ cells and sex hormones
Ducts	Sperm migration, site of fertilization, transport of the fertilized ovum to the uterus
Uterus	Site of fixation, development and growth of the conceptus
Vulva	Copulation (the vagina receives the semen from male penis)
Bartholin Glands	Secretions may lubricate
Mammary glands	Feeding of the newborn

Table 2. Functions of female reproductive system.

2.3 Regulation of the reproductive system

In females, the secretion of hormones and the reproductive events they regulate are cyclic. Whereas males produce sperm continuously, females release only one egg or a few eggs at a specific time during each cycle (Campbell and Reece, 2005).

The secretory and gametogenic functions of the gonads are both dependent on the secretion of the anterior pituitary gonadotropins, FSH, and luteinizing hormone (LH) (Figure 1). The sex hormones and inhibin B feedback to inhibit gonadotropin secretion. In males, gonadotropin secretion is noncyclic; but in postpubertal females an orderly, sequential secretion of gonadotropins is necessary for the occurrence of menstruation, pregnancy, and lactation (Barrett et al., 2010).

Sperm production and androgen synthesis are controlled by a complex feedback loop involving the testes, hypothalamus, and pituitary gland. The pituitary controls the function of the testis by producing follicle-stimulating hormone (FSH) and luteinizing hormone (LH). FSH stimulates spermatogenesis, in part by affecting Sertoli cells, while LH stimulates androgen production by interstitial cells. Pituitary production of these hormones depends on secretion of gonadotropin-releasing hormone (GnRH) by the hypothalamus which can be

stimulated by the cerebral cortex. Elevated levels of GnRH initiate puberty. The production of LH is controlled by the actions of testosterone on the hypothalamus and pituitary. The testis can control brain function. If testosterone concentration is elevated, this hormone inhibits production of GnRH by the hypothalamus; subsequently, LH and FSH production decreases (Palladino, 2002). Hormones also coordinate functions in several different organs at the same time. Considerable coordination among the organs of the female reproductive tract is required. Reproduction will not be successful unless ovulation at the ovary occurs near the time when the uterus is prepared to receive the pre-embryo and, soon thereafter, begin forming the placenta.

Without a functional placenta the pregnancy will not continue very long after implantation of the blastocyst. Surrounding the tubules are clusters of interstitial cells, which synthesize testosterone secretion into the bloodstream. Testosterone is present in infant boys, although synthesis increases dramatically at puberty around the age thirteen. This increase stimulates the onset of spermatogenesis and development of accessory sex glands. All male reproductive organs require testosterone for functions such as protein synthesis, fluid secretion, cell growth, and cell division. Androgens also play an important role in the male sexual response and stimulate secondary sex characteristics such as skeletal development, facial hair growth, deepening of the voice, increased metabolism, and enlargement of the testes, scrotum, and penis.
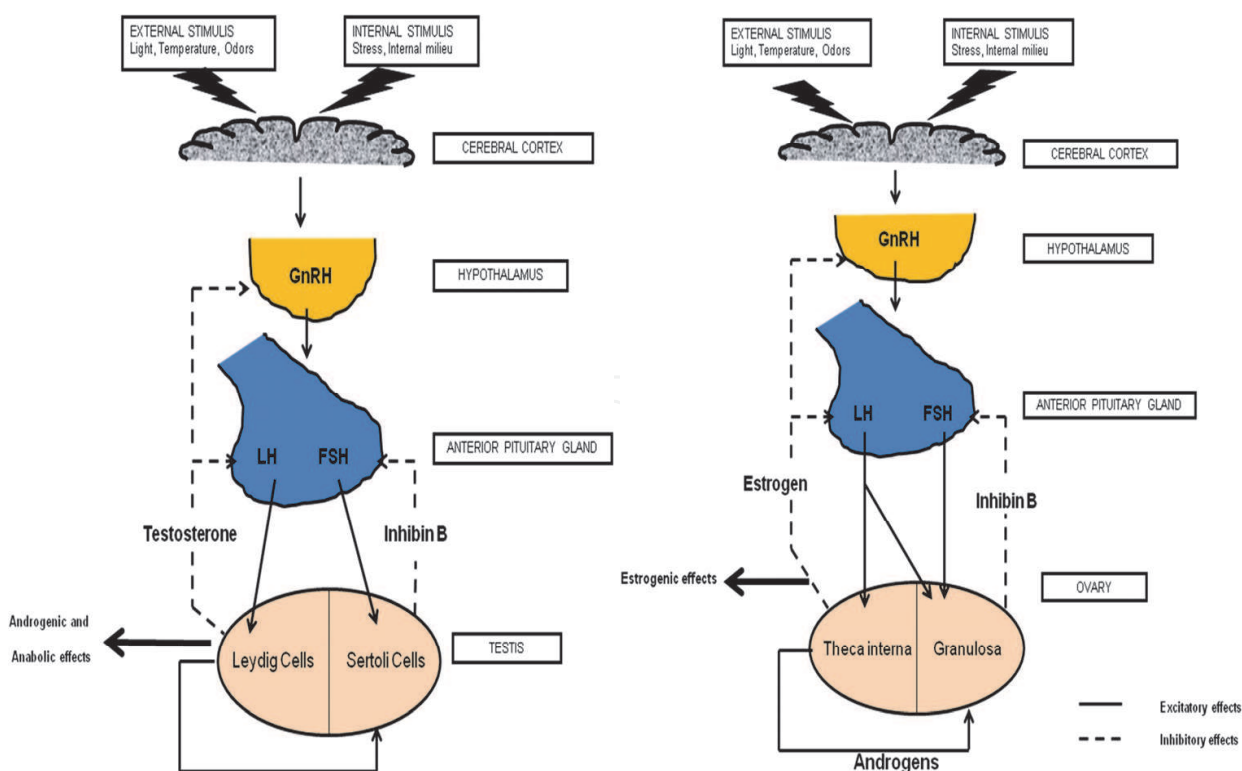

Fig. 1. Postulated mechanisms of regulation of male (on the left) and female (on the right) reproductive function (Barrett et al., 2010 modified).

2.4 fertilization, growth and development of conceptus

Fertilization occurs when sperm and oocyte cell membranes fuse. Once in the female reproductive tract, prostaglandins in the semen cause thinning of the mucus at the opening of the uterus and stimulate contractions of the uterine muscles, which help move the semen up the uterus. The alkalinity of the semen helps neutralize the acidic environment of the vagina, protecting the sperm and increasing their motility. When ejaculation takes place, the semen coagulates, making it easier for uterine contractions; then anticoagulants liquefy the semen, and the sperm begin swimming through the female tract (Campbell and Reece, 2005). Following coitus, exposure of sperm to the environment of the female reproductive tract causes capacitation, removal of surface glycoproteins and cholesterol from the sperm membrane, enabling fertilization to occur. Fusing of the first sperm initiates the zona reaction. Release of cortical granules from the acrosome causes biochemical changes in the zona pellucida and oocyte membrane that prevent polyspermy (Klein and Enders, 2007). Development begins with fertilization, the process by which the male gamete (sperm), and the female gamete (oocyte), unite to give rise to a zygote (Sadler, 2006). Fertilization of an egg by a sperm also called conception in Human occurs in the oviduct about 24 hours later, the resulting zygote begins dividing, a process called cleavage. Cleavage continues, with the embryo becoming a ball of cells by the time it reaches the uterus 3 to 4 days after fertilization. By about 1 week after fertilization, cleavage has produced an embryonic stage called the blastocyst, a sphere of cells containing a cavity. In a process that takes several more days for completion, the blastocyst implants into the endometrium. The embryo secretes hormones that signal its presence and control the mother's reproductive system. One embryonic hormone, human chorionic gonadotropin (HCG), acts like pituitary LH to maintain secretion of progesterone and estrogens by the corpus luteum through the first months of pregnancy in the absence of this hormonal override, the decline in maternal LH due to inhibition of the pituitary would result in menstruation and loss of the embryo (Campbell and Reece, 2005). In human, growth in length is particularly striking during the third, fourth, and fifth months, while an increase in weight is most striking during the last 2 months of gestation. In Human, the length of pregnancy is considered to be 280 days, or 40 weeks after the onset of the last normal menstrual period (LNMP) or, more accurately, 266 days or 38 weeks after fertilization. There are high risks of malformation during the embryogenesis. Birth defect, congenital malformation, and congenital anomaly are synonymous terms used to describe structural, behavioral, functional, and metabolic disorders present at birth. Terms used to describe the study of these disorders are teratology and dysmorphology (Sadler, 2006).

3. Insecticides

3.1 Definition and classification

Insecticides are a group of substance belonging to pesticides. Pesticides previously known as agricultural chemicals are economic poisons that are used to control, kill or repel pest. Depending on the target pest, pesticide can be subclassified into a number of categories namely algicide, fungicide, herbicide, nematocide, mollucide, insecticide, acaricide, rodenticide etc. Depending on the toxicity, formulation concentration, and the pattern use, pesticides can be classified as "general" or "restricted" used. The United States Environmental Protection Agency (US EPA) has developed "category use" definitions based on toxicity. Thus Category I pesticides are highly hazardous, classified as restricted use and

have an oral LD_{50} less than or equal to 1.0mg/kg of body weight; category II are moderately toxic pesticides with an oral LD_{50} less or equal to 500mg/kg; category III are generally non toxic pesticides and have an oral LD_{50} less or equal to 15 000 mg/kg The primary classes of pesticides in use today are fumigants, fungicides, herbicides and insecticides (Hodgson, 2004).

Insecticides can be divided into:

Organochlorines which are insecticides that contain carbon, hydrogen and chlorine. They are also known as chlorinated hydrocarbons, chlorinated organics, chlorinated insecticides, or chlorinated synthetics. Today this group is scarcely used.

Organophosphates (OPs) is the generic term that includes all insecticides containing phosphorus. All Ops are esters of phosphorus having varying combination of oxygen, carbon, sulfur and nitrogen attached.

Organosulfurs contain two phenyl rings with sulfur as the central atom (instead of carbon like in DDT).With very low toxicity to insects, they are used only as acaricides (miticides).

Carbamates are insecticides derivatives of carbamic acid. They inhibit cholinesterase as OPs do.

Formamidines comprise a small group of insecticide used to control OP-and carbamate-resistant pests.

Dinitrophenols have a broad range of toxicity as herbicides, insecticides, ovicides, and fungicides.

Organotins is mainly used as an acaride.

Pyrethroids are very stable in sunlight and are generally effective against most agricultural insect pest when used at the very low rates.

Nicotinoids are new class of insecticides with a new mode of action.

Spinosyns are represented by spinosad which is a fermentation metabolite of the actinomycete *Saccharopolyspora spinosa.*

Fiproles (or Phenylpyrazoles) are used for the control of many soil and foliar insects.

Pyrroles are used as insecticide-miticide on cotton and experimentally on corn, soybeans, vegetables, tree and vine crops etc.

Pyrazoles consist of tebufenpyrad and fenpyroximate which are miticides with limited effectiveness on psylla, aphids, whitefly, and thrips.

Pyridazinones has only Pyridaben as a member of this class. It is a selective insecticide and miticide, aloso effective against thrips, aphids, whiteflies and leafhorpprs.

Quinazolines offer a unique chemical configuration, consisting only of one insecticide, fenazaquin which is a contact and stomach miticide.

Benzoylureas are a group of insecticides that act as insect growth regulators. Their greatest value is in the control of caterpillars and beetles larvae.

Botanicals are natural insecticides, toxicants derived from plants.

Synergist (or Activators) are not themselves considered toxic or insecticidal, but are materials used with insecticides to synergize or enhance the activity of insecticides.

Antibiotics comprise *avermectins* which are insecticidal, acaricidal.

Fumigants are small, volatile, organic molecules that become gases at 40°F. They are generally heavier than air and commonly contain one or more of the halogens (Br, Cl or F).

Insect repellents include smoke, plants hung in dwelling or rubbed on the skin as the fresh plant or its brews, oils, pitches, tars, and varied earths applied to the body (Ware, 2001).

4. Reproductive toxicity of insecticides

4.1 Effects of insecticides on male reproductive system

Insecticides can affect the male reproductive system at one of several sites or at multiple sites. These sites include testes, the accessory sex glands, and the central nervous system, including the neuroendocrine system (Moline et al., 2000). Insecticides may directly damage spermatozoa, alter Sertoli cell or Leydig cell function, or disrupt the endocrine function in any stage of hormonal regulation (hormone synthesis, release, storage, transport, and clearance; receptor recognition and binding; thyroid function; and the central nervous system). These mechanisms are described with respect to the effects of insecticides exposure in vitro and in vivo (Mathur et al., 2010).

4.1.1 Effects of carbamate insecticides on male reproductive system

Subchronic administration of Methomyl, a Carbamate insecticide, to male rat significantly decreased the fertility index, weight of testes and accessory male sexual glands, serum testosterone level and sperm motility and count, but increased sperm cell anomalies. It induced testicular lesions characterized by moderate to severe degenerative changes of seminiferous tubules and incomplete arrest of spermatogenesis. These toxic effects are not persistent (Shalaby et al., 2010). Propoxur (2-isopropoxy-phenyl-N-methylcarbamate), a carbamate pesticide, administered to adult male Wistar rats for 90 successive days led to a concentration-dependent increase in relative weights of testis and epididymis and a decrease in sperm density, serum and intratesticular total cholesterol concentrations, and intratesticular total proteins in treated rats. Propoxur had no significant effect on gestation, fertility and parturition indices, average birth weight, litter size and pups sex ratio of untreated female rats mated with treated males rats (Ngoula et al., 2007a).

Two studies at a carbaryl manufacturing factory have shown that carbaryl exposure affects the quantity and quality of sperm produced by the workers. A second study of the same sperm samples found that the number of sperm anomalies was increased in workers who were being exposed to carbaryl (Wyrobeck et al., 1981). Rani et al. (2007) evaluated the carbaryl exposure and showed distorted shape of seminiferous tubules, disturbed spermatogenesis, and accumulation of cellular mass in the lumen of tubules, oedema of the interstitial spaces and loss of sperms of varying degrees in testes.

Studies on laboratory animals in addition to limited human data showed an association between carbaryl exposure and decreased semen quality.

4.1.2 Effects of organochlorine insecticides on male reproductive system

The chlorinated hydrocarbon insecticides were introduced in the 1940s and 1950s and include familiar insecticides such as DDT, methoxychlor, chlordane, heptachlor, aldrin, dieldrin, endrin, toxaphene, mirex, and lindane. The chlorinated hydrocarbons are neurotoxicants and cause acute effects in the transmission of nerve impulses.

Detectable levels of lindane, DDT, and dieldrin were found in German men, with the highest levels in chemistry students (Alegakis et al., 1996). DDE, aldrin, endosulfan, and isomers of hexachlorocyclohexane (HCH), were detected in men in India (Potashnik et al., 1987).

Exposure to persistent organoclorine pollutants has been associated with human perturbations of the sperm X:Y chromosome ratio (Niederberger, 2005). On the other hand, a high dose of 2-bromopropane decreases spermatogenesis by adversely affecting

spermatogonia followed by depletion of spermatocytes, spermatids, and spermatozoa, with subsequent testicular atrophy (Hwa–Young et al., 1999). Methoxychlor induces oxidative stress in the epididymis and epididymal sperm by decreasing antioxidant enzymes, possibly by inducing reactive oxygen species (Latchoumycandane et al., 2003).

Pant et al. (1995) reported a dose dependent decrease of the weight of epididymides, seminal vesicles, ventral prostate and coagulating glands in male rats exposed to Carbofuran (0.1, 0.2, 0.4 or 0.8 mg kg-1 body weight, 5 days/week for 60 days). Decreased sperm motility, reduced epididymal sperm count along with increased morphological abnormalities in head, neck and tail regions of spermatozoa were observed in rats exposed to 0.2, 0.4, or 0.8 mg carbofuran kg-1 body weight. Histologically, the results indicated the toxicity of carbofuran on testes depending on the doses. The changes predominantly consisted of moderate oedema, congestion, damage to Sertoli cells and germ cells, along with the accumulation of cellular debris and presence of giant cells in the lumen of a few seminiferous tubules which showed disturbed spermatogenesis with the higher doses of carbofuran.

A recent study suggests that endosulfan exposure may delay sexual maturity and interfere with hormone synthesis in male children (Narayana et al., 2004). Jaiswal et al. (2005) reported pre-treatment with 5-aminosalicylic acid (5-ASA) significantly reduced sperm-shape abnormalities in endosulfan-treated rats. The number of abnormal sperm in the epididymis was markedly increased by endosulfan treatment. Histopathological analysis of seminiferous tubules and Leydig cells showed significant protection from endosulfan-induced tissue damage such as necrosis. The population of Sertoli cells increased and the lumen of the seminiferous tubules contained a greater number of spermatids. There was a corresponding increase in the number of Leydig cells. Rao et al. (2005) investigated the effect of L-ascorbic acid on postnatal exposure of endosulfan induced testis damage in the rat. Endosulfan affected the testicular function enhancing the incidence of abnormal spermatozoa, decreasing the sperm count and sperm motility.

In a study carried out on the reproductive functions of 32 sprayers men exposed to 2,4-D, and after four days of sexual inactivity the results of their sperm analysis, compared with unexposed workers, showed a significantly high levels of asthenospermia, necrospermia and teratospermia (Lerda and Rizzi, 1991). An increase in the germ cells and sperm head abnormalities was observed after oral administration of 2,4-D at 3.3 mg kg(-1) in male rats for three and five consecutive days (Amer and Aly, 2001).

2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD) induces oxidative stress in the epididymis and epididymal sperm by decreasing the antioxidant enzymes through induction of reactive oxygen species. Male rats exposed to TCDD display reduced fertility, delayed puberty and altered reproductive organ weights (Bell et al., 2007). TCDD- exposed male rats displayed decreased numbers of sperm and increased numbers of abnormal sperm in the epididymis (Faqi et al., 1997).

HCH exposure (50 mg or 100 mg kg-1 body weight day-1, 5 days in a week for 120 days) also led to a decrease in epididymal sperm count, sperm motility and an increase in the percentage of abnormal sperm (Prasad et al., 1995).

Lindane, an organochlorine pesticide, impairs testicular functions and fertility. Lindane has direct action on reproduction and also carcinogenic properties. Treatment with 1-40 mg of lindane/kg body weight disrupted testicular morphology, decreased spermatogenesis and impaired reproductive performances in males (Page et al., 2002).

The weights of the testis, epididymis, seminal vesicles and ventral prostate decreased in methoxychlor treated rats (Latchoumycandane and Mathur 2002). The activities of antioxidant enzymes such as superoxide dismutase, catalase, glutathione reductase and glutathione peroxidase decreased in testes. The levels of hydrogen peroxide generation (H2O2) and lipid peroxidation increased in testis of the rats treated with methoxychlor.

According to Waissmann (2003); Hakin and Oates (1997), DDT and some organic solvents lead to decreased fertility and altered sperm counts DDT can also delay puberty (Santamarta, 2001; Jequier, 2002; Waissmann, 2003; Metzler, 2002; Moreira and Wolff 2003).

Dioxins can affect libido and fertility, causing changes in the sexual behavior of male fish, birds, mammals, and reptiles as reported by Assunção and Pesquero (1999), Ribeiro (2003), Giwercman et al. (1993). Tetrachloro-dibenzo-p-dioxin (TCDD) can interfere with libido (Hakin and Oates, 1997). The effects of high exposure to TCDD and "TCDD-like" compounds on important sites for development and reproduction have been also been recognized by Eskenazi and Kimmel (1995).

Endosulfan exposure in male children may delay sexual maturity and interfere with sex hormone synthesis (Saiyed et al., 2003).

Ben et al. (2001) evaluated the reproductive toxicity of DDT in adult male rats exposed to 50 and 100 mg/kg body weight (b.wt) day-1 for 10 successive days and concluded that DDT led to reduction of testicular weight and the number as well as the percentage of motile spermatozoa in the epididymis. Histological observations of the testicle revealed a marked loss of gametes in the lumen of seminiferous tubules. Hu and Wang (2008) showed the joint toxicity of phoxim (Pho) and fenvalerate (Fen) on the spermatogenesis of male rats. Phoxim and Fenvalerate jointly impaired spermatogenesis in a dose- and time- dependent manner. Their joint action exhibited a synergetic effect and increased toxicity.

4.1.3 Effects of organophosphate Insecticides on male reproductive system

Organophosphate pesticides (OPs) are phosphoric acid esters or thiophosphoric acid esters and are among the most widely used pesticides for insect control.

Dimethoate at $28\,mg\,kg^{-1}\,day^{-1}$, deltamethrin at $5\,mg\,kg^{-1}\,day^{-1}$ and their mixture at $5\,mg\,kg^{-1}\,day^{-1}$ were associated with a significantly decreased sperm count, motility and viability and significantly increased percent morphologically abnormal spermatozoa (Abdallah et al., 2010).

Subchronic exposure of male rat to dimethoate (2, 8 and 20 mg/kg for 90 days) induced a decrease in relative testis weights (Sayým, 2007). In light microscopic examinations, histopathological observation of treated rats revealed that dimethoate caused dose-related testicular damage characterized by moderate to severe seminiferous tubule degeneration as sloughing, atrophy, germ cell degeneration and by partial arrest of spermatogenesis. Farag (2007) demonstrated the adverse effects of dimethoate on the reproductive performance of male mice. The sperm viability, motility and density were reduced in dimethoate treated mice. Ngoula et al. (2011) also obtained similar results in male rats treated with Dimethoate. Testicular and epididymal sperm density were decreased in rats treated with malathion. Pre and post fertility test showed 80% negative results after treatment. Biochemical profile of the testis revealed a significant decline in the contents of sialic acid and glycogen. Whereas a significant increase in the protein content of testis and testicular cholesterol was observed. The activity of testicular enzyme acid phosphatase increased significantly, while decreased alkaline phosphatase activity was found (Choudhary et al., 2008).

Histopathological studies of the intoxicated rats (Treated with methomyl orally 17 mg/kg in saline daily for two months) revealed variable degrees of degenerative changes in the seminiferous tubules up to total cellular destruction (Mahgoub and EI-Medany, 2006).

A single injection of parathion (organophosphate agro pesticide) to immature male mice led to a decrease in testis weight and early damage of germ cells of the mice. The effect is reversible and recovers at longer intervals (Sobarzo and Bustos-Obregon, 2000). In adult Wistar rats orally treated with pirimiphos-methyl (41.67, 62.5 or 125 mg/kg) for 90 days, a decrease in relative testis and epidiydimis weights and intra-testicular cholesterol level was recorded. whereas a decrease in serum total protein, sperm density and motility, fertility and parturition indices and pups sex-ratio (M/F) was recorded in animals treated with 125 mg/Kg of pirimiphos methyl. Histological findings also indicated enlargement of interstitial space, inhibition of spermatogenesis, rarefaction of Leydig cells and oedema in testes of treated rats (Ngoula et al., 2007[b]).

A single injection of the organophosphorous agroinsecticide parathion (6.67 mg/kg bwt corresponding to 1/3 of LD_{50} dose) to immature male mice (upon the onset and installation of spermatogenesis in immature CF1 mice) led to a decrease of testis weight and an early damage of germ cells in treated mice. The effects are reversible and recover at long intervals (Sobarzo and Bustos-Obregón, 2000[b]).

Quinalphos a commonly used organophosphorus insecticide reduce prostatic acid phosphatase activity and fructose content of the accessory sex glands, and plasma levels of testosterone and FSH and LH (Rey et al., 1991) as well as relative weights of the testis and accessory sex organs. Dimethoate orally exposed to male rats increase relative weights of testis and prostate, sperm density and motility, serum and testis levels of protein and cholesterol, activity of prostatic acid phosphatase. Testicular and epididymal histology generally shown in the testis, spams of Sertoli cells destruction and disorganization of germinal epithelium and in the epididymis, the proliferation of epithelial cells. The lumen of seminiferous tubules and epididymis were generally poor in sperm (Ngoula et al., 2011).

Methyl parathion adversely affect male rat reproductive organs by inducing vacuolization of the epithelium of seminiferous tubules, nuclear pyknosis and brush border disruption in the ductus deferens with the presence of immature cells in the lumen. Also, the activity of acid phosphatase was reduced (Narayana et al., 2006). Methyl Parathion caused significant decrease in the weight of testis, epididymis, seminal vesicle and ventral prostate with marked pathomorphological changes. Also, marked reduction in epididymial and testicular sperm counts was observed in exposed male rats. Fertility test showed 80% negative fertility in treated animals. A significant reduction in the sialic acid contents of testis, epididymis, seminal vesicle, ventral prostate and testicular glycogen were noticed, while the protein and cholesterol content were raised significantly (Suresh at al.,2003).

Methyl Parathion orally administered to male rats at levels of 50, 150 and 250 mg/kg for 60 days reduced the weight of the testes, epididymis, seminal vesicle and ventral prostate. Testicular and epididymal sperm density were also decreased in the treated animals. Pre and post fertility test showed 80% negative results after treatment Choudhary et al. (2003).

Co- treatment of malathion-exposed rats with vitamins E and C had a protective effect on sperm counts and sperm motility. Degenerative changes in the seminiferous tubules were also observed in the rats which received malathion and supplemented with vitamins C and E, but milder histopathological changes were observed in the interstitial tissues (Uzun et al., 2009).

Body and testis weights decreased in methyl parathion (0.28 mg/kg b.wt per day for 7 weeks) treated rats. It was observed that, at the end of 4th and 7th weeks there was a statistically significant decrease in sperm counts and sperm motility, increase in abnormal sperm morphology Meltem et al. (2007). Joshi et al. (2007) investigated the effects of chlorpyrifos on testes. Chlorpyrifos methyl orally administered to male rats at the dose levels of 7.5, 12.5 and 17.5 mg/kg b. wt. /day for 30 days showed marked reduction in epididymal and testicular sperm counts in exposed males. Histopathological examination of testes showed mild to severe degenerative changes in seminiferous tubules at various dose levels. Fertility test showed 85% negative results.

4.1.4 Effects of pyrethroid Insecticides on male reproductive system

Pyrethrin is an extract from several types of chrysanthemum, and is one of the oldest insecticides used by humans. There are six esters and acids associated with this botanical insecticide. Pyrethrin is applied at low doses and is considered to be nonpersistent. Mammalian toxicity of pyrethrins is quite low, apparently due to its rapid breakdown by liver microsomal enzymes and esterases. Exposure to the higher concentration of cypermethrin disturbed the reproductive behaviour of the parr. They displayed fewer courting events, spent less time near the nesting females and had lower volumes of strippable milt. They also had significantly lower amounts of 11-ketotestosterone (11-KT) in the blood plasma. Further, in control fish, higher plasma levels of 17,20-P were observed in parr interacting with a female compared to those with no female contacts (Jaensson et al., 2007).

Yao & Wang (2008) observed a new type of pesticides and because of their high performance and low toxicity, pyrethroid insecticides are widely used in place of organochlorine insecticides both in agriculture and in the home. Recent researches indicates that pyrethroid insecticides can reduce sperm count and motility, cause deformity of the sperm head, increase the count of abnormal sperm, damage sperm DNA and induce its aneuploidy rate, as well as affect sex hormone levels and produce reproductive toxicity. Meeker et al. (2008) reported reduced semen quality and increased sperm DNA damage in relation to urinary metabolites of pyrethroid insecticides.

4.2 Effects of insecticides on female reproductive system

Insecticides that target the female reproductive system can cause a wide variety of adverse effects. Changes in sexual behavior, onset of puberty, cyclicity, fertility, gestation time, pregnancy outcome, and lactation as well as premature menopause are among the potential manifestations of female reproductive toxicity: all can disrupt a female reproduction.

4.2.1 Effects of organochlorine insecticides on female reproductive system

Residue levels of chlorinated insecticides continue to be found in the environment and, although the concentrations are low approaching the limit of delectability, there stil play a big role. Organochlorine compounds are known to interrupt the estrus cycle in rats (Martinez and Swartz, 1991; Uphouse et al, 1984; Swartz and Mall, 1989).

Chronic treatment of young female rats with 5, 10, 20, and 40 mg/kg lindane delayed vaginal opening and disrupted ovarian cyclicity up to approximately 110 days of age. Thereafter, regular ovarian cycles were present in the majority of females (Ralph et al., 1989). In addition, exposure of mink to Lindane from conception resulted in a decrease in

reproductive efficiency when they were subsequently mated, leading to a 60% reduction in the number of kits born (Beard and Rawlings, 1998). Acephate treatment was associated with a decreased number of implantations and live fetuses, and an increased number of early resorptions at 28 mg/kg/day (Farag et al., 2000).

Study on infertile German women found association between endometriosis and elevated levels of chlorinated hydrocarbon pesticides (Gerhard et al., 1999). However, no association was found in wives of pesticide applicators in Minnesota, or with levels of chlorinated hydrocarbon pesticides in infertile women in Canada (Lebel et al., 1998).

A study done in Florida at a time of heavy application of DDT in agricultural showed that 14 ppb concentration level was found in black babies and 6 ppb in whites. However, other studies have found low levels of DDE and hexachlorocyclohexane in California women in their second trimester of pregnancy (Moses, 1995). The presence of pesticides in cord blood is evidence of transplacental passage. Most tests of maternal/fetal pairs are for persistent pesticides in the DDT family. The highest reported level of DDE was found in Mexican babies born in 1997 (4700 ppb), and DDT levels were also higher (880 ppb). The highest level of hexachlorobenzene (HCB) was reported in 1985 from Tunisia (37 ppb) while the lowest levels were found in babies in Nicaragua (6.39 ppb), Spanish babies born between 1997 to 1999 (1.1 ppb) and German babies born in 1994 (0.5 ppb). Higher levels of DDT and lindane were found in stillbirt babies in India but the levels were not significant from full term births babies (Sancewicz-Pach et al., 1997).

Chlordecone (0.015, 0.03, 0.06 and 0.125 mg in 0.05 ml sesame oil) intra pertitonally injected 10 times during 12 days to one-day-old female mice may produce distinct morphological alterations in the epithelium lining both the vagina and uterus. The changes in the neonate mouse reproductive tract appeared dose related in that increased doses of administered chlordecone accelerated development of the vaginal epithelium leading to keratinization while cellular hypertrophy, hyperplasia, and glandular formation were observed in the uterus. These changes appeared identical to the developmental changes induced by the estradiol (Eroschenko and Moussa, 1979).

Treatment of immature rats with chlordane, dieldrin, heptachlor, lindane, p,p'-DDT, p,p'DDE, or toxaphene for 7 days stimulates the metabolism of estrone by liver microsomal enzymes and inhibited the increase in uterine wet weight caused by estrone (Welch et al., 1971). Another study in German found no significant differences in the levels α-β-γ isomers of hexachlorcyclohexane, heptachlor, dieldrin, and total DDT in the subcutaneous fat of children who died of Sudden Infant Death Syndrome (SIDS) compared to children who died of known causes (Kleemann et al. 1991).

The pesticide heptachlor may cause disrupted and prolonged estrus cycles (Oduma et al., 1995). Treatment with DDT and chlordecone resulted in persistent estrus in rats. Lindane induced marked disturbances in the estrus cycle, prolonging the proestrus phase considerably and thereby delaying ovulation (Chadwick et al., 1988; Pages et al., 2002, Lahiri et al., 1985).

4.2.2 Effects of organophosphate insecticides on female reproductive system

No reports on organophosphate pesticides in cord blood were found. Studies in California and Florida found decreased cholinesterase activity, a biomarker of organophosphate exposure. Since these pesticides are not persistent, the findings reflect recent exposure. Monocrotophos, an organophosphate insecticide, administered to female rats provoked

embryonic resorptions. Fertility and parturition indices were reduced in dose dependent fashion. However, gestation index was not affected. Viability and lactation indices were highly reduced in rats of high dose group. Birth weight and crown-rump length of pups in high dose group were significantly less, with no effect on average litter size (Adilaxmamma et al., 1994).

Methyl Parathion (MP) (oral gavage for five days a week for four weeks at a daily dose) led to delections in microvilli and Marked loss in kinocillia of surface epithelium of fallopian Tube (Mehmet et al., 2007). In addition, the number of estrus cycles and the duration of each phase of the estrus cycle were significantly affected after treatment of rats with methyl parathion (Asmathbanu and Kaliwal, 1997; Dhondup and Kaliwal, 1997). The pesticides dimethoate, malathion, and sumithion gave similar results (Kumar and Uppal, 1986; Gouda and Sastry, 1979)

4.2.3 Effects of pyrethroid insecticides on female reproductive system

Permethrin exposure has caused embryo loss in pregnant rabbits (US EPA, 1997) and in pregnant rats (Spencer and Berhane, 1982). Moreover, in pregnant rabbits, feeding of cyfluthrin causes both miscarriages and resorption of fetuses. In a three-generation study of rats, feeding of cyfluthrin caused pups to have "decreased viability" and decreased weight (US EPS, 1988). Cyfluthrin may also have more subtle effects on the ability of humans and other animals to reproduce. The researchers advise protection from any form of contact or ingestion of the pyrethroids in order to prevent any undesirable effects on the human reproductive syste (Eil et al., 1990).

In sexually mature female rats orally intubated with the organophosphorus insecticide, Pestban at a daily dosage of 7.45 or 3.72 mg/kg bwt. respectively for 14 days during premating, mating and throughout the whole length of gestation and lactation periods showed reduced fertility with increasing the dose. In addition, the number of implantation sites and viable fetuses were reduced in pregnant females. However, the number of resorptions, dead fetuses, and pre-and postimplantation losses were increased. The behavioral responses as well as fetal survival and viability indices were altered during the lactation period (Morgan, 2008).

4.2.4 Effects of other insecticides or mixture of insecticides on female reproductive system

A single dose of Frontline approximately doubled the time between periods of estrus in female rats (Ohi et al., 2004). Higher doses of Frontline also reduced the number of female rats who were able to become pregnant following mating (Ohi et al., 2004). Offspring of rats fed fipronil during pregnancy were smaller than offspring of unexposed rats. In addition, male offspring from exposed mothers took longer than offspring of unexposed mothers to mature sexually. These effects occurred at all but the lowest dose level tested. In another study, fipronil reduced litter size, fertility, and the survival of offspring. These effects occurred at the highest dose level tested (U.S. EPA, 1998[1]). Offspring of rats exposed to fipronil had smaller brains than the offspring of unexposed rats. In addition, the fipronil exposure caused a variety of behavioral changes. All of these effects occurred at the highest dose level tested (U.S. EPA, 1997 and 1998).

Carbofuran affected the estrus cycle by showing a decrease in the number of estrus cycles and the duration of each phase, which may be due to a direct effect on the ovary or on the

hypothalamus-pituitary-ovarian axis causing hormonal imbalance (Baligar and Kaliwal, 2002).

Another pesticide found in cord blood is the widely used insect repellent deet. In a study in Thailand deet was found in 8% of babies whose mothers used the repellent in the second and third trimester of pregnancy (Moses, 1995).

4.3 Effects of Insecticides on endocrine system

The fate and detoxification of organochemicals have not been well defined, but these agents can disrupt the hypothalamic-pituitary-tesicular axis affecting the endocrine and reproductive functions. Since environmental exposure is due to a mixture of various endocrine disruptors, the effect of their combined toxicity becomes more important.

Development of a fetus into a phenotypic male depends, first, on testis formation and second, on hormone production by the fetal testis. Disorders of testicular hormone production or action can lead in severe cases to phenotypic abnormalities or can predispose towards impaired reproductive health. Though it is concluded that no direct evidence links human exposure to environmental chemicals and male reproductive disorders that stem from disturbed testis development, this is based mainly on lack of information (Sharpe, 2001).

4.3.1 Effects of organochlorine insecticides on endocrine system

Organochlorine insecticide Lindane lower serum testosterone levels in animals, block steroid hormone biosynthesis in leydig cells by reducing StAR protein expression (Walsh et al., 2000; Walsh et Stocco, 1998). DDT, a commonly used pesticide, and its metabolites (o,p-DDT, and p,p'DDE) have estrogenic effects in males by blocking the androgen receptor (Whorton et al., 1977; Mattison, 1983; Kelce et al., 1995). DDT inhibited the cAMP response to follicle-stimulating hormone (FSH), the major endocrine control of Sertoli cell development, and to a β2-agonist, isoproterenol. DDT exposure decreased the level of FSH binding sites. The DDT inhibitory effect on the FSH response was also observed in Ser W3 cells, a Sertoli cell-derived immortalized cell line (Bernard et al., 2007). DDE, a metabolite of DDT, has anti-androgenic action and can also jeopardize estrogen metabolism in its synthesis or breakdown and physiological elimination (Toppari, 1996; Kelce, 1995). DDE may also inhibit the expression of transferin (Tf) and upmodulate expression of ABP in cultured rat Sertoli cells (XianZhi et al., 2006).

Young females rats exposed to Lindane (20 and 40 mg/kg) presented smaller pituitary and uterine weights, lower serum and pituitary luteinizing hormone (LH) and prolactin, serum estrogen concentrations and higher pituitary follicle stimulating hormone (FSH) concentrations. Thus, indane may effectively block the response of estrogen-dependent tissues to this ovarian steroid hormone and that this apparent antiestrogenic effect of lindane is responsible for the disturbances observed in the neuroendocrine control of ovarian function in the rat (Cooper et al., 1989). It is shown that chronic administration of lindane results in endocrine disruption in birds as well as in mammals (Saradha et al. 2009). Treatment with 1-40 mg of lindane/kg body weight, inhibited testicular steroidogenesis, reduced plasma androgen concentrations and impaired reproductive performances in males (Page et al., 2002).

Toxic manifestations of dermally applied hexachlorocyclohexane (50 mg or 100 mg kg-1 body weight day-1, 5 days in a week for 120 days) on testes led to a decrease in serum testosterone levels Prasad et al. (1995).

2,3,7,8-Tetrachlorodibenzo-p-Dioxin (TCDD) can have an anti-androgenic and anti-estrogenic effect (Eskenazi and Kimmel, 1995), inducing a decrease in the testicular response to LH (Eskenazi and Kimmel, 1995; Bush et al., 1996).

4.3.2 Effects of organophosphate insecticides on endocrine system

Quinalphos a commonly used organophosphorus insecticide reduce prostatic acid phosphatase activity and fructose content of the accessory sex glands, and plasma levels of testosterone and FSH and LH (Rey et al., 1991) as well as relative weights of the testis and accessory sex organs. Thus, Quinalphos exert suppressive effects on the functional activity of accessory sex glands by decreasing testicular testosterone production following inhibition of pituitary gonadotrophins release (Rey et al., 1991). Quinalphos also reduce prostatic acid phosphatase activity and fructose content of the accessory sex glands, and plasma levels of testosterone and FSH and LH.

Chlorpyrifos orally administered to male rats at the dose levels of 7.5, 12.5 and 17.5 mg/kg b. wt. /day for 30 days showed a decrease in serum testosterone concentration (Joshi et al., 2007). Treatment of rats with the insecticide heptachlor suppressed estradiol concentrations in blood and reduced the production of estradiol by ovarian cells of treated rats (Oduma et al., 1995; Rami et al., 1995). Lindane, also cause a decrease in circulating estradiol levels in rats (Eldridge et al., 1994; Gojmerac et al., 1996). In monkeys, ovulatory levels of estradiol were reduced after high doses of hexachlorobenzene (Foster et al., 1995), which also induced anovulatory cycles and suppression of circulating levels of estradiol (Muller et al., 1978), and a dose dependent suppression of serum progesterone concentrations during the luteal phase (Foster et al., 1992). Progesterone levels may be decreased by exposure to methoxychlor as well, especially during the estrus phase of the estrus cycle in rats (Chapin et al., 1997; Cumming and Lasley, 1993). During early pregnancy, progesterone concentrations decreased after treatment with DDT in rabbits (Lindeneau et al., 1994).

4.3.3 Effects of carbamate insecticides on endocrine system

Methomyl, a Carbamate insecticide administered to male rat daily for 65 successive days at two doses (0.5 and 1 mg/kg body weight) significantly decreased serum testosterone level (Shalaby et al., 2010).

Subchronic exposure to *methomyl (Carbamate)* induce a significant decrease in the level of *testosterone* in the intoxicated rats, while the levels of FSH, LH and *prolactin* significantly increased (Mahgoub and EI-Medany, 2006). The hormonal changes and testicular damage continued for 30 days after withdrawal of the insecticide indicating a persistent effect (Mahgoub & EI-Medany, 2006). Subchronic exposure of male rats to methomyl also provoked a decrease in the level of testosterone (Choudhary et al., 2008; Afaf et al., 2000), while the level of FSH, LH and prolactin increase (Afaf et al., 2000). The rats given malathion alone or in combination with vitamins also had lower plasma FSH, LH and testosterone levels than the control rats (Uzun et al., 2009).

4.3.4 Effects of pyrethroid insecticides on endocrine system

Experimental studies have reported that pyrethroid insecticides affect male endocrine and reproductive function, but human data are limited. Serum reproductive hormones levels of 161 men recruited from an infertility clinic as well as the pyrethroid metabolites 3-phenoxybenzoic acid (3PBA) and cis- and trans-3-(2,2-dichlorovinyl)-2,2-

dimethylcyclopropane carboxylic acid (cis-DCCA and trans-DCCA) in spot urine samples were determined. When adjusting for potential confounders, categories for all three metabolites, as well as their summed values, were positively associated with FSH. Suggestive positive relationships with LH were also found. In addition, cis-DCCA and trans-DCCA were inversely associated with inhibin B (p for trend=0.03 and 0.02, respectively). Finally, there was evidence that trans-DCCA was inversely associated with testosterone and free androgen index (Meeker et al., 2009).

Wistar rats received daily (po), from day 6 of pregnancy to day 21 of lactation, deltamethrin (D) and endosulfan (E) concomitantly: D: 2.0 mg/kg + E: 1.5 mg/kg, or D: 3.0 mg/kg + E: 2.0 mg/kg, or D: 4.0 mg/kg + E: 3.0 mg/kg. Results from the uterotrophic assay indicate absence of in vivo estrogenic activity of D + E. No significant variations in reproductive endpoints of females were observed (Kenia et al., 2005).

Permethrin affects both male and female reproductive systems. It binds to receptors for androgen, a male sex hormone, in skin cells from human males (Eil and Nisula, 1990). Permethrin also binds to a different receptor, called the peripheral benzodiazepine receptor, which stimulates production of the male sex hormone testosterone (Ramadan et al., 1988). Cyfluthrin also binds with peripheral benzodiazepine (PBZ) receptors. PBZ receptors are found in high concentration in the testes and appear important in "hormonal responsiveness (Ramadan et al., 1988).

A research documented the ability of six synthetic pyrethroids, as well as the naturally occurring pyrethrins, to bind with androgen (a male sex hormone) receptors, and disrupt normal androgen function (Eil et al., 1990).

5. Developmental toxicity of insecticides

Developmental toxicity conferred to any structural or functional alteration or perturbation, caused by environmental insult, reversible or irreversible, which interferes with homeostasis, normal growth, differentiation, development and/or behaviour (Rochelle, 1988). Developmental abnormalities constitute a significant medical problem and greatly contribute to animal and human suffering. Protective barrier of placenta is not always enough to shield the developing embryo or foetus from chemical exposure via the mother. This chemical can be toxic, lethal or cause birth defects in the developing embryo or foetus. The developmental process is particularly vulnerable to adverse environmental conditions including chemical pollutants such as insecticides which have been ubiquitous because of its widespread manufacture, and disposal all over the world. They have direct effects resulting in impaired fertility, high rates of abortions, and abnormal pregnancies. In fact, every developmental stage is vulnerable to any environmental insult which encompasses a spectrum of possible effects which includes malformation of fertilized egg or zygote, of the embryo during organogenesis, the foetus in the post embryonic period of gestation and the postnatal until sexual maturity of offspring.

5.1 Effects of insecticides on fertilization

Incubation of sea urchin *Paracentrotus lividus, eggs* for 1 h in the presence of increasing concentrations of lindane, methoxychlor, or dieldrin up to 100μM, rinsed in filtered sea water and then fertilized with a final 10^4 -fold sperm dilution led to the decrease of fertilization rate. Treatment of eggs with each pesticide did not prevent fertilization, but increased the rate in polyspermy, delayed or blocked the first mitotic divisions, and altered

early embryonic development. Moreover, all pesticides could alter several intracellular biochemical pathways that control first mitotic divisions and early development, including intracellular calcium homeostasis, MPF (mitosis promoting factor) activity and formation of the bipolar mitotic spindle. Lindane was the most potent of the three pesticides (Pesando et al., 2003). Dieldrin, methoxychlor, and lindane, can alter oocyte maturation in mammals and in marine invertebrates. The effects were observed at relatively high doses of pesticides (Picard et al., 2003).

The reproductive process ranges from the development and maturation of both female and male reproductive systems, to successful mating and a resulting healthy, normal viable offspring. Exposure of an organism to these chemicals can cause damage to the spermatogonial cells which represents male genome or cause damage to spermatozoid undergoing maturation (Oakes et al., 2002). These damages to spermatogenesis would lead to increased adverse fertilization effects when the males mated with females. The rapidly dividing spermatogonia are susceptible to toxicity induced by insecticides which affect cells division.

Some insecticides have been reported to have weak steroid activities at the level of the ovary, attenuating its sensitivity to gonadotropins and altered sperm motility in the oviduct (Khan-Dawood and Satyaswaroop, 1995). According to Blomqvist et al. (2005), roosters exposed to the chlorinated insecticide DDT and its persistent metabolites during their embryonic development resulted in persistent effects on epididymal-testicular structure and function had a significantly reduced semen production in adult stage.

5.2 Effects of insecticides on prenatal development

Many organotin compounds which are widely used in agriculture and industry have biocidal properties and are used in agriculture as insecticides. Their widespread use has caused increasing amounts to be released into environment. Exposure of an organism to insecticides at any time during foetal life can produce structural defects in developing organ systems such as the kidneys, the nervous system, and the skeleton. At this time, exposure to insecticides may also cause cancer in the prenatal or postnatal periods, altered growth, functional deficits, and prenatal death or premature senescence (Michal et al., 1993). These phenomena may result from interference with the endocrine system (Ema and Harazono, 2000) which disturb hormonal regulation during pre and postnatal development.

During embryonic stage of development, the conceptus is very vulnerable to environmental insult including insecticides because of differences from adult include the following:

- The organismic plasticity of small cell numbers found in the pre-embryonic stage of development is lost with the transition from presumption to determined cell status.
- Interference of rapid rates of cell proliferation during embryonic stage with the process of rapid synthesis of energy sources such ATP and GTP may preclude normal differentiation and growth, and may translate into growth retardation or malformation.
- The limited metabolic capability to produced enzymes responsible detoxifying xenobiotics.
- Lack of recognition capability of immunosurveillance systems due to the immaturity of embryonic cells as compared to postnatal cells with altered surface markers which can easily distinguish "self" and "non self".

The finding of Blomqvist *et al*. (2005) showed that embryonic exposure to DDT or EE_2 (17alpha-ethynyl estradiol) induced a persistent effect on testicular function, and impaired fertility because of the reduced output of spermatozoa. Insecticides developmental delays in prenatal development is detected by reduced foetal or neonatal body weights in mammals, reduced absolute and relative organ weights, and reduced ossification of skeletal elements in foetus which it is conventionally evaluated during gestational day 20 or 21 in rats, day 17 or 18 in mice, and day 29 or 30 in rabbits (Rochelle, 1988). Due to totipotent cells which comprise the conceptus during pre-embryonic stage of development, which begins with fertilization and ends at implantation, and lasts approximately 5 to 8 days in most mammals, the conceptus is considered relatively refractory to the chemical compounds used in agriculture.

Chlorpyrifos-methyl (CPM) exhibit weak reproductive toxicity in F0 rats exposed at adulthood and negligible effects in F1 offspring exposed in utero and via lactation at weanling, but induce anti-androgenic effect and hypothyroidism after long term exposure from in utero through sexual maturation of F1 rats (Sang-Hee et al., 2006).

A study conducted by Rope et al. among male workers who were exposed to various mixtures of pesticides such as DDT, BHC, endosulfan; and organophosphorus pesticides i.e. malathion, methyl- parathion, dimethote, monocrotophos, phosphamidon and quinalphos; synthetic pyrethroids such as fenvelrate and cypermethrin during mixing and spraying showed male mediated adverse reproductive outcome such as abortion, stillbirths, neonatal deaths, congenital defects, etc. (Rupa et al., 1991).

5.3 Effects of insecticides on postnatal development

In some developing countries, women from the majority of the agricultural work force bringing them into contact with uncontrolled use of pesticides and other chemicals used in agriculture which may adversely affect reproduction and increase contamination of breast milk (Michal et al., 1993). There are many pathways for exposure: in drinking water from contaminated wells, in food, from household insecticide use, from residues on plants as they are picked or on machinery as it is being handled or repaired, from insecticide drift as it is being sprayed, from spills during transport and from dermal exposure during mixing or application. The paper by Nurminen et al. (1995) in the issue of epidemiology of birth defect from women exposure to insecticides revealed 95% of chance for the risk of having a child or stillborn infant with a structural birth defect among women employed in agricultural work.

Embryonic and postnatal exposure to high doses of insecticides like DDT and its derivatives induced a significant reduction in the average area of the seminiferous tubules of the male testis, indicating that an increased amount of interstitial tissue in the testis accompanies the decrease in tubular area (Blomqvist et al., 2005). A positive correlation between the diameter of the seminiferous tubules and sertoli cell size has been observed in Syrian hamster (Hikim et al., 1989), and experiments in rats have shown that sertoli cell development is modulated by estrogen (Sharpe et al., 1998). This report is supported by the finding that rats neonatally exposed to estrogens had fewer sertoli cells and a decreased diameter of the seminiferous tubules (Aceitero et al., 1998; Atanassova et al., 1999). Testicular deformations such as abnormal shape and blisters and a stunted epididymis were also reported by the finding of Blomqvist et al. (2005) on domestic rooster embryonically exposed to DDT. These effects were mainly seen in the left testis which has an ambisexual potential and is more sensitive to estrogen. As shown in gulls,

quail, and chicken (Fry and Toone, 1981; Berg et al., 1998), exposure to insecticides causes feminization of the left testis in bird embryo.

In contrast to testis, ovotestis formation appears to be a transient effect of embryo exposure to estrogenic substances. Several earlier studies on quail, and rooster embryonically exposed to insecticides are in agreement that ovotestis did not persist until adulthood (Scheib, 1983; Halldin et al., 1999). Likewise, quail exposed embryonically to 150 µg DDT/g egg did not show ovotestis as adults (Halldin et al., 2003).

Insecticides developmental delays in postnatal offspring may be indicated by reduced body weight or weight gain, considered a sensitive and consistent measure of developmental effect (Rochelle, 1988).

6. Perspectives of research in developmental and reproductive toxicity of insecticides

Expensive studies that are able to incorporate direct exposure assessments on large populations are needed. Before this can be justified as other studies have suggested (Rowland, 1995), the basic question which needs further attention is to know if "people who perform agriculture work at increased risk"? There are substantial differences in the ways insecticides are used within different types of farming that may not have been adequately appreciated in the past. Collaboration between registries and pooling of cases when case-control studies are planned is worth considering. Since adverse reproductive outcome may be an indirect measure of the exposure effect, it is urgent to rethink what has long been standard approach to modelling toxicity of environmental insults and develop alternative methods for doing more quantitative-based insecticides exposure assessments. To incorporate these methods into more accurate exposure assessments in case-control studies of reproduction defects and insecticides, epidemiologists and industrial hygienists will need to work together to characterize determinants of insecticide exposure that are region and crop specific.

7. References

Abdallah, F. B., Slima, A. B., Dammak, I., Keskes-Ammar, L. and Mallek, Z. Comparative effects of dimethoate and deltamethrin on reproductive system in male mice. *Andrologia* 2010; 42: 182–186.

Aceitero, J., Llanero M., Parrado, R., Pena, E., Lopez-Beltran, A. Neonatal exposure of male rats to estradiol benzoate causes rete testis dilation and backflow impairment of spermatogenesis. *Anatomy Research*, 1998; 252(1): 17-23.

Adilaxmamma, K., Janardhan, A. and Keddy, K.S. Monocrotophos: Reproductive toxicity in rats. *Indian Journal of Pharmacology* 1994; 26: 126-129.

Alegakis, A. K., Koumantakis, E., and Troulakis, G. Experiences with acute organophosphate poisonings in Crete. *Vet. Hum. Toxicol.* 1996; 38(2): 101-107.

Amer, S.M. and Aly, F.A. Genotoxic effect of 2, 4-dichlorophenoxy acetic acid and its metabolite 2,4- dichlorophenol in mouse. *Mutat. Res.* 2001; 494: 1-12.

Andersen, A.G., Jensen, T.K., Carlsen, E., Jorgensen, N., Andersson, A.M., Krarup, T., Keiding N, et Skkaek, N.E. Fréquence élevée de qualité de sperme inférieure à la moyenne chez une population non sélectionnée d'hommes jeunes: *Reproduction Humaine* 2000; 15 (2): 366-372.

Asmathbanu, I, Kaliwal, B.B. Temporal effect of methyl parathion on ovarian compensatory hypertrophy, follicular dynamics and estrous cycle in hemicastrated albino rats. *J Basic Clin Physiol Pharmacol* 1997; 8:237-254.

Assunção, J.V., Pesquero, C.R. Dioxinas e furanos: origens e riscos. *Rev Saúde Pública* 1999; 33:523-30.

Atanassova, N., McKinnell, C., Walker, M., Turner, K.J., Fisher, J.S., Morley, M., Millar, M.R., Groome, N.P., and Sharpe, R.M,. Permanent effects of neonatal estrogen exposure in rats on reproductive hormone levels, Sertoli cell number and the efficiency of spermatogenesis in adulthood. *Endocrinology* 1999; 140: 5364-5373.

Aziz, N, Walliullah, S.S. and Aziz, R.N. Histological Changes in Male Rat Reproductive Organs Post-Treated With Insecticide Carbofuran (Furadan). *Annals of Microscopy* 2008 ; 8 : 83-89.

Baligar, P.N., Kaliwal, B.B. Reproductive toxicity of carbofuran tothe female mice: effects on estrous cycle and follicles. *Ind Health* 2002; 40:345-352.

Barrett, K.E., Barman, S.M., Boitano, S. and Brooks, H.L. Ganong's Review of medical physiology 23rd Edition McGraw Hill 2010.

Beard, A. P. and Rawlings, N. C. Reproductive effects in mink (Mustela vison) exposed to the pesticides Lindane, Carbofuran and Pentachlorophenol in a multigeneration study. *Journal of Reproduction and Fertility* 1998; 113, 95-104.

Bell, R., Sally, C., Ming, Q., Alwyn, F., Paul, M. F., Tao, J., George, L., Alan, M.N., Brian, G., Rose, L., Tran, k. and Shaun, W.: Toxicity of 2,3,7,8- tetrachlorodibenzo-p-dioxin in the developing male Wistar (han) rat. I: no decrease in epididymal sperm count after a single acute dose. *Toxicological Sciences* 2007; 99: 214–223.

Ben Rhouma, K., Tebourbi, O., Krichah, R.N. & Sakly, M. Reproductive toxicity of DDT in adult male rats. *Human Experimental Toxicology* 2001; 20 (8): 393-397.

Blomqvist, A., Berg, C., Holm, L., Brandt, I., Ridderstrale, Y., & Brunetröm, B. Defective reproductive organ morphology and function in domestic Rooster embryonically exposed to O,P'-DDT or ethynylestradiol. *Biology of Reproduction* 2006; 74(3): 481-486.

Bush, B., Lambert, G., Tarbell, A. Polychlorinated biphenyl (PCB) and dichlorodiphenyl dichloroethylene (DDE) exposure among Native American men from contaminated Great Lakes fish and wildlife. *Toxicol Ind Health* 1996; 12:361-8.

Cabello, G., Valenzuela, M. & Vilava, A. A rat mammary Tunor Model Induced by the Organophosphorous pesticides Parathion and Malathion, possibly through Acetylcholinesterase inhibition. *Environmental Health perspectives* 2001; 109 (5): 471-479.

Campbell, N.A. & Reece J.B. Biology 7th Edition, Binjamin Cummings, San Francisco, Boston, New York 2005; 1231p.

Chadwick, R.W., Cooper, R.L., Chang, J., Rehnberg, G.L., McElroy, W.K. Possible antiestrogenic activity of lindane in female rats. *J Biochem Toxicol* 1988; 3:147-158.

Chapin, R.E., Harris, M.W., Davis, B.J., Ward, S.M., Wilson, R.E., Mauney, M.A., Lockhart, A.C., Smialowicz, R.J., Moser, V.C., Burka, L,T., Collins, B.J. Theeffects of perinatal/juvenile methoxychlor exposure on adult rat nervous, immune, and reproductive system function. *Fundam Appl Toxicol* 1997; 40:138-157.

Choudhary, N., Goyal, R. & Joshi, S.C.. Effect of malathion on reproductive system of male rats. *Journal of Environmental Biology* 2008; 29(2): 259-262.

Choudhary, N., Goyal, R. and Joshi, S.C. Reproductive toxicity of endosulfan in male albino rats. *Environ. Contam. Toxicol* 2003; 70:285–289.

Chung, M.K., Kim, J-C., Han, S.S. Developmental toxicity of flupyrazofos, a new organophosphorus insecticide, in rats. *Food and Chemical Toxicology* 2002; 40: 723–729.

Clark, G., Garry, V., Burroughs, B., Holland, S., Chu, M. & Brown, D. Endocrine disruptors. Relationships between exposure to dioxin-like chemicals, testosterone levels, and sex of the children of pesticide applicators. *Organohalogen Compounds* 2002; 56: 73-76.

Colborn, T., Myers, P.J. & Dumanoski, D. Our Stolen Future. Penguin Boocks, USA Inc., New York. Consensus d'actualisation SFAR - Médecine d'Urgence 1996; 18 p.

Colborn, T., Vom Saal, F.S. & Soto, A.M. Developmental effects of endocrine-disrupting chemicals in wildlife and humans. *Environmental Health Perspectives* 1993; 101: 378-384.

Cooper, R.L., Chadwick, R.W., Rehnberg, G. L., Goldman, J.M., Booth, K.C., Hein J.F. & W. Keith McElroy. Effect of lindane on hormonal control of reproductive function in the female rat. *Toxicology and Applied Pharmacology* 1989; 99(3) : 384-394.

Corwin, E. J. Handbook of Pathophysiology, 3rd Edition, Lippincott Williams & Wilkins 2008.

Cummings, A.M., Laskey, J. Effect of methoxychlor on ovarian steroidogenesis: role in early pregnancy loss. *Reprod Toxicol* 1993; 7:17-23.

Darren, M.R., Ayanthi, K., Nick, A.B., Gamini, M,H., Sheriff, R. & Eddleston, M. Influence of pesticide regulation on acute poisoning deaths in Sri-Lanka. *Bulletin of World Health Organization* 2003; 81: 112-120.

Delemarre-van de Waal, H.A. Environmental Factors Influencing Groth and Pubertal Development. *Environmental Health Perspectives* 1993; Supplément 101. 39-44.

Dhondup, P., Kaliwal, B.B. Inhibition of ovarian compensatory hypertrophy by the administration of methyl parathion in hemicastrated albino rats. *Reprod Toxicol* 1997, 11:77-84.

Eil, C. and Nisula B.C. The binding properties of pyrethroids to human skin fibroblast androgen receptors and to sex hormone binding globulin. *J. Steroid Biochem*. 1990; 35(3/4):409-414.

Eldridge, J.C., Fleenor-Heyser, D.G., Extrom PC, Wetzel, L.T., Breckenridge, C.B., Gillis, J.H., Luempert, L.G. III, Stevens, J.T. Short-term effects of chlorotriazines on estrus in female Sprague-Dawley and Fischer 344 rats. *J Toxicol Environ Health* 1994; 43:155-167.

Eroschenko, V.P. & Mousa, M. A. Neonatal administration of insecticide chlordecone and its effects on the development of the reproductive tract in the female mouse. *Toxicology and Applied Pharmacology* 1979 ; 49 (1) : 151-159.

Eskenazi, B., Kimmel, G. Workshop on perinatal exposure to dioxin-like compounds. II. Reproductive effects. *Environ Health Perspect* 1995; 103:143-5.

Faqi, A.S., Dalsenter, P.R., Ligensa, A., Merker, H.J. and Chahoud, I.: Effect on male fertility and testis concentrations of low dose of 2,3,7,8- tetrachlorodibenzo-p-dioxin (TCDD) in offspring of rats exposed during pregnancy and lactation. *Teratology* 1997; 56: 403.

Farag, A. T., Ahmed, F., Aswad, E. and. Shaaban, N. A.: Assessment of reproductive toxicity of orally administered technical dimethoate in male mice. *Reprod. Toxicol* 2007; 23: 232-238.

Farag, A.T., Eweidah, M.H., El-Okazy, A.M. Reproductive toxicology of acephate in male mice. *Reprod Toxicol* 2000; 14(5):457-462.

Farag, AT, Eweidah, MH, Tayel, SM, El-Sebae, AH. Developmental toxicity of acephate by gavage in mice. *Reproductive Toxicology* 2000; 14: 241–245.

Foster, W.G., McMahon, A., Villeneuve, D.C., Jarrell, J.F. Hexachlorobenzene (HCB) suppresses circulating progesterone concentrations during the luteal phase in the cynomolgus monkey. *J Appl Toxicol* 1992; 12:13-17.

Foster, W.G., McMahon, A., Younglai, E.V., Jarrell, J.F., Lecavalier, P. Alterations in circulating ovarian steroids in hexachlorobenzeneexposed monkeys. *Reprod Toxicol* 1995; 9:541-548.

Gerhard, L., Monga, B., Krahe, J., Runnebaum, B. Chlorinated hydrocarbons in infertile women. *Environ Res* 1999; (80-4) : 299-310.

Giwercman, A., Carlsen, E., Keiding, N., Skakkebaek, N.E. Evidence for increasing incidence of abnormalities of the human testis: a review. *Environ Health Perspect* 1993; 101:65-71.

Gojmerac, T., Kartal, B., Curic, S, Zuric, M., Kusevic, S., Cvetnic, Z. Serum biochemical changes associated with cystic ovarian degeneration in pigs after atrazine treatment. *Toxicol Lett* 1996; 85:9-15.

Gouda, H., Sastry, M.S. Effect of 0,0-Dimethyl-0 phosphorothicate (sumithion) on reproductive performance in rats and oestrogenic activity in mice. *Indian J Pharmacol* 1979; 11:287-292.

Hakin, L.S., Oates, R.D. Non-surgical treatment of male infertility: specific therapy. In: Lipshultz LI, Howards SS, editors. Infertility in the male. St. Louis: Mosby Year Book; 1997. p. 395-402.

Halldin, K., Berg, C., Brandt, I.& Brunström, B. Sexual behaviour in Japanese quail as a test end point for endocrine disruption: effects of in ovo exposure to exposure to ethinylestradiol and diethylstilbestrol. *Environ Health Perspect* 1999; 107: 861-866.

Halldin, K., Holm, L., Ridderstrale, Y., & Brunström B. Reproductive impairment in Japanese quail (Corturnix japonica) after in ovo exposure to O'P'-DDT. *Archive of Toxicology* 2003; 77: 116-122.

Hikim, A.P., Amador, A.G., Klemcke, H.G., Bartke, A.& Russell, L.D. Correlative morphology and endocrinology of Sertoli cells in hamster testes in active and inactive states of spermatogenesis. *Endocrinology* 1989; 125: 1829-1843.

Hodgson, E. A textbook of Modern Toxicology 3rd Edition A John Wiley&Sons Publication 2004.

Hwa–Young, S., Yong–Bum, K., Boo–Hyon, K., Sung–Whan, C. Chang–Su, H., & Jung–Koo R.. Effects of 2-bromopropane on spermatogenesis in the sprague–dawley rat. *Reproductive Toxicology* 1999; 13 (3): 179–187.

Jaensson, A., Scott, A.P., Moore, A., Kylin, H. & Olsen, K.H. Effects of a pyrethroid pesticide on endocrine responses to female odours and reproductive behaviour in male parr of brown trout (Salmo trutta). *Aquatic Toxicology* 2007; 81: 1-9.

Jaiswal, A., Parihar, V. K., Sudheer, K. M., Manjula, S.D., Krishnanand, B. R., Shanbhag, R. and Unnikrishnan, M. K.: 5-Aminosalicylic acid reverses endosulfan-induced

testicular toxicity in male rats. *Genetic Toxicology and Environmental Mutagenesis* 2005; 585: 50-59.

Jequier, A.M. Male infertility – a guide for the clinician. Oxford: Blackwell Science; 2002.

Joshi, S.C., Mathur, R. and Gulati, N.: Testicular toxicity of chlorpyrifos (an organophosphate pesticide) in albino rat. *Toxicol. Ind. Health* 2007; 23: 439-444 .

Kelce, W.R., Stone, C.R., Laws, S.C., Gray, L.E., Kemppainen, J.A. & Wilson, E.M. Persistent DDT metabolite p,p'-DDE is a potent androgen receptor antagonist. *Nature* 1995; 375: 581-585.

Khan-Dawood, F.S. & Satyawaroop, P.G. Toxic effects of chemicals and drugs on the sex accessory organs in the nonpregnant female. In: Raphael J.Witorsch (edt), Reproductive Toxicology, Second edition. Raven Press, Ltd., New York 1995. 159-173.

Kleemann, W.J., Weller, J.P., Wolf, H., Troger, H.D., Bluthgen, A. & Heeschen W. Heavy metals, chlorinated pesticides and polychlotinated biphenyls in Sudden Infant Dead Syndrome (SIDS). *International Journal Legal Medicine* 1991; 104:71-75

Klein, R.M. & Enders, G.C. Anatomy, Histology and Cell Biology 3rd Edition. McGraw-Hill Medical. New York 2007; 618p

Kumar, R., Uppal, R.P. Effect of malathion on estrous cycle and reproductive performance of rats. *J Environ Biol* 1986; 7:35-39.

Lahiri, P., Chakravarty, S., Mondal, A. & Sircar, S. Effect of lindaneon cytology and cytochemistry of exfoliated vaginal cells. *Exp Clin Endocrinol* 1985; 85:303-308.

Latchoumycandane, C. & Mathur, P. P. Effect of methoxychlor on the antioxidant system in mitochondrial and microsome-rich fractions of rat testis. *Toxicology* 2002; 176: 67-75.

Latchoumycandane, C., Chitra, K.C. & Mathur, P.P. The effect of 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD) induces oxidative stress in the epididymis and epididymal sperm of adult rats. *Arch. Toxicol.* 2003; 77: 280–284.

Lebel, G., Dodin, S., Ayotte, P., Marcoux, S., Ferron, L.A. & Dewailly, E. Organochlorine exposure and the risk of endometriosis. *Fertil Steril* 1998; 69:221-228.

Lenselink, D.R., Midtling, J.E. & Kolesari, G.L. Teratogenesis associated with oxydemeton-methyl in the stage 12 chick embryo. *Teratology* 1993; 48, 207–211.

Lerda, D. & Rizzi, R.: Study of reproductive function in persons occupationally exposed to 2,4- dichlorophenoxyacetic acid (2,4-D). *Mutat. Res.* 1991; 262:47–50.

Lindenau, A., Fischer, B., Seiler, P., Beier, H.M. Effects of persistent chlorinated hydrocarbons on reproductive tissues in female rabbits. *Hum Reprod* 1994; 9:772-780.

Makoto, E. & Akira, H. Development and reproductive toxicity of tributyltin and its metabolite, dibutylin, in rats. *Congenital Anomalies* 2000; 40: 108-120.

Makoto, E. & Emiko, M. Suppression of uterine decidualization correlated with reduction in serum progesterone levels as a preimplantation embryonic loss induced by diphenyltin in rats. *Reproductive toxicology* 2002; 16: 309-317.

Martin, S., Harlow, S.D. and Sowers, M.F.: DDT metabolite and androgens in African American farmers. *Epidemiology* 2002; 13: 454-458.

Martinez, E.M .& Swartz, W.J. Effects of methoxychlor on the reproductive system of the adult female mouse. Gross and histologic observations. *Reprod Toxicol* 1991; 5:139-147.

Mattison, D.R. The mechanisms of action of reproductive toxins. *Am J Ind Med* 1983; 4: 65_79.

Meeker, J.D., Barr, D.B. & Hauser, R. Human semen quality and sperm DNA damage in relation to urinary metabolites of pyrethroid insecticides. *Hum Reprod* 2008; 23(8):1932-1940.

Meeker, J.D.& Barr, D.B,, Hauser R. Pyrethroid insecticide metabolites are associated with serum hormone levels in adult men. *Reproductive Toxicology*. 2009; 27: 155-160.

Mehmet, G., Baha, O., Hilmi, D., Gulnur, T., Seren, G. G., Irfan, A., Tamer, M. Fallopian damage induced by organophosphate insecticide methyl parathion and protective effect of vitamins E and C on ultrastructural changes in rats. *Toxicology and Industrial Health* 2007; 23: 429-438.

Meltem, U., Yusuf, K., Kerem, D., Suna, K., Ayse, O. and Fatma, B.: Acute, subacute and subchronic administration of methyl parathion-induced testicular damage in male rats and protective role of vitamins C and E. *Pesticide Biochemistry and Physiology* 2007; 87:115-122.

Metzler, M., editor. The handbook of environmental chemistry. Berlin: Springer-Verlag; 2002.

Michal, F., Kenneth, M. G., Negro-Vilar A, and Skakkebæk M. Impact of the environment on reproductive health: executive summary. *Environment Health Perspective* 1993: 101(2): 159-167.

Moline, J.M., Golden, A.L., Bar-Chama, N., Smith, E., Rauch, M.E., Chapin, R.E., Perreault, S.D., Schrader, S.M., Suk, W.A. & Landrigan, P.J. Exposure to hazardous substances and male reproductive health: A research framework. *Environmental Health Perspectives* 2000; 108(9): 803-813.

Moreira, J.C., Wolff, M. Dietary and reproductive determinants of plasma organochlorine levels in pregnant women in Rio de Janeiro. *Environ Res* 2003; 91:143-50.

Morgan, C., & Ashraf, M. Reproductive Toxicity Evaluation of Pestban Insecticide Exposure in Male and Female Rats *Toxicological Research* 2008; 24(2): 137-150.

Muller, W.F., Hobson, W., Fuller, G.B., Knauf, W., Coulston F., Korte, F. Endocrine effects of chlorinated hydrocarbons in rhesus monkeys. *Ecotoxicol. Environ. Saf.* 1978; 2:161-172.

Narayana, K., Narayan, P. & D'Souza, U.J. Is our drinking water a slow poison? *Indian J. Med. Sci.* 2004; 58:528-530.

Narayana, K., Prashanthi, N., Nayanatara, A., Kumar, S.G., Kumar, H.H.C., Bairy, K.L., & D'Souza, U.J.A. A broad-spectrum organophosphate pesticide *O,O*-dimethyl *O*-4-nitrophenyl phosphorothioate (methyl parathion) adversely affects the structure and function of male accessory reproductive organs in the rat. *Environmental Toxicology and Pharmacology* 2006; 22: 315–324.

Ngoula, F., Watcho, P., Bouseko, T. S., Kenfack, A., Tchoumboué. J., Kamtchouing, P. Effects of propoxur on the reproductive system of male rats. *Afr J Reprod Health*. 2007; 11 (1):125-32.

Ngoula, F., Watcho, P., Dongmo, M-C., Kenfack, A., Kamtchouing, P., Tchoumboué. J. Effects of pirimiphos-methyl (an organophosphate insecticide) on the fertility of adult male rats. *Afr Health Sci.* 2007; 7 (1):3-9.

Ngoula, F., Tchoumboue, J., Watcho, P., Kenfack, A., Defang Fualefac, H., Manga Nzouck, J., Kamtchouing, P. Effects of dimethoate (organophosphate insecticide) on the

reproductive system and fertility of adult male rats (*Rattus norvegicus*). Presented at the international Conference for Toxicological Sciences. 31st may – 03rd June 2011, University of Buéa-Cameroon. THEME: "Searching for African Solutions to Human and Environmental Toxicological Challenge".

Nidhi, M., Pandey, G. & Jain, G.C. Pesticides: A Review of the male reproductive toxicity. *Journal of Herbal Medicine And Toxicology* 2010; 4 (1): 1-8.

Niederberger, C. Exposure to persistent organochlorine pollutants associates with human sperm Y:X chromosome ratio. *Hum Reprod* 2005; 20: 1903-1909.

Nurminen, T., Rantala, K., Kurppa, K. & Holmberg, P.C. Agricultural work during pregnancy and selected structural malformations in Finland. *Epidemiology* 1995; 6: 63-65.

Oakes, D.J., Webster W.S., Brown-Woodman P.D.C., and Ritchie H.E. A study of the potential for herbicide formulation containing 2,4-D and Picloram to cause male-medieted developmental toxicity in rats. *Toxicology Sciences* 2002; 68: 200-206.

Oduma, J.A., Wango, E.O., Makawiti, D.W., Einer-Jensen N. & Oduor-Okelo, D. Effects of graded doses of the pesticide heptachlor on body weight, mating success, oestrous cycle, gestation length and litter size in laboratory rats. *Comp Biochem Physiol C Pharmacol Toxicol Endocrinol* 1995a, 110:221-227.

Oduma, J.A., Wango, E.O., Oduor-Okelo, D., Makawiti, D.W. & Odongo. H. In vivo and in vitro effects of graded doses of the pesticide heptachlor on female sex steroid hormone production in rats. *Comp Biochem Physiol C Pharmacol Toxicol Endocrinol* 1995b; 111:191-196.

Ohi, M., Dalsenter, P.R., Andrade, A.J. & Nascimento, A.J. Reproductive adverse effects of fipronil in Wistar rats. Toxicol. Lett. 2004; 146:121-127.

Pages, N., Sauviat, M.P., Bouvet, S. & Goudey-Perriere, F. Reproductivetoxicity of lindane. *J Soc Biol* 2002; 196:325-338.

Palladino, M.A. Male reproductive system. In *Biology* Vol 3, Robinson R.(Ed). Macmillan Reference USA, New York, Thomson Gale 2002; 56-59pp.

Pant, N., Prasad, A.K., Srivastava, S.C., Shankar, R. and Srivastava, S.P.: Effect of oral administration of carbofuran on male reproductive system of rat. *Hum. Exp. Toxicol.* 1995; 14: 889-894.

Pesando, D., Robert, S., Huitorel, P., Gutknecht, E., Pereira, L., Girard, J-P., Ciapa, B. Effects of methoxychlor, dieldrin and lindane on sea urchin fertilization and early development. *Aquatic Toxicology*, 2004; 66: 225–239.

Pesticides Action Network (PAN) Belgium. Pesticides a usage domestique risques pour la sante. 1999 84 p.

Picard, A., Palavan, G., Robert, Ste-P., Pesando, D. & Ciapa, B. Effect of Organochlorine pesticides on Maturation of Starfish and Mouse Oocytes. *Toxicological Sciences*, 2003 ; 73 : 141–148.

Potashnik, G. & Abeliovich, D. Chromosomal analysis and health status of children conceived to men during or following dibromochloropropaneinduced spermatogenic suppression. *Andrologia* 1985; 17:291-6.

Prasad, A.K., Pant, N., Srivastava, S.C., Kumar, R. & Srivastava, S.P.: Effect of oral administration of carbofuran on male reproductive system of rat. *Hum. Exp. Toxicol.* 1995; 14: 484-491.

Presibella, K.M., Kita, D.H., Carneiro, C.B., Andrade, A.J., Dalsenter, P.R.. Reproductive evaluation of two pesticides combined (deltamethrin and endosulfan) in female rats. *Reprod Toxicol*. 2005; 20(1):95-101.

Ramadan, A.A.; Bakry, N.M.; Marei, A.S.M.; Eldefrawi, A.T. & Eldefrawi, M.E. Actions of pyrethroids on the peripheral benzodiazepine receptor. *Pesticide Biochemistry and Physiology* 1988; 32: 106-113.

Rani, A., Sahai, A., Srivastava, A.K. & Rani, A. Carbaryl induced histopathological changes in the testis of albino rats. *Journal of the Anatomical Society of India* 2007; 56: 4-6.

Rani, B.E., Krishnakumari, M.K. Prenatal toxicity of heptachlor in albino rats. *Pharmacol Toxicol* 1995; 76:112-114.

Rao, M., Narayana, K., Benjamin, S. & Bairy, K.L. L-ascorbic acid ameliorates postnatal endosulfan induced testicular damage in rats. *Indian J. Physiol. Pharmacol.* 2005; 49(3): 331-336.

Ray A, Chatterjee S, Ghosh S, Kabir SN, Pakrashi A, Deb C. Suppressive effect of quinalphos on the activity of accessory sex glands and plasma concentrations of gonadotrophins and testosterone in rats. *Arch Environ Contam Toxicol.* 1991; 21(3):383-387.

Ribeiro, G. Os pesticidas como disruptores endócrinos nos peixes.
        http://www.fmv.utl.pt/stf/ sem0001/G04.htm.

Rochelle, W.Tyl. Developmental toxicity in toxicologic research and testing. In Bryan Ballantyne (edt): Perspectives in basic and applied toxicology wright. Butterworth and Co (Publishers), London, Baston, Durban, Singapore, Sydney, Toronto, Wellington. 1988; pp 206-239.

Rowland, A.S. Pesticides and birth defects. *Epidemiology* 1995; 6 (1): 6-7.

Rupa, D.S., Reddy, P.P. and Reddi, O.S.: Reproductive performance in population exposed to pesticides in cotton fields in India. *Environ. Res.* 1991; 55: 123-128.

Sadler, T.W. Langman's Medical Embryology 10th Edition 2006; 358p

Sancewicz-Pach, K., Groszek, B., Pach, D., Klys, M. Acute pesticides poisonings in pregnant women, Przegl. Lek 54 1997; 10: 741-744.

Sang-Hee, J., Byung-Yong, K., Hwan-Goo, K., Hyun-Ok, K. & Joon-Hyoung, C. Effect of chlorpyrifos-methyl on steroid and thyroid hormones in rat F0- and F1-generations. *Toxicology* 220 (2006) 189–202.

Santamarta, J. Por um futuro sem contaminantes orgânicos persistentes. *Agroecologia e Desenvolvimento Rural Sustentável* 2001; 2:46-56.

Saradha, B., Vaithinathan, S. & Mathur, P.P. Single exposure to low dose of lindane causes transient decrease in testicular steroidogenesis in adult male Wistar rats. *Toxicology* 2008, 244: 190–197.

Saradha, B., Vaithinathan, S. & Mathur, P.P.: Lindane induces testicular apoptosis in adult Wistar rats through the involvement of Fas-FasL and mitochondria-dependent pathways. *Toxicology* 2009; 255:131-139.

Sayým, F. Histopathological effects of dimethoate on testes of rats. *Bulletin of Environmental Contamination and Toxicology* 2007; 78: 479-484.

Scheib, D. Effects and role of estrogens in avian gonadal differentiation. *Differentiation*, 1983; 23 (suppl): 87-92.

Shalaby, M.A., El Zorba, H.Y. & Ziada, R. M. Reproductive toxicity of methomyl insecticide in male rats and protective effect of folic acid. *Food and Chemical Toxicology* 2010 ; 48: 3221–3226.

Sharpe, R.M. Hormones and testis development and the possible adverse effects of environmental chemicals. *Toxicology Letters* 2001; 120: 221–232.

Sharpe, R.M., Atanassova, N., McKinnell, C., Parte, P., Turner, K.J., Fisher, J.S., Kerr, J.B., Groome, N.P., Macpherson, S., Millar, M.R. & Saunders, P.T. Abnormalities in functional development of the Sertoli cells in rats treated neonatally with diethylstilbestrol: a possible role for estrogens in Sertoli cell development. *Biology of Reproduction* 1998; 59: 1084-1094.

Sobarzo, C. & Bustoos-Obregón E. Sperm quality in mice acutely treated with parathion. Asian *Journal of Andrology*, 2000a; 2: 147-150.

Sobrazo, C. & Bustos-Obregon E. Acute effect of parathion on the seminiferous epithelium of immature mice. *Revista Chilena de Anatomia* 2000b; 18(1): 6-68.

Spencer, F. and Z. Berhane. Uterine and fetal characteristics in rats following a post-implantational exposure to permethrin. *Bull. Environ. Contam. Toxicol.* 1982; 29:84-88.

Suresh, C.J., Reena, Ma., Anita, G. &Tripta, S. Influence of methyl parathion on reproductive parameters in male rats. *Environmental Toxicology and Pharmacology* 2003 ; 14: 91-98.

Swartz, W.J., Mall, G.M. Chlordecone-induced follicular toxicity inmouse ovaries. *Reprod Toxicol* 1989; 3:203-206.

Talens, G. & Wooley, D. Effects of parathion administration during gestation in the rat on development of the young. *Proceedings of the Western Pharmacological Society* 1973; 16: 141–145.

Toppari, J. Male reproductive health and environmental xenoestrogens. Environ Health Perspect 1996; 104:741-803.

U.S. EPA. Data evaluation record: Developmental neurotoxicity study - rat; OPPTS 870.6300. (MRID 44501102.) Washington, D.C. 1997.

U.S. EPA. Data evaluation record-supplemental: Developmental neurotoxicity study - rat; OPPTS 870.6300. (MRID 44039002.) Washington, D.C. 1998[2]

U.S. EPA. Office of Pesticide Programs. "Tox one-liners": Cyfluthrin. Washington, D.C. 1989.

U.S. EPA. Office of Pesticide Programs. Health Effects Division. Tox oneliners: Permethrin. Washington D.C. 1997.

U.S. EPA. Office of Prevention, Pesticide and Toxic Substances. Fipronil for use on rice (Regent®, Icon®) and pets (Frontline®). HED risk assessment. Washington, D.C. 1998[1], 22. Pp.19,20,22.

Uphouse, L., Mason, G. & Hunter, V. Persistent vaginal estrus and serum hormones after chlordecone (kepone) treatment of adult female rats. *Toxicol Appl Pharmacol* 1984, 72:177-186.

Uzun, F.G., Kalender, S., Durak, D., Demir, F. & Kalender, Y. Malathion-induced testicular toxicity in male rats and the protective effect of vitamins C and E. *Food Chem. Toxicol.* 2009; 47: 1903-1908.

Vaithinathan, S., Saradha, B. & Mathur, P.P. Transient inhibitory effect of methoxychlor on testicular steroidogenesis in rat. *Arch. Toxicol.* 2008; 82: 833-839.

Van Emden, H.F. & Pealall, D.B. Beyond Silent Spring, Chapman & Hall, London, 1996; 322p

Vartiainen, T., Kartovaara, L. & Tuomisto, J. Environmental Chemichals and Changes in Sex Ratio: Analysis Over 250 Years in Finland. *Environmental Health Perspectives* 1999; Volume 107(10).

Villeneuve, D.C., Willes, R.F., Lacroix, J.B. & Phillips, W.E.J. Placental transfer of 14C-parathion administered intravenously to rats. *Toxicology and Applied Pharmacology* 1972; 21: 542–548.

Vogin, E.E., Carson, S. &Slomka, M.B. Teratology studies with dichlorvos in rabbits. *Toxicology and Applied pharmacology* 1971; 19: 377–378.

Waissmann, W. Endocrinopatologia associada ao trabalho. In: Mendes R, organizador. Patologia do trabalho. São Paulo: *Editora Atheneu*; 2003; p.1093-138.

Walsh, L.P. & Stocco D.M. The effects of roundup and dimethoate on steroidogenesis acute regulatory (Star) protein in mouse MA-10 Leydig cells. *Proceedings of the Society For the Study of Reproduction* 1998; 8-11: 182.

Walsh, L.P., McComick, C., Martin C., & Stocco D.M. Roundup inhibits Steroidogenesis by disrupting steroidogenic acute regulatory (StAR) protein expression. *Environmental Health Perspectives* 2000; 108 (8): 769-776.

Ware, G.W. & Whitacre DM. The Pesticide Book, 6th Ed. Meister Media Worldwide, Willoughby, Ohio. 2004; 496 pp.

Ware, G.W. An introduction to insecticides 3rd Edition 2001; p. 7

Weck, M.A. Female reproductive system. In *Biology* Vol2, Robinson. (Ed). Macmillan Reference USA, New York, Thomson Gale 2002; 77- 81 pp

Whorton, D., Krauss RM, Marshall S, Milby TH. Infertility in male pesticide workers. *Lancet* 1977; 2: 1259-61.

Wikibooks Producers. Human Physiology. 2007; 426p

Wyrobek, A.J., Watchmaker, G. and Gordon, L. Sperm shape abnormalities in carbaryl-exposed employees. *Environ. Health Perspect*. 1981; 40: 255-26

Insecticides - Advances in Integrated Pest Management
Edited by Dr. Farzana Perveen

ISBN 978-953-307-780-2
Hard cover, 708 pages
Publisher InTech
Published online 05, January, 2012
Published in print edition January, 2012

This book contains 30 Chapters divided into 5 Sections. Section A covers integrated pest management, alternative insect control strategies, ecological impact of insecticides as well as pesticides and drugs of forensic interest. Section B is dedicated to chemical control and health risks, applications for insecticides, metabolism of pesticides by human cytochrome p450, etc. Section C provides biochemical analyses of action of chlorfluazuron, pest control effects on seed yield, chemical ecology, quality control, development of ideal insecticide, insecticide resistance, etc. Section D reviews current analytical methods, electroanalysis of insecticides, insecticide activity and secondary metabolites. Section E provides data contributing to better understanding of biological control through Bacillus sphaericus and B. thuringiensis, entomopathogenic nematodes insecticides, vector-borne disease, etc. The subject matter in this book should attract the reader's concern to support rational decisions regarding the use of pesticides.

How to reference
In order to correctly reference this scholarly work, feel free to copy and paste the following:

Ferdinand Ngoula, Omer Bébé Ngouateu, Jean Raphaël Kana, Henry Fualefac Defang, Pierre Watcho, Pierre Kamtchouing and Joseph Tchoumboué (2012). Reproductive and Developmental Toxicity of Insecticides, Insecticides - Advances in Integrated Pest Management, Dr. Farzana Perveen (Ed.), ISBN: 978-953-307-780-2, InTech, Available from: http://www.intechopen.com/books/insecticides-advances-in-integrated-pest-management/reproductive-and-developmental-toxicity-of-insecticides