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ARTICOLO SPECIALE

IL RISCHIO DI DISORDINI RIPRODUTTIVI TRA LE DONNE CHE LAVORANO NELLE SERRE

THE RISK OF REPRODUCTIVE DISORDERS AMONG WOMEN WORKING IN GREENHOUSE

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Riassunto

I pesticidi sono sostanze altamente tossiche, utilizzate in agricoltura convenzionale per la difesa delle piante, il cui impiego continuativo può comportare effetti nocivi per la salute umana e l'ambiente.

Recenti studi scientifici hanno dimostrato che molte di queste sostanze rientrano fra gli inferenti endocrini (endocrin disruptors), molecole in grado di interferire, anche a dosi bassissime, con le funzioni ormonali, immunitarie, metaboliche e riproduttive.

In particolare le donne che lavorano nelle serre, dove i cicli di crescita sono rapidi e c'è un microclima che favorisce lo sviluppo di agenti patogeni, sono maggiormente sottoposte a fattori di rischio chimico a causa dell'intensa frequenza dei trattamenti fitosanitari e all'uso non appropriato degli adeguati dispositivi di protezione.

Studi condotti su operatrici sericole alla prima gravidanza hanno dimostrato la probabile correlazione tra l'esposizione delle donne ai pesticidi e la comparsa di fenomeni che interferiscono con la riproduzione.

La normativa europea con la Direttiva 2009/128/CE[13], istituisce un *"quadro per l'azione comunitaria ai fini dell'utilizzo sostenibile dei pesticidi"*, e si propone di ridurre i rischi e l'impatto dei pesticidi sulla salute umana e sull'ambiente e di promuovere l'uso della difesa integrata e di tecniche agricole alternative .

Questi obiettivi dovranno essere perseguiti attraverso l'adozione di Piani d'Azione Nazionali da parte degli Stati Membri i quali, a seconda delle loro specifiche realtà agricole ed ambientali, dovranno fissare obiettivi quantitativi *"per ridurre la dipendenza dall'utilizzo di pesticidi"*.

Per salvaguardare le operatrici sericole e ridurre i rischi legati all'impiego dei pesticidi, l'alternativa sembra essere rappresentata oggi dall'applicazione, anche nelle produzioni in serra, della coltivazione sostenibile che consente di ridurre l'uso dei pesticidi prediligendo metodi di coltivazione alternativi e integrati.

Parole chiave: Pesticidi, Distruttori endocrini, Alterazioni riproduttive, Tecniche agricole alternative, Direttiva 2009/128/EC

Abstract

The Risk of Reproductive disorders Among Women working in Greenhouse

Pesticides are intrinsically highly toxic, and the benefits accruing from their use should be viewed in tandem with the undesired effects they produce on human health and the environment. In recent years, scientific evidence has shown that some pesticides are potential endocrine disruptors, that interfere with the reproductive processes of

exposed workers. Especially for women working in greenhouses, where growing cycles are rapid and there is a microclimate that encourages the development of pathogens, there are more chemical risk factors due to the intense use of plant protection treatments and the non-use of appropriate personal protective equipment. Studies conducted on first-time pregnant women workers in greenhouses have shown that there is likely correlation between women's exposure to pesticides and the appearance of phenomena that interfere with reproduction. Directive 2009/128/EC[13], establishing "a framework for Community action to achieve the sustainable use of pesticides", sets out to reduce risks and the impact on human health and the environment and to promote the use of integrated pest management and alternative agricultural techniques. This aim will have to be pursued by the adoption of national plans by Member States which, depending on their specific agricultural and environmental conditions, will have to fix quantitative objectives "to reduce dependency on the use of pesticides". To safeguard women workers, reduce production costs and obtain healthier and more eco-friendly crops, it is thus necessary to steer greenhouse production towards alternative or integrated pest management methods with a view to reducing the use of pesticides.

Key words: Pesticides, Endocrine disruptors, Reproductive alterations, alternative agricultural techniques, Directive 2009/128/EC

Introduction

Nursery industry (ornamental plants, fruit, vegetables, forestry) is an agricultural sector based on an industrial-scale propagation and production of plants in greenhouses for the production of trees, shrubs and herbaceous plants to be sold on the market.

Greenhouse farming is in any case an activity that has a considerable impact on the environment due to the amount of energy needed to support production, with the consequent emission of greenhouse gases (heating), the use of technical means (protective structures, fertilisers, pesticides), and the agricultural operations involved (irrigation, cultivation).

Yet despite ongoing climate changes, there is bound to be an increase in greenhouse farming, since this form of agriculture allows a greater control over meteorological conditions and reduces the negative effects of winds, drought and too much rain, and allows a continuous-cycle cultivation, regardless of seasons and the availability of land. In Italy greenhouse growing is common in the south of the country, particularly in Sicily, where 26% of the 31,500 Italian enterprises in this sector are concentrated, with 30% of the 22,000 hectares of land occupied for this type of production at a national level. In this region the surface area set aside for protected crops is over 8,500 ha (25-30% of the national surface area destined for protected crops).

Furthermore, women are often employed in the flower-growing nursery sector. Inside greenhouses, where growing cycles are rapid and there is a microclimate that encourages the spread of pathogens (fungicides, insecticides, pesticides, etc.), women workers work under particular conditions in terms of temperature and humidity. This raises chemical risk factors owing to the intense use of fertiliser and pesticide treatment. Plant protection treatment is often carried out manually, with high-pressure pumps. Fixed machines are not used since "they cannot comply with regulations".

The risks for female agricultural workers in greenhouses include contact with treated crops and with plant protection products of various chemical categories, non-use of PPE because of difficult microclimatic conditions and re-entry in the greenhouse, for manual and mechanical operations, before decay times are complete. There may be particular risks for women workers due to soil sterilisation operations, the use of high-dosage pesticides (the warm and humid greenhouse environment causes a greater spread of parasites), unfavourable microclimatic conditions (opening of windows during work tasks that should not be performed during the hotter hours of the day in spring and summer), exposure to noise and vibrations due to the use of machinery, and adoption of inappropriate postures because of limited space. The most common pathologies are:

- allergopathies, including dermatitis, conjunctivitis, rhinitis, asthma (possibly

Sigle

ED: Endocrine Disruptors
DHEA: dehydroepiandrosterone
PCB: polychlorinated biphenyl
PBDE: polybrominated diphenyl ethers
PFOS: perfluorooctane sulfonate
PFOA: perfluorooctane acid
HCB: hexachlorobenzene
TTP: time to pregnancy
TT4: total Thyroxine
TSH: thyroid stimulating hormone
OP: Organophosphoric pesticides

asthmatic bronchitis), farmer's lung, hymenopteran bites, caused by:
  a) chemical agents (in particular pesticides);
  b) biological agents such as pollen, mites, mycete, contact with animals (dog/cat fur, wool, etc.)
- dermopathies and bronco-pneumopathies that may arise from exposure to chemical irritants (pesticides, fertilisers), biological agents (bacteria, mycete, etc.); these may be aggravated by exposure to cold or to humidity (unfavourable climatic or microclimatic conditions).
- zoonosis (reported in accident reports)
- diseases caused by physical agents:
  a) noise;
  b) vibration transmitted by the use of power hoes and harrows, tractors, or transmitted by other machinery. This pathology may include angiopathies caused by vibrating tools and tunnel syndrome. The effects of exposure to vibrations may be compounded by micro-traumas causing bone and joint disorders.

Exposure to sunlight may also cause epitheliomas and melanomas, while exposure to unfavourable microclimatic conditions may be a cause of heat stress. Risks from pesticide contamination and from occupational diseases are recorded mainly in greenhouses where the level of mechanisation is low. Chemical risk depends on the toxicity and dangerousness of the intrinsic properties of the product, exposure levels and duration, the degree of absorption through the airways, mouth, skin and mucous membranes, and usage methods and frequency[1,16]. The incorrect use of pesticides may also give rise to dangerous environmental contamination. On this point the European Directive on a Strategy for the sustainable use of pesticides has among its objectives the promotion of a type of agriculture that uses few pesticides, with greater protection of the aquatic environment, regular and mandatory inspection of pesticide equipment, appropriate management and storage of pesticide packaging and residues, adequate personnel training and greater awareness building among the population. To safeguard women workers, reduce production costs and obtain healthier, more eco-friendly crops, it is thus necessary to steer workers towards alternative or integrated plant protection practices in order to reduce the use of pesticides[4,23,26].

Many of these substances may be considered as Endocrine Disruptors (ED). In Weybridge, in 1996 Endocrine Disruptors were defined as *"…an exogenous substance or mixture that alters functions of the endocrine system, causing adverse health effects of an organism, or its progeny or (sub)populations"*[5]. The term endocrine disruptor actually indicates a heterogeneous group of substances, both natural and synthetic, present in the environment and in foods which, considerable differences at a molecular level, are capable of disrupting endocrine homeostasis, in particular of the thyroid hormones and steroid sex hormones[27]. Numerous animal species (crustaceans, fish, birds, mammals), including humans, are subject to the action of endocrine disruptors, but the extent of their impact for human beings is still not fully known. *In vivo* and *in vitro* studies have however shown impairment of reproductive capacity, the presence of morphological or functional defects at the birth and the emergence and growth of tumours[3]. Some types of pesticides indeed can disrupt a woman's reproductive system, sometimes bringing about serious effects on the foetus.

The effects of EDs

EDs may[29]:
- interfere with the synthesis, conveyance, metabolism and excretion of natural hormones, altering their physiological concentrations and endocrine functioning;
- bind in a competitive manner with hormonal receptors and block the action of natural hormones;
- perform the action of natural hormones (same chemical reactions and same effects);

The biological actions of hormones [estrogen, androgen, progesterone, thyroxin, pregnenolone and dehydroepiandrosterone (DHEA)], are mediated by receptors of high-affinity proteins situated in the *target* cells. Some steroids, such as estrogens, normally circulate in their sulfated (inactive) form, while the free hormone is released in the *target* tissue through sulphatase present in the same tissue. Other steroid hormones circulate in the blood bound to a *carrier protein* or to serum albumin. These hormones are all lipo-soluble and quickly pass through the cell membrane, subsequently interacting with dimeric protein receptors, which in the case of estrogens are ER-alpha and ER-beta, even though recent studies propose the existence in fish and some mammals of a third receptor, ER-gamma[12]. From malformations to molecular mechanisms in the male: three decades of rese-

arch on endocrine disrupters; APMIS, 109: 263-72). EDs too are lipophilic in nature, thus they are able to spread by means of the cell wall, and once receptors for steroid hormones are bind they can accumulate in the adipic tissue. Their bioaccumulation is of considerable importance in toxicological terms, since through the fats ingested with food (meat, milk, etc.) numerous substances deriving from environmental pollution enter the organism.

The best known endocrine disruptors are those binding the intracell receptors of the estrogens, the main female sexual hormones. Once formed, the steroid-receptor complex is bind to specific target regions of the DNA, activating a cascade of reactions that mediate the organism's response to the hormone itself. It was believed that endocrine disruptors acted through purely genomic mechanisms, i.e. as agonists of the steroid hormones used to bind the receptor. It appears however that some of these compounds can mediate non-genomic effects. Some of them, in fact, can also alter the synthesis and availability of endogenous hormones. Steroids form out of cholesterol, through a series of reactions involving the isoforms of cytochrome P450, enzymes that appear to be induced by atmospheric contaminants. Two nuclear receptors, SXR/PXR and CAR, are important regulators of the metabolism of xenobiotics and steroid hormones. They are widely formed in the liver and the intestine, where they mediate the induction of enzymes of the cytochrome family P450, conjugation enzymes and conveyors, in response to ligand xenobiotics and endogenous hormones. SXR activates the transcription after the bond with the ligand, while CAR is constitutively active, and its high basal activity is repressed by steroids relating to androstenol and by SXR ligands.

Effects similar to estrogen have been demonstrated *in vivo* and *in vitro* for some natural substances too (mycotoxins produced by some fungi and phytoestrogens of vegetables such as soya), which are potentially present in foodstuffs.

The most common effects caused by EDs on the female reproductive neuroendocrine system relate to:

- thyroid: the effect of some substances used as pesticides (metabolites of ethylenebisdithiocarbamate) on the thyroid has been posited, but further studies are needed;
- ovaries: aneuploidy, polycystic ovary syndrome and alterations to the menstrual cycle;
- uterus: endometriosis, uterus fibromas, restriction of foetal growth, miscarriage (it has been suggested that paternal exposure in early pregnancy to some substances used as pesticides might raise miscarriage rates among mothers);
- mammary glands: impossible to feed or reduced breast-feeding period, cancer. Some studies suggest that exposure to substances such as DDT, dioxin and polychlorinated biphenyl (PCB) may increase the risk of breast neoplasia among women. There is also a possible connection between the early onset of puberty among daughters and the mother's exposure during pregnancy to the same substances[9].

Endocrine disruptors mainly influence the reproductive process in a *continuum* going from the production of gametes to fertilisation, intrauterine and postnatal progeny development, with the formation of the foetus' reproduction apparatus and high sensitivity to hormones[27]. These effects were observed mainly among men, where the process of sexual differentiation and masculinisation is chiefly governed by hormones, rendering males more open to the action of EDs. This greater susceptibility is shown by the high incidence among young males of pathologies such as cryptorchidism and hypospadia, which have become more common in recent years. Among genitourinary malformations hypospadia is an alteration of sexual differentiation, whose precise aetiology remains unknown in the majority of cases, despite the continuing validity of risk factors given in literature, such as delayed intrauterine growth, low weight at birth, endocrinological factors and foetal exposure to EDs[3]. Studies conducted on the gene for the androgen receptor have assessed the length of CAG triple repeats and the state of methylation of the gene itself in preputial blood and tissue samples obtained from patients suffering from isolated hypospadia.

Results showed that compared with the control group's tissue, as expressed by the androgen receptor, subjects had a lower amount of protein and a higher level of methylation of the AR gene mediated by the DNA enzyme methyltransferase 3a (Dnmt3a)[3]. *In vitro* studies on fibroblasts extracted from the prepuce, verifying the results observed *in vivo*, suggest that some EDs, in particular those with antiandrogenic activity, can increase the methylation of the AR gene as well as reduce its expression. These results appear to assign an aetiopathogenetic role to androgens and its receptors for

some malformations, especially genital defects, also with reference to EDs[3]. Human milk moreover is in many cases the only food ingested by the newborn in the first months of life. It can be analysed to estimate the intake of contaminants. Studies conducted on milk samples of women residing in the town of Siena and province showed the presence in all samples of p,p'-DDE, a DDT metabolite, and of the majority of sought PCB congeners; hexachlorobenzene (HCB) and flame retardant polybrominated diphenyl ethers (PBDE) were found only in some samples. Among contaminants p,p'-DDE was prevalent in all the samples analysed[8]. In another study conducted on women living in the town of Siena and province, out of 41 milk samples analysed 13 contained perfluorooctane sulfonate (PFOS), while perfluorooctane acid (PFOA) was present in a single sample[17]. Exposure to endocrine disruptors through maternal milk may be important in determining ever more common problems among children, such as growth-related problems.

The WHO promotes breastfeeding, in the absence of sufficient scientific evidence on risks relating to the presence of contaminants in milk, and considering its nutritional and psychological importance, but further action must be taken to ensure that the fall in concentration of pollutants, which began in the 1990s, continues over time. The benefits of breastfeeding are substantial, and the best way of maximising such benefits is to reduce maternal exposure, in particular avoiding or reducing the intake of potentially contaminated foods[30].

Pesticides exposure

Women working in greenhouses are exposed to atmospheric contaminants, including pesticides, which may cause acute harmful effects, as well as long-term effects, following low-dosage chronic exposure. In 2009 Rosano A. et al. conducted a study on 145 women working in greenhouses in the province of Latina who during their first pregnancy had been exposed to pesticides[31]. Exposure to pesticides was classified as high or low accordng to job type and duration of exposure. The alteration of fertility was measured in terms of time to pregnancy (TTP), the number of months taken by the couple to conceive, for the first pregnancy, after having suspended the use of contraceptives). The control group was selected among P.A. women workers in the same province. The study showed that women workers exposed to pesticides had reduced fertility, with TTP over 50% higher than the control group. The issue under study is complex however, since occupational exposure is a condition that must be considered with care, bearing in mind that other factors can have a bearing on reproductive health (emotional state, susceptibility due to congenital or acquired factors).

Chlorinated organic pesticides

Chlorinated organic pesticides (DDT, methoxychlor, chlordecone, kepone) have proved to be responsible for the acceleration of vaginal dilatation, the inhibition of luteal functions and reduced fertility, interfering with ovulation and the ovum in the uterus[35]. Methoxychlor is a chlorinated insecticide with estrogenic action. Exposure may occur through direct use and consumption of lipidic foods (especially from outside the EU). They inhibit folliculogenesis and stimulate the production of anti-Mullerian hormone, involved in the polycystic ovary syndrome[36]. Numerous studies have been conducted on the effects of DDT and its metabolites (*p,p'*-DDE, DDE, *o,p'*-DDT, *p,p'*-DDD) in numerous animal species, but data on humans is limited and comes from studies carried out on groups of workers in DDT synthesis plants and from epidemiological studies on the general population. Because of the insufficiency of available data these compounds cannot be considered as a direct cause of anomalies of the endocrine system taken into consideration. It is clear however that DDT and its metabolites may potentially have effects on human health. Acting as an endocrine disruptor, DDT and its metabolites may activate a steroidogenic *pathway* mediated by alpha and beta receptors of estrogens (ER)[10].

In particular, depending on the model system studied, for *p,p'*-DDE estrogen action has been ascertained[8], as well as anti-estrogen[38], anti-androgen[11], anti-progestin and anti-glucocorticoid action[25].

DDT, being an antagonist of nuclear receptors, also acts on oxidative stress, apoptosis and cellular proliferation processes[34]. DDT can act as a competitive receptor binding with estrogens. Intracellular receptors such as those of sexual and suprarenal steroids, thyroid hormones, vitamin D and retinal acid regulate the ligand-dependent genic transcription through their interaction with sequences of specific DNAs. The competitive binding between DDT and estrogen for the same ER is due to a structural similarity between the two compounds (presence of the benzene ring). The effect of

the molecule and its metabolites is seen, chiefly in critical periods of development such as pregnancy or peri-puberal, in the ability to alter the differentiation and maturing of male and female sexuality[7,22,23].

DDT and its metabolites are able to alter the properties and functions of the female reproductive system, and are detected in follicular fluid and in serum[2,20]. Among women that have undergone *in vitro* artificial insemination there is a correlation between high levels of DDE in follicular fluid and unsuccessful insemination[40] since the follicular fluid plays an important role in forging a close link between granulosa cells and the developing oocyte. The presence of DDT and DDE in the follicular fluid alters the production of steroids on the part of granulosa cells, acting in the crucial phases of development and differentiation of the oocyte[19]. Concentrations of DDE similar to those of the follicular fluid (of between 0.61 and 1.07 ng/ml) may not interfere with the vitality of the oocyte, yet alter the production of progesterone of the granulosa cells and thus the microenvironment around the oocyte. The *o,p'*-DDT, despite binding with the ER, in a similar way to 17-beta estradiol, does not appear to stimulate a proliferation of endothelial cells of the human endometrium[24,28]. Microarray analyses have shown that the molecule reduces in a dose-dependent way the proliferation of endothelial cells, raising cellular necrosis. DDT acts in biological processes of endometrial angiogenesis (menstrual cycle, cellular division, defence responses, lipid and steroid metabolism) on cell elements (plasma membrane and chromosomes), on molecular functions involved in signal transduction, on receptor activity and on cytokines. The structure and functionality of the endometrium are regulated by estradiol and progesterone, so small disturbances could hinder its normal functions[4,5]. Surplus estradiol in the early phases of folliculogenesis may speed up oocyte maturation, such as to create an asynchrony in cytoplasm-nucleus maturation, leading to non-fertilisation. The stimulation of DDE may also have a paracrine effect on the proliferation of granulosa cells[39]. A recent study also showed that male infertility can be associated with the exposure of mothers to *p,p'*-DDE, the effects of which are manifested during the intrauterine lifecycle, and cannot therefore be determined in the blood or seminal fluid of adults[6].

DDT is also believed to be a *thyroid disruptor*, i.e. a substance capable of altering the homeostasis of the thyroid gland. A recent study focused on the role of *p,p'*-DDE, *p,p'*-DDT and *p,p'*-DDD on the thyroid hormonal system during foetal growth. A comparative analysis of concentrations of *p,p'*-DDE, *p,p'*-DDT, *p,p'*-DDD present in the serum of mothers and the umbilical cord of children, with a concentration of TSH present in umbilical cord serum, shows that the presence of the pesticide and its metabolites in maternal serum and in that of the umbilical cord is inversely proportional to the presence of total Thyroxine (TT4), confirming the alteration of the hormonal system during foetal growth[1]. Other *in vitro* studies have shown that the DDT molecule can reduce the constitutive activity of the thyroid stimulating hormone receptor (TSHr) and inhibit the accumulation of cAMP following TSH stimulation.

The inhibitory effect may occur through a non-competitive mechanism, and the action mechanism may be justified by an allosteric alteration of the transmembrane domain of the receptor or by a possible direct effect on adenylyl cyclase[32,33]. Another possible effect of alterations to the endocrine system is a percentage modification of bone mineral density, regulated by the antagonistic effect of androgens and estrogens. It has been shown that *in vitro* DDT is capable of modulating the intake of calcium on the part of the trophoblast. There may be a weak association between serum levels of the pesticide and its metabolites and the reduction in bone densit[12,15].

Organophosphoric pesticides

Organophosphoric pesticides (OP), have effects on reproduction. Insecticides and fungicides have been seen to cause an induction of ovulation and lower LH and progesterone levels in the blood. Herbicides have been seen to have fetotoxic effects. Studies on healthy women have shown lower levels of cholinesterase in the first three months of pregnancy (range 17-46%) and a return to normal levels in the final quarter[35]. This is an unknown phenomenon of falling levels of plasma activity of the cholinesterase during pregnancy, for which no mechanism has been proposed. This fact may however be considered when there is an inexplicable drop in cholinesterase[18]. A therapeutic abortion was carried out on a 24-year-old woman two months after she had injected herself with malathion during the third month of pregnancy in a suicide attempt, since the pregnancy was deemed to be at risk, although the state of the foetus was not described[14]. Two patients in the second and third quarters of pregnancy who had ingested organophosphoric pesticides in suicide attempts made complete recoveries[21], and the

pregnancy was brought to a successful conclusion through the management of acute cholinergic effects and of the intermediate stages of poisoning. Weis et al. reported a 21-year-old patient who was in the 34th-35th week of pregnancy and hospitalised with signs of serious poisoning from organophosphoric pesticides[21]. A caesarean delivery was carried out 11 hours after admission to allow the mother an optimal dose of atropine. Acetylcholinesterase levels were less than 2% of the normal level for the newborn, and atropine was given for eight days. Both mother and child recovered without further problems, and were released from hospital 30 days after hospitalisation[21].

Many organophosphoric pesticides have been tested for their mutagen potential. It is not possible to generalise, since only some compounds are mutagenic, while others are not. Over the past decade numerous experimental studies have been conducted on the neurotoxicity of CPF in laboratory rodents. It has been noted that neonatal neurotoxicity of CPF occurs due to exposure to doses that do not produce systemic intoxication, and in the absence of significant inhibition of cerebral AChE. Preliminary studies appear to show that brief neonatal exposure to CPF noticeably reduces in adult life the behavioural response to an anti-depressant drug in the Porsolt test. The mechanisms behind this alteration need to be studied further, with special reference to the role of serotonin in the modulation of emotional states and neuroendocrine mechanisms associated with these states.

In 2001 the EPA introduced tight restrictions on the use of CPF and m-CPF due to their potentially high degree of neurotoxic action on developing organisms. Experimental studies show that their effects are particularly significant on more vulnerable categories, such as pregnant women, foetuses and children. In these phases CPF may interfere permanently with neurobehavioural development[37]. Numerous pesticides act as Endocrine disruptors[26], but it has not yet been seen whether organophosphorics have the ability to alter hormonal regulation mechanisms (Table 1). CPF may thus be considered an EDs, with long-term mechanisms and effects on neuro-endocrine and thyroid regulation, which have still to be fully understood. This action mechanism could also relate to other organophosphoric pesticides, which would pose a problem for food safety. This needs to be dealt with by taking into due account residue limits for pesticides in foodstuffs, so as to protect more vulnerable categories, such as foetuses and children. It would also be useful to assess the presence in foodstuffs of more than one pesticide having the same action mechanism and possible synergistic interactions.

Discussion and conclusion

Pesticides are a problem not only for the safety of agricultural workers and the environment, but also for the food safety of consumers. It should always be necessary to take into due account the limits for pesticide residues

Table 1 *- Effects of organophosphoric pesticides on reproduction*
Tabella 1 *- Effetti dei pesticidi organofosforici sulla riproduzione*

Effects of organophosphoric pesticides on reproduction	
Birth defects	limb defects; urogenital anomalies; central nervous system defects; cleft lip and palate; heart defects; eye anomalies.
Time to pregnancy	Longer time to pregnancy. In studies that did not show this association data on exposure and effects related to males.
Fertility	drop in fertility; increased risk of sterility was noted among women that had worked with OP 2 years prior to attempting conception; reduction males fertility appears to be related to the aneuploidy of the sexual chromosome in the sperm or to erectile dysfunction.
Abnormalities of fetal delevopment	risk factor for chronic illnesses in adult life; relationship was noted between exposure and altered foetal development.
Fetal death	miscarriage, stillbirth and neonatal death.
Other reproductive alterations	higher rate of placental infarction.

present in the environment and in foodstuffs, to safeguard more vulnerable categories, such as foetuses and children. New European legislation would appear to be capable of meeting the growing interest in the application in agriculture of low-impact plant protection products in order to reduce risk levels for farmworkers, consumers and the environment. This new legislation promotes the use of alternative pest control systems.

The U.E. has adopted two new laws regarding pesticides, the Regulation 1107/2009 of the European Parliament and of the Council of 21 October 2009 regarding the placing of plant protection products on the market (Regulation (EC) No 1107/2009;), and the Directive 2009/128/EC of the European Parliament and of the Council of 21 October 2009, establishing a framework for Community action to achieve the sustainable use of pesticides[13]. The regulation introduces the so-called "cut-off criteria" (excluding *a priori* active substances identified as dangerous for the health of humans, animals or the environment) and a list of "active substances that are candidates for substitution"). Directive 2009/128/EU "on the sustainable use of pesticides" governs, for the first time in a European context, the use of plant protection products, supporting integrated pest management and alternative techniques to reduce risks and the impact on human health and on the environment. These plans shall include measures and time frames for reducing risks relating to the use of plant protection products on human health and on the environment, increasing the number of controls on the use and distribution of pesticides. The aim is thus to reduce levels of harmful active substances, in particular replacing the most dangerous ones with safer alternative substances (including non-chemical elements), encouraging a type of agriculture that uses limited amounts of pesticides or even eliminates them (starting in 2014 the users of plant protection products will have to adopt principles of integrated pest management). This legislation would also appear to be able to control parasites, weeds and plant diseases and guarantee the quality, convenience and safety of foods by applying high standards of safety and striking the right balance between costs and benefits. One of the possible safety standards is based on the evaluation of pesticide action as endocrine disruptors.

Numerous studies have been conducted or are ongoing to gauge the action of pesticides as endocrine disruptors and to assess the presence in foodstuffs of several pesticides having the same action mechanism and possible synergistic interactions.

The promotion of pest management making little use of pesticides, giving incentives for integrated pest management and establishing measures needed for its application (crop rotation, use of adequate cultivation techniques, use of resistant/tolerant "cultivars" and standard/certified seed and planting material, use of balanced fertilisation, liming and irrigation/drainage practices, preventing the spread of harmful organisms by hygiene measures, protection and enhancement of important beneficial organisms and encouraging the spread of organic farming, can reduce risks for women working in greenhouses, consumers and the environment.

Dichiarazione di conflitto di interesse

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