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Is There a Link Between Human Infertilities and Exposure to Pesticides?

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Pesticides are chemicals commonly used in homes and current agronomy to eradicate or keep away pests or halt their reproduction. Diverse series of chemicals such as insecticides, fungicides, rodenticides, pediculicides and biocides are subcategories within this category of chemicals.

Contact to pesticides can be through inhalation of contaminated air, ingestion of food residues or/and contaminated water, dermal contact or across the placenta. Most of the pesticides are readily accessible to the human body as they are persistent and remain intact for long periods of time. According to the latest Stockholm Convention on Persistent Organic Pollutants, 16 out of 22 the most hazardous and persistent chemicals are pesticides. Henceforth, these truths have made a mounting distress about the safety of pesticides and human health (<http://chm.pops.int/Implementation/NewPOPs/Overview/tabid/667/Default.aspx>).

Health risks that are associated with human pesticide exposure are cancer, adverse effects on immune systems, neurodevelopment dysfunction, metabolic diseases such as diabetes, endocrine system disruption and infertility (Gilden *et al.*, 2010; Rahimi and Abdollahi, 2007; Mostafalou and Abdollahi, 2012a). Pesticides also may cause difficulty in breathing, headaches, neurological or psychological defects, irritation of skin and mucous membranes and skin disorders. Dose, timing and duration of exposure are critical to the ability of a pesticide to cause harmful effects.

The adverse effects of pesticides on human reproduction has been documented more than 30 years ago (Whorton *et al.*, 1977). Although, most of the studies that have been conducted in human and animals showed the potential reproductive health risks of pesticides exposure but there is still essential to screen adverse reproductive outcomes of pesticides exposure in human.

Pesticides may influence their adverse effects on reproduction on selected stages of development including prenatal stage, prepubertal stage or the adult, resulting in damage to the reproductive organs and/or impaired fertility (Malik *et al.*, 2011). They may directly make their

action as (1) a reactive chemical and cause germ cell damage (e.g., alkylating agents) and (2) taking structural similarity to endogenous molecules, e.g., hormone agonists/antagonists. Pesticide also may indirectly act and interrupt reproduction (1) by metabolism to a direct-acting compound or reactive intermediate, (2) via endocrine alterations such as increased/decreased steroid clearance and (3) by stimulating or inhibiting neuroendocrine responses at the level of the thyroid, hypothalamus or pituitary (Iyer and Makris, 2010).

In case of male reproduction, pesticides may act through hormonal or genotoxic pathways (Shadnia *et al.*, 2005). They may penetrate the blood-testis barrier to potentially affect spermatogenesis, either by affecting genetic integrity or hormone production (Perry, 2008) leading to poor semen quality and reduced male fertility (Roeleveld and Bretveld, 2008). In female, they may disrupt the hormonal function of the female reproductive system and in particular the ovarian cycle may result in modulation of hormone concentrations, ovarian cycle irregularities and impaired fertility. Epidemiological studies on females showed that exposure to pesticides has been associated with menstrual cycle disturbances, reduced fertility, prolonged time-to-pregnancy, spontaneous abortion, stillbirths and developmental defects, which may or may not be due to disruption of the female hormonal function (Bretveld *et al.*, 2006).

Exposure to pesticides may occur by virtue of occupational or environments. It has been shown that occupational exposures to pesticides adversely influence male and female fertility (Bian *et al.*, 2004; Bretveld *et al.*, 2006; Snijder *et al.*, 2012). Agricultural and horticultural occupations are of importance as it has been shown that occupational exposure to pesticides in these cases appears to consistently reduce fertility and/or fecundability (Mendola *et al.*, 2008).

Some of the epidemiological studies showed that employment in agriculture for men increases the risk of specific morphological abnormalities in sperm, including the decreased sperm count per ejaculate and declined percentage of viable sperm (Hanke and Jurewicz, 2004)

and spermatozoa DNA damage (Bian *et al.*, 2004). In addition, two studies amongst cotton field workers in India reported increased male infertility, negative pregnancy outcome and higher rates of abortions in their wives (Rita *et al.*, 1987; Rupa *et al.*, 1991). In women, agricultural pesticides exposure may affect menstrual cycles (Farr *et al.*, 2004) and may cause spontaneous abortions, congenital defects, pre-maturity births, delay in conception and infertility (Figa-Talamanca, 2006). Moreover, studies suggested that parental employment in agriculture exposed to pesticides could decrease fecundability ratio and increase the risk of congenital malformations in the off springs (Hanke and Jurewicz, 2004).

This is more severe in developing countries, in particular, that high exposure to pesticides due to overused and misused of pesticides by farmers have been reported (Wilson and Tisdell, 2001; Tariq *et al.*, 2007; Panuwet *et al.*, 2012). Therefore, it would be rational to conclude that in less developed countries, farmers due to occupational exposure (Antle *et al.*, 1998; Tariq *et al.*, 2007) and the people living in rural areas due to environmental contamination exposure (Panuwet *et al.*, 2012) are at higher risk for acute and chronic health effects associated with pesticides (Figa-Talamanca *et al.*, 2001; Atreya, 2008). In this regard, adverse effects on human reproduction could be one of the consequences which several studies showed male and female reproductive issues in farmers from developing/less developed countries (Rita *et al.*, 1987; Rupa *et al.*, 1991; Antle *et al.*, 1998; Tariq *et al.*, 2007; Atreya, 2008; Panuwet *et al.*, 2012).

Showing the importance of the concern, recently the contribution of exposure to pesticides and incidence of human diabetes has been bolded, an issue that is going to be one of the global health dilemmas (Mostafalou and Abdollahi, 2012b). In fact, pesticides by their major toxicity as inducers of free radical damage inside the whole body can disrupt many organs or defect their function (Abdollahi *et al.*, 2004). All together, occupational exposures to pesticides particularly agricultural and horticultural occupations appear to have serious adverse effects on male and female reproduction. Farmers, especially those from less developed countries are in high exposure to pesticides and subsequently more chance for potential pesticides human reproductive issues. Therefore, a great need to increase awareness and education to safe use for the workers and farmers who are occupationally exposed to pesticides are essential. Furthermore, more epidemiological studies should be conducted to elucidate the occupational exposure adverse effects of pesticides on human reproduction in particular

farmers from less developed countries. At the moment nobody can claim that there is no link between pesticides exposure and reproductive toxicity but yet it is impossible to state how many of human infertilities are due to pesticide exposure.

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