

MINISYMPOSIUM: REPRODUCTIVE HEALTH IN RELATION TO PESTICIDES AND AGRICULTURAL WORK

EXPOSURE ASSESSMENT ISSUES IN REPRODUCTIVE PESTICIDE STUDIES

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Background and aims: Most epidemiological studies on the health effects of occupational or environmental pesticide exposure use qualitative exposure assessment methods, based on, for instance, job titles, self-reported data from questionnaires or interviews, expert judgement, or regional differences in use of pesticides. Complicating factors are the vast number of pesticides formulations on the market, shifts in use of specific pesticides over time, and seasonal and other time-dependent fluctuations in pesticide use. The latter is especially important in reproductive studies in which long-term exposure is usually not an issue, but the timing of exposure and the exposure pattern are critical for the effects that could be expected. The large variation in application methods, work practices, and exposure situations further complicates exposure assessment. Especially for women, pesticide exposure is often 'invisible' as they usually do not apply pesticides themselves, but get exposed through re-entry work in crops that have been treated with pesticides and/or by living on a farm or in a pesticide-exposed area.

Methods: A literature study was undertaken to find all studies on reproductive disorders in relation to occupational pesticide exposure or agricultural work. In addition, the literature on exposure assessment for pesticides was reviewed.

Results: During the mini-symposium, an overview will be given of the different exposure assessment methods used in reproductive pesticide and agricultural studies and their consequences for validity and comparability of the results. In addition, several exposure assessment issues that are specific to studying reproductive disorders will be addressed, such as the variability in critical exposure time windows (e.g. life-time exposure, preconceptional exposure, month-by-month exposure during pregnancy) and exposure metrics (e.g. continuous exposure, repeated short-term exposure, peak exposure) related to different effect parameters, as well as male versus female and combined exposure.

Discussion and conclusions: Eventually, the advantages and disadvantages of using qualitative, semi-quantitative, and quantitative exposure assessment methods in reproductive pesticide studies will be explored from both a practical and a methodological point of view.

PESTICIDE EXPOSURE AS A REPRODUCTIVE HAZARD FOR CHILDHOOD LEUKEMIA IN COSTA RICA

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Background and aims: Workforce includes women of reproductive age who are exposed to workplace hazards, such as chemical toxicants (heavy metals, pesticides, endocrine disruptors) and physical, environmental or biological-infectious agents. Exposure transmission through parents includes a) transplacental transmission during gestation and b) postnatal direct contact with plants, pets and soil; parents' take home exposures; direct physical contact with parents (hand-body contact, breastfeeding) and indoor surface contamination.

Leukemias are the most common pediatric cancers in most populations and have multifactorial etiologies and mother-fetus exposure transmission involving interactions between environmental and genetic aspects. This is a review of the plausibility, mechanisms and exposure routes involved, proposed in the empirical data on the pesticide-related etiology of cancer.

Methods: In a case-control study of childhood leukemia and its association with parents' occupational exposure to pesticides performed in Costa Rica, mothers' and fathers' exposures to pesticides during pregnancy were associated with the risk. We compare here our epidemiological findings with available mechanistic data.

Results: Excesses of total leukemia were found for mothers and fathers exposed to organophosphates and for fathers exposed to benzimidazoles. The specific pesticides that showed an association were picloram, benomyl, paraquat, phoxim, mancozeb and malathion, compounds not addressed in previous epidemiological studies, with the exception of malathion. Human, animal and mechanistic data suggest carcinogenic potential for benomyl, mancozeb and malathion; some of the mechanisms suggested are: genotoxic damage, aneuploidy, apoptosis and chromosome aberrations. An association with adult human leukemia has been found for mancozeb.

Discussion and conclusions: Epidemiological, animal and mechanistic evidence related to carcinogenicity in the offspring of particular pesticides compounds is still limited. Existing epidemiological evidence for childhood leukemia risk can be associated with other cancer-related evidence for benomyl, mancozeb and malathion. Both initiator and later effects are possible. Pesticides ought to be of serious concern for health promotion programs of women in reproductive age.

EXPOSURE TO PESTICIDES AND FERTILITY

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Background and aims: Pesticides are a widely used group of toxic chemicals. The aim of the paper is to present epidemiological evidence on the impact of pesticide exposure on fertility.

Methods: A literature survey was conducted on studies on pesticide exposure and couple fertility published in 1983 to 2008. Outcomes of interest included time to pregnancy, infertility, or delayed conception with a reference to fertilization success among in vitro fertilization patients (IVF) and fertility in the second generation. In total, 19 studies on male effects and 13 studies on female effects were found. The studied populations consisted of occupational cohorts (10 male and 6 female studies), population samples (3 and 4 studies), and clients in infertility clinics (6 and 3 studies).

Results: Findings from three studies conducted in occupational settings indicated reduced fertility among men with occupational exposure to pesticides. Four studies either came up with a suggestive finding or simply observed an association for instance in a subset of primiparous couples, whereas three studies were entirely negative. Similarly, the studies focusing on pesticide exposure in women indicated mixed findings, although five of the six studies were either positive or suggestive. A two-generation study focused on fecundability in daughters of mothers exposed to DDT produced the following result: the higher mother's serum p,p'-DDT concentration, the lower the daughter's fecundability. However, the opposite effect was seen for the metabolite p,p'-DDE. IVF studies have shown a decreased fertilizing ability but an increased implantation rate in couples in which the male partner had been exposed to pesticides.

Discussion and conclusions: There is some evidence on declining fertility among male and female workers occupationally exposed to pesticides. The potential associations are difficult to attribute to specific pesticides because mixtures of pesticides have been used. Comparison between studies is difficult because pesticides used by workers and exposure levels vary across studies. Also, many studies suffer from methodological shortcomings such as selection bias, inadequate control of confounding, or exposure misclassification, including problems in ascertaining exposure for pregnancy attempt times. Fertility effects of pesticide exposure may extend to the next generation. IVF studies provide an opportunity to focus on the potential mechanisms of these effects.

BIOLOGICAL MARKERS OF MALE REPRODUCTIVE FUNCTION

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Background and aims: It has been known for decades that some pesticides may seriously harm male reproductive function, but the effects of common used pesticides on male reproductive function is less clear. The aim of the present presentation is to give an overview of the effects of occupational pesticide exposure on male reproductive function.

Methods: Effects of pesticide exposures on male reproductive function was identified through a Pubmed search, using the search string (semen or sperm or hormones) and pesticides and occupational, limited to human studies. Only studies evaluated as relevant based on the abstract was included. In addition, relevant references referred to in the identified papers were included.

Results: Dibromochloropropane (DBCP) seriously harm male reproductive function including findings of azoospermia and genetic alterations of sperm cells, in workers at DBCP factories or agricultural workers exposed to this product. These findings back in the 70s and 80s prompted a series of studies on male workers exposed to other pesticides. Fortunately, the effects of other pesticides has not been demonstrated to be as strong as DBCP, but several examples of pesticide induced alterations of male semen quality and reproductive hormones has been observed in almost every class of pesticide used. Generally, the present use of pesticides in industrialized countries is not suspected to cause major alterations of male reproductive function.

Discussion and conclusions: Pesticide induced alterations of semen quality has been observed in several occupational studies of farmers, gardeners or workers at pesticide producing plants.

Exposure in the prenatal period may be more sensitive to reproductive disturbances than adult exposure. It should be noted that the majority of the studies are conducted in industrialised countries, whereas the use of compounds with potential harm on male reproductive function is much less regulated and less safety precautions are taken while using these compounds in the less developed countries.

OCCUPATIONAL EXPOSURE TO PESTICIDES AND FEMALE REPRODUCTION: THE EPIDEMIOLOGIC EVIDENCE

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Background and aims: The hypothesis that exposure to pesticides may interfere with the human reproductive function was first documented among male workers exposed to DBCP almost thirty years ago. In the years that followed, many studies attempted to determine possible similar effects from other pesticides to both male and female workers. The investigations among females with well defined exposures to pesticides are not numerous, but often show negative reproductive effects such as spontaneous abortions, congenital defects and developmental effects. The evidence is not always consistent, mostly because the levels and types of exposures to pesticides are often ill defined

Methods: The paper is a selective review of the epidemiologic literature published after 2000.

Results: The most frequently studied outcome up to now has been spontaneous abortion, and delay in conception through time to pregnancy. The presentation will summarize the data of a few of the more recent studies on the possible association between occupational pesticide exposure of women and spontaneous abortion, LBW/SGA and selected birth defects of the newborn.

Greenhouse workers have repeatedly been shown to be more likely to suffer adverse reproductive effects, probably because of their exposure to pesticides is higher and more continuous. Reduction in fecundability was observed among greenhouse workers in Denmark, Finland and increased risk of fetal loss in Italy. There is sufficient evidence therefore that handling of pesticides by female workers might have negative effects on their reproductive health.

Additional evidence comes from studies of non occupational settings, where the population has been exposed to pesticides (ex. following residential treatment) or in ecological studies of large agricultural areas. In a study in Ontario for example, an excess in spontaneous abortion in the exposed population was associated specifically with the use of phenoxy herbicides. Two studies, where exposure was measured through biological monitoring of the metabolite (DDE) of one pesticide (DDT), found an association between maternal serum concentration of DDE and preterm and SGA babies, and the other found an association of serum levels of DDT with spontaneous abortion. Recent studies of dietary exposures to pesticides also provide useful evidence in this regard. The evidence on the possible link between maternal exposure to pesticides during pregnancy and the risk of these birth defects, is suggestive but not conclusive

Discussion and conclusions: Several of the more recent studies, (all conducted in western countries) find no significant association of occupational exposure to pesticides and negative pregnancy outcome, attributing this to efficient preventive measures. This positive result is unlikely to apply to the less developed countries