OCFP 2012 Systematic Review of Pesticide Health Effects: Executive Summary

The second Ontario College of Family Physicians (OCFP) Systematic Review of Pesticide Health Effects reviewed the relevant literature published since 2003. Of this literature, 142 studies met the inclusion criteria, covering three groups of health effects:

1. Reproductive health outcomes and pesticide exposure (update of 2005 review) – 75 studies
2. Neurodevelopmental behavioural health outcomes and pesticide exposure in children (expanded from 2005 review to include all neurodevelopmental outcomes) – 32 studies
3. Respiratory health outcomes and pesticide exposure in children and adults (new outcome area not covered in 2005 review) – 35 studies

Each study was assessed by two independent trained reviewers and scored using criteria adapted from the modified Downs and Black Quality Assessment Tool (see Chapter 2: Methods, Appendix A).

Reproductive health outcomes and pesticide exposure

This review provides evidence that non-organochlorine pesticides may cause deleterious reproductive outcomes. The most suggestive evidence is of an association between fetal growth outcomes and pesticide exposure. Of the ten studies that considered fetal growth outcomes, eight reported significant associations. Most of these positive associations were for birth weight, and were from well-designed cohort studies. As low-birth-weight babies are at increased risk of mortality, morbidity, and disability in infancy and childhood and of long-term adverse health outcomes in adult life, reducing low-birth-weight rates should be a public health priority. However, the associations found for a given type of pesticide in one study were not always replicated in other studies of that pesticide. These inconsistencies, which could be due to differences in sample size, methodology, and study design, make it challenging to draw definitive conclusions. While it appears that there is an association between pesticide exposure and birth weight, this relationship varies according to the type of pesticide, with some giving rise to less than consistent findings.

Decreased head circumference, as suggested in several studies, is of particular concern because small head circumference is linked to lower cognitive abilities in older children and adults.

All of the high-quality birth defect studies reported positive associations. However, as a group they considered a diversity of pesticides, which makes comparisons between the studies difficult. Nevertheless, associations were found with hypospadias, neural tube defects, and congenital diaphragmatic hernia. The associations with hypospadias are further supported by an earlier systematic review of nine other studies. Three of four studies of quality <13 out of 20 found a positive association, and both studies ranked >13 had positive findings. The finding of an association between gastroschisis and pesticide exposure is interesting given its largely unknown etiology and warrants further investigation.

Only two studies examined preterm birth as an outcome, and both found positive associations. Both cited biologically plausible explanations for these effects (e.g., organophosphate pesticides can affect enzymes that stimulate contractions of the uterus, thereby decreasing gestational duration). Additional studies with individual-level data would provide further insight into these associations.

In contrast, there is less suggestive evidence in this review that the organochlorine pesticides affect reproductive outcomes. Most of the studies were conducted in countries where DDT and other organochlorine pesticides had been banned for several decades and levels were generally low in the general population. As with the non-organochlorine studies, exposure measurements were almost all by biomarker.

It is possible that associations were not found due to the small sample sizes in most of the studies. Many authors also commented on the low concentrations of the examined organochlorines in maternal and cord blood as well as breast milk. However, some of the studies in which levels were considered high still did not find associations, or if they did, the wide range of exposure levels, lack of dose–response relationships, and other methodological deficiencies make it difficult to draw conclusions. Some of the studies did report a few positive findings that did not attain statistical significance and therefore were reported as negative; however, many of these did not follow a dose–response relationship and therefore could have been spurious.

Certainly, the results of this study would indicate that there are benefits to reducing exposure of pregnant women to commonly used pesticides. In 2004, the birth weights of infants born after rather than before a household ban on two frequently used insecticides were found to be significantly higher in New York City, illustrating the possible benefit of pesticide bans within a few years of implementation. In Canada, several provinces and many municipalities have mandated bans and phase-outs of many pesticides in the past several years, and research into reproductive outcomes resulting from these policies is recommended.

Neurodevelopmental/behavioural health outcomes and pesticide exposure in children

The studies in this systematic review show that prenatal pesticide exposure is consistently associated with measurable deficits in child neurodevelopment across a wide age range from birth to adolescence.

Neonates with prenatal organophosphate exposure had absent or hypotonic reflexes and deficits in attentiveness to stimuli. After prenatal organochlorine exposure, neonates displayed irritability on neurological testing. In organophosphate-exposed **children aged 12–36 months**, consistent deficits in the Mental Development Index of the Bayley Scales for Infant Development were found in three large cohort studies. For exposure to the main metabolite of the organochlorine pesticide DDT, there were deficits in both scales but with stronger effects for the Psychomotor Development Index. For these early childhood deficits, the relative risks (RRs) are usually in the 1.5–2.0 range. However, even a small increase in the incidence of such complex childhood

conditions impacts both the healthcare system and the learning and later earning potential of affected individuals.

In **older children aged 3–10 years**, attention problems such as ADHD, reduced overall IQ, and other conditions including autism spectrum disorder and pervasive developmental disorder were more common in children who had higher levels of organophosphate or DDT/DDE exposure during pregnancy. Typically, statistically significant health effects were seen primarily in children in the highest 20–25% of exposure. On the other hand, there are rarely unexposed control groups, which may result in underestimation of the risk of ADHD. Some studies of ADHD and autism associated with prenatal exposure have higher RRs in the 6.0–7.0 range. In a birth cohort of 30-year-olds in the UK, both males and females diagnosed with attention deficit at age 10 were found to have "lower employment rates, worse jobs, lower earnings if employed, and lower expected earnings overall." In addition, children diagnosed with ADHD also have a much higher likelihood of engaging in criminal behaviour as adults, with high attendant social costs.

In multi-scale IQ tests, working memory and verbal comprehension appeared to be most consistently affected by pesticide exposure. The effects were modest, with RRs usually less than 2.0. However, the reductions found in total IQ (ranging from –2 to –7 points) have substantial impacts on school performance and later earning potential when viewed from a population perspective. In 2001, Environment Canada scientists estimated the cost of the loss of 5 IQ points at CAD 30 billion per year for Canada, and the cost of neurodevelopmental deficits and hypothyroidism at CAD 2 billion per year for Ontario alone. The proportion of those conditions (and costs) considered attributable to environmental exposures was at least 10% and as high as 50%.

Our understanding of the association between pesticide exposure and child neurodevelopment has benefited from several large longitudinal studies of birth cohorts from the USA, Spain, and Mexico. The cohorts were all recruited from groups thought to have higher than average exposure to pesticides. In the future, it will be important to study the associations with health effects in cohorts with typical exposures. This is important, as some endocrine-disrupting pesticides, such as atrazine, appear to have health effects at very low doses.

Taken as a whole, the results of the systematic review of pesticide exposure and child neurodevelopment suggest that children are experiencing neurodevelopmental problems throughout childhood that are associated with prenatal and childhood pesticide exposures. This suggests that vigilance is required to minimize the pesticide exposures of pregnant women and children from all potential sources, including dietary, indoor and outdoor air, water, and farm and domestic use exposures. The currently used organophosphate insecticides are consistently implicated in neurodevelopmental deficits, as are the organochlorines, such as endosulfan, still heavily used as crop pesticides in agricultural settings.

Respiratory health outcomes and pesticide exposure in children and adults

Overall, there is evidence that exposure to pesticides, and to organophosphate or carbamate insecticides in particular, is associated with the development of respiratory symptoms and a spectrum of obstructive and restrictive lung diseases. Studies of asthma in children reported an association between maternal exposure to organophosphate and organochlorine insecticides, while respiratory tract infections in infants were linked to maternal exposure to organochlorine insecticides in two of three reviewed studies.

Twelve studies investigated the effects of asthma, of which nine studies of medium to high quality found a positive association between organophosphate and carbamate insecticides and atopic asthma, with odds ratios above 2.0. This association was found for occupational, domestic, and environmental exposures, particularly after exposure to the organophosphate insecticides parathion and coumaphos. While the possibility remains that these results could reflect the aggravation of pre-existing asthma, asthma-related respiratory problems are nonetheless associated with pesticide exposure. In children, the evidence is consistent, with all included studies finding a positive association with pesticide exposure, specifically maternal organochlorine insecticide, organophosphate insecticide, biocide (disinfectant), and fungicide exposure. Specifically, in utero and post-natal exposures in the first year of life were associated with asthma and wheeze up to six years of age. Breastfeeding was shown to have a protective effect, despite increased organochlorine pesticide levels in the infants.

The evidence linking chronic bronchitis to pesticide exposure in adults is not as prolific or as robust as that regarding asthma. While three studies did find a positive effect, the resulting odds ratios were below 2.0, with large confidence intervals. In particular, two studies that used data from the Agricultural Health Study found an association between exposure to insecticides and the development of chronic bronchitis. Organochlorine, organophosphate, carbamate, and pyrethroid insecticides all showed an association in farmers, while the herbicide paraquat showed the strongest relationship in their spouses through paraoccupational exposure. In addition, one large retrospective study found that the relationship between insecticide exposure and the development of chronic cough and bronchitis in Ontario farm children did approach significance, but only for girls.

Studies of occupational workers across many industries that use pesticides (e.g., farming, pesticide manufacturing, and pesticide spraying) showed a subtle yet persistent association between decreased lung function and exposure to a broad range of herbicides and insecticides. Exposure to the now-banned organophosphate insecticide chlorpyrifos resulted in a particularly strong association with wheeze, chronic cough, and shortness of breath in many studies. Studies of these occupationally exposed populations linked organophosphate and carbamate insecticides in particular to decreased FEV1/FVC ratios, indicative of obstruction, and to decreased mid-expiratory flow rates (FEF 25–75%). These outcomes may reflect effects of chronic exposures and as well possibly direct toxic effects on the airways due to inhibition of acetyl-cholinesterase and resulting acute bronchoconstriction.

Two studies of exposure to neonicotinoid insecticides and organophosphates also showed associations with restrictive lung function changes. However, a study of chronic, low-level exposures to paraquat found no restrictive lung disease. Finally, sarcoidosis and farmer's lung (hypersensitivity pneumonitis) were both associated with occupational exposure to insecticides.

The risk of developing farmer's lung increased after exposure to organochlorine and carbamate insecticides in particular.

The relationship between respiratory tract infections in children and the organochlorine insecticide metabolite dichlorodiphenyldichloroethylene (DDE) was assessed in three high-quality studies with varying results. Two studies showed a positive association between in utero exposure and respiratory tract infections, while a third paradoxically showed that higher levels during pregnancy were in fact protective. In addition, one study found that upper, but not lower, respiratory tract infections in infants were associated with increased exposure to organochlorines.

The sum of the evidence would indicate that reducing or eliminating exposure to all pesticide types, and to organophosphate, carbamate, and organochlorine insecticides in particular, would be prudent in both occupational and domestic settings with respect to preventing negative respiratory health consequences. While the study of agricultural occupational pesticide exposure and negative health outcomes remains challenging, the accumulation of studies showing significant associations between exposure and asthma, chronic obstructive lung diseases, and decreased lung function highlight the importance of reducing exposure when possible and of using proper personal protective equipment when exposure is necessary.

Implications for family practice

Family physicians can counsel to prevent or reduce pesticide exposure in several settings:

1. In preconception and prenatal patient encounters, counsel to reduce pesticide exposure and help reduce negative birth outcomes, neurodevelopment problems, and childhood asthma outcomes associated with prenatal pesticide exposure. Prevention of these effects has an extended benefit in reducing the frequency of adult chronic diseases associated with suboptimal birth outcomes. History taking should focus on occupational exposures and the indoor use of pesticides during pregnancy and early childhood.
2. Advise parents to minimize exposure of older children by reducing use of indoor and home and garden pesticides. Pyrethroids are still approved for many indoor uses, are detected in 100% of Canadian children, and are associated with health effects in children.
3. Alert new parents to the risks of paraoccupational (i.e., take-home) exposures and the protective benefits of wearing personal protective equipment for patients who have unavoidable occupational exposure.
4. Educate patients in occupations at high risk of pesticide exposure about the health effects associated with these exposures.
5. Consider community-based education and action in circumstances in which children are unnecessarily exposed to pesticides. Previous bans on pesticides with high health effect burdens have been shown to reduce health risks to children and reduce detection frequency in children and the environment.