

# Pesticides and human health

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Pesticides, including herbicides, insecticides, fungicides, fumigants and rodenticides, provide important benefits in public health, food production and aesthetics (<http://www.epa.gov/agriculture/ag101/pestbenefits.html>). Unlike most other important chemicals, pesticides are designed to impact living systems (<http://www.cdc.gov/niosh/docs/81-123/>). Consequently there has long been a concern about environmental and human consequences of widespread pesticide use. Carson<sup>1</sup> effectively voiced this concern and documented some problems in her 1962 book, *Silent Spring*. Global pesticide use increased dramatically between the 1960s and 1990s, and more slowly thereafter, but large increases continue to occur in many developing countries.<sup>2</sup> The estimated worldwide use in 2007 was 5211 million pounds of active ingredients, with herbicides accounting for the major use in agriculture, and about 40% of the use overall.<sup>3</sup> To place this figure in context, it is close to one pound for each of the 6.6 billion people then inhabiting the globe, albeit with unequal distribution.

Human occupational exposure is expected during pesticide production and application, but the general population can also be exposed through drift, contamination of water and food supplies, and biological concentration through the food chain.<sup>4</sup> In addition, pesticide use for vector control and elimination of nuisance pests is an important exposure source for a considerable portion of the world population, and is an especially important source of exposure indoors.<sup>5</sup> These varied pathways have resulted in such ubiquitous exposure that persistent pesticides or their

metabolites can be found at low levels in biological tissues of much of the world's population. This includes many who may be especially susceptible to deleterious effects from pesticide exposure, such as children, the elderly, developing fetuses and the immunosuppressed.

How hazardous are pesticides to humans? We really do not know and the answer is most certainly dependent on the specific chemicals and health effects being considered. Pesticides include dozens of chemical families, with hundreds of active ingredients, thousands of different formulations and many known or suspected adverse health outcomes. In addition to the active ingredients, pesticides also contain chemicals known as 'inerts' such as solvents, surfactants, preservatives, which may have toxic actions distinct from the active ingredients.<sup>6</sup> Some contaminants come from the production process. Dioxin, for example, is a contaminant of production of some phenoxyacetic acid herbicides, and is classified as a human carcinogen.<sup>7</sup>

Acute effects from intentional and unintentional pesticide poisoning are well established, but recent worldwide estimates do not exist. Previous estimates of 3 000 000 poisonings and 220 000 deaths worldwide in the 1980s<sup>8</sup> are out of date and are likely severe underestimates given the increase in pesticide use since that time. Scattered, but abundant, case reports and surveys from multiple regions in the world show that acute pesticide poisonings, both occupational and non-occupational, with mild-to-fatal effects, continue to be a major issue and there is an urgent need for a valid global estimate.

For chronic effects, the evidence is even less clear because of the challenge in accurate assessment of exposures during the relevant time period, which may be years before diseases or symptoms develop and only recently have certain health effects, for example, immunotoxicity, endocrine disruption and neurodevelopmental toxicity received much research attention.<sup>9 10</sup> What is clear is that the spectrum of suspected pesticide—chronic human disease associations continues to grow and that human and/or experimental data suggest links between some pesticides and cancer at multiple sites<sup>11 12</sup> and

deleterious effects on the immune, nervous, respiratory, endocrine and reproductive systems.<sup>13–15</sup>

Evidence for carcinogenic effects of pesticides comes from experimental and epidemiological studies.<sup>11</sup> Cancers of the lung, prostate, and lymphatic and haematopoietic system have been the sites most frequently associated in epidemiological studies.<sup>11 12</sup> Childhood cancer has also been linked with environmental and parental occupational pesticide exposure.<sup>16</sup> Experimental and mechanistic studies suggest that many pesticides are not mutagenic, but that some may operate through epigenetic mechanisms and at a late stage of the carcinogenic process.<sup>11 12</sup> To date, however, no active ingredient (other than arsenic) has been classified as a definite human carcinogen by an authoritative body. There is a sufficient literature to indicate that there is a need for a chemical by chemical evaluation and the International Agency for Research on Cancer in 2014 announced plans to review of a number of pesticides in the monograph programme.

In addition to cancer, there are several other chronic health effects that may be linked to pesticides. The nervous system is particularly vulnerable to many pesticides of several distinct chemical classes. It is well known that acute poisoning with organophosphates causes long-term neurobehavioral deficits and depression, but health effects from low-dose exposures without clinical poisoning are less clear.<sup>13</sup> A recent meta-analysis of studies investigating low-dose organophosphate exposures found small-to-moderate associations with reduced psychomotor speed, executive function, visuospatial ability, and work and visual memory.<sup>17</sup> Neurodevelopmental effects have been reported in a number of studies of children with prenatal and early childhood exposure to organophosphates.<sup>18</sup> Reviews have also linked organochlorine, organophosphate and other pesticides with Alzheimer, other dementias and amyotrophic lateral sclerosis, with the most consistent results reported for Parkinson disease.<sup>19</sup> There have now been a number of studies reporting joint effects between common genetic variants and an increasing number of pesticides on the risk of Parkinson disease suggesting numerous different mechanistic pathways<sup>20 21</sup> may be involved and that pesticide–gene interactions need to be included in future studies. Recently, pesticides have also been associated with hearing loss,<sup>22</sup> diabetes and obesity,<sup>23</sup> and non-malignant respiratory disease.<sup>24</sup>

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Much of the evidence on potential human hazards associated with pesticides has come from studies in developed countries. However, the use has been heavy, and mostly uncontrolled in many developing countries,<sup>2–25</sup> which may result in high exposures to large numbers of people and lead to more severe and widespread health effects.

The growth in use of pesticides,<sup>2</sup> the large number of people exposed during application or production and through various environmental exposure pathways, and the possible role of pesticides in the development of many different diseases and ill-health outcomes underscores the need to fully understand the risks associated with use of these chemicals, so that their overall benefits can be appropriately gauged. Also a thorough assessment of potential human health hazards from newly developed pesticides must be undertaken before they are widely used. As with many chemicals of modern society, there has been a tendency to replace the use of pesticides with known hazards by substances for which there is not as much known about their potential health effects, particularly long-term. Future research needs to focus not only on specific active ingredients and various formulations, but also on the possible cumulative and interactive effects from exposure to multiple pesticides over time.<sup>26</sup> To adequately assess the total health burden that might arise from the widespread use of pesticides requires sophisticated research approaches involving multiple disciplines with development of new methods to assess health effects from multiple exposures and sources. In the meantime efforts should be made to inform the public about the potential harm from pesticides exposure, especially vulnerable populations, and to limit or prevent human exposures. Development, strengthening and implementation of sustainable methods in agriculture and vector control are urgently needed to minimise pesticide use globally and, in particular, in developing countries.

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