# Study fails tests: The debate over pesticide use in Toronto was fed a report that ignored prior data, regulatory actions, plausibility and criteria of risk

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I have been asked by the editor to examine and comment on the recent Pesticides Literature Review prepared by the Ontario College of Family Physicians. I understand the review, published on April 23, became an important element in the City of Toronto's debate over whether to ban the use of pesticides. In my view, the OCFP report fails several important science tests and should not be used as a guide to setting policy on pesticide use. Indeed, I question whether the OCFP paper should have been made public, given that it was not subject to rigorous external peer scrutiny.

The OCFP report reviews a portion of the pesticide epidemiology literature. Epidemiology is the science of searching for possible connections between disease and environmental factors, in this case pesticide exposure. By definition, epidemiology cannot show a cause-and-effect relationship.

My first and continuing impression of this review was that the authors see all pesticides as a common group of chemicals for which an effect by one may be associated with any other. If chemical A is carcinogenic, then so is chemical B. Numerous specific pesticides that are clearly established as being non-carcinogenic by international regulatory action are thrown into this amorphous collection for which an alarm is sounded about cancer. This philosophy is the same as considering all therapeutic drugs as just medicine. By this thinking, the nature of the chemical, its behavior in the body, the specific intended effect on the patient, the potential toxicity (side effects) all become unimportant, and the practice of medicine becomes very simple. The problem with such an approach is obvious.

All chemicals are different. An evaluation of potential risk of use of any given substance is possible only if the entire spectrum of its unique chemical, physical and biological properties is considered. In the OCFP report, the only information considered is possible associations between some indirect estimate of "pesticide" contact and disease. As important as this connection is for specific chemicals, it is usually the least precise information about chemical effects. The authors comment on the need for "linkage with animal studies, clinical case literature and other sources of information on particular pesticide use and toxicity." But then they ignore the extensive body of data describing individual chemicals, particularly their ability to affect genetic material or to cause cancer or reproductive effects or other toxicity.

In short, there is no recognition of national, international and state regulatory actions. These regulatory judgments -- by the U.S. Environmental Protection Agency, Health Canada and others -- are not made by a few people over coffee, but depend on analyses of effects down to the genetic level and over a lifetime, with several levels of expert review. Would the OCFP have the same dismissive attitude toward the enormous body of non-human study that enables preclinical and clinical trials of the therapeutic drugs prescribed by physicians?

Epidemiology depends on a core precept: Findings must meet standards of plausibility. Plausibility can be determined only by examination of all available information about each chemical of concern. Do the findings make sense? The OCFP review fails that test. First, it lumps grossly unlike chemicals together. Second, it fails to consider the mass of fundamental biological and environmental data available for each substance.

Along with the overriding principle of plausibility, the review also did not attend to several other vital precepts in epidemiology. I will briefly discuss only one: strength of association. This means that an estimate of added risk must be supported by dependable diagnoses, good exposure information, identification of other possible contributors to the risk, a large enough population of affected and presumably unaffected people (controls) and other factors. With all these qualifications, the estimated risk must be high enough relative to normal background risk that it is likely to be real. Depending on the kind of study, normal risk for a given effect is represented as one or 100, and if the estimated risk in the study population is more than one the initial implication is that risk has been increased.

It is not that simple, however. Low numbers of cases, unreliable exposure estimates, exposure to other carcinogens and other factors make such numbers unreliable, including the normal high background risks. The total background risk of cancer in North America is one case in the lifetime of every three or four people. A statistical range into which the risk estimate will fall is the Confidence Interval (CI). Usually the estimate (odds ratio) is stated to have a 95% probability of falling somewhere between the two extremes of the CI. If the lower limit of the CI is one (normal risk) or less, the estimate is usually considered to not represent an increased risk. The lower value can only approach zero, but the upper end has no limit. Reliability decreases as that gap widens. The OCFP authors have included numerous studies showing little strength of association to support their overall contention.

The OCFP tendency to find meaning where it is questionable can be illustrated with a couple of references, from among hundreds in the study. One is a reference to a 1999 report by Hardell and Eriksson of Sweden on a large number of herbicides and other substances, suggesting that several herbicides cause non-Hodgkins lymphoma. However, the estimated risks are low and the low end of most CIs are one or less, indicating non-significant risk. The positive associations appear in groups so small that a single misdiagnosis could change the result. Furthermore, almost half of the respondents were next of kin, trying to recall activities of someone else 10 or 20 years earlier. In two lists of 33 substances in the Hardell paper, almost all odds ratios (risk estimates) were similar. Such similarity in a large group of widely divergent kinds of chemicals is biologically implausible, unless none has a significant effect. Another example: A 2001 paper by T.E. Arbuckle and others was stated to have "revealed an association between phenoxy herbicides and spontaneous abortions" and may "possibly point" to critical exposure "when the fetus may be more vulnerable to toxic exposures." In fact, the authors of the Arbuckle paper looked at exposure to nine different chemicals and stated they intended only to develop hypotheses for further work. They also acknowledged the difficulties with such studies. Most of the findings are below or just at statistical significance and therefore similar, which, again, is improbable unless there is no effect.

The OCFP literature search strategy is also questionable. The primary search term was "pesticides," with various modifiers, but apparently no specific chemicals were searched.

There is no rationale given for ignoring the useful research conducted before 1990; certainly there was no great leap forward in methods at that time. I won't attempt to list the more recent work they missed. It is useful, however, to comment on their rejection of two studies that were funded by the "chemical industry" because of presumed bias. Perhaps they are not aware that such work by industry is subject to scientific and political scrutiny from every quarter. Flaws in industry studies carry a much higher penalty than does, say, the OCFP flaws. The willingness to exclude valid studies on that basis itself suggests a bias that can influence the way they interpret research. Perhaps this is expressed in their advocacy of political action to address "this public health issue," and recommend avoiding pesticides on purchased foods. It is likely that they are not aware that almost all produce actually meets organic standards for pesticide residues.

Reviews in the OCFP paper also appear to be selective toward positive findings. An excellent example is the study by Fleming who found an association between pesticide use and prostate cancer. OCFP didn't mention that the same study found no associations with cancer of the lungs, breast, pancreas, kidney, colon or leukemia and non-Hodgkins lymphoma. Fleming also mentioned that the applicators were consistently healthier than the general population. One of the stronger claims by OCFP in this review was the potential for pesticides to cause prostate cancer. It was based on a portion of the National Cancer Institute Agricultural Health Study, including more than 55,000 applicators.

However, the positive association occurred only with use of methyl bromide, a fumigant rarely used in Canada and scheduled for cancellation in North America. OCFP didn't consider it important to note that cancer incidence from all sites was significantly less than expected, or that for 35 other pesticides no association with prostate cancer was observed.

Selectivity also extends to exposure criteria. In many cases, this review comments that exposure data are inadequate or questionable, but then goes forward with a statement about evident outcomes.

I have to wonder if philosophical issues may have caused good science to be pushed aside. It is not inappropriate that the authors use Rachel Carson's Silent Spring as a backdrop for their report, but almost no present-day pesticides fit her concerns. Carson was somewhat a visionary, but her rationale at that time made sense. Unfortunately, Colborn's Our Stolen Future is also considered fundamental. Amidst the author's frequent self-congratulation, this book also lumps all pesticides together, speaking of endocrine disruption and other effects, and only at the end do we find that she is really talking about persistent chlorinated hydrocarbons. The book doesn't belong on the same table with Carson's. (The authors of the OCFP report were wise enough to ignore these substances.)

These brief comments are not a thorough review of the OCFP report but are sufficient to seriously question its value. As it stands, this document does not describe the health impact of pesticides. It should not supplant the judgment of Health Canada on regulatory policy issues.

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