Pesticide residues and cancer risks

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Although the calculation of potential cancer risks from pesticide residues in foods involves much scientific uncertainty, estimates of risk are currently used to guide policy decisions. Since risk estimates may vary by several orders of magnitude depending on the assumptions used in the calculations, it is imperative that assumptions be based on the best available scientific data.

The issue of pesticide residues in the human food chain is of considerable interest to consumers, consumer advocates, food producers, processors, retailers, the chemical industry, and government agencies. It is a highly controversial and extremely complicated subject. This report highlights the value of information in assessing potential carcinogenic risks from pesticide residues and recommends changes that could improve the accuracy of scientific data used in risk assessment. Of particular note are our recalculations of the National Research Council's dietary cancer risk estimates for several pesticides and selected foods, using alternative assumptions about exposure. The results differ markedly, calling into question the value of many current assumptions that generally underlie the risk assessments used in guiding regulatory decisions.

Risk assessment—quantification of the potential adverse effects of pesticides—is a critical component of our present regulatory system. Estimates of dietary risks from pesticide residues for selected pesticides and crops depend on (1) sound toxicology, to assess the potential for adverse health effects of specific pesticides; (2) information on pesticide use patterns, specifically to determine which materials may result in residues on food crops; (3) good data on the levels, if any, of residues that can be expected to occur; and (4) up-to-date estimates of the foods people eat, sufficiently identified by age, sex, ethnicity, and location to determine likely exposure levels. As greater reliance on risk assessments to guide regulatory policy develops, complete and accurate information concerning these variables is critical to effective and economically efficient regulation.

Although regulatory agencies use quantitative risk assessment methodology to estimate human health effects from exposure to toxic substances such as pesticides, it is an evolving science. Risk assessment suffers from many sources of uncertainty; knowledge of how chemicals cause cancer is far from complete. Uncertainty arises from the need to extrapolate from the high doses necessary to induce tumors in animals to the lower doses to which humans are likely to be exposed. Data from cancer studies of many pesticides are limited, and data on both pesticide use and residues on raw crops and in processed foods are insufficient to conduct aggregate risk analyses. Up-to-date information on dietary patterns of various population groups is also lacking.

To compensate for these uncertainties, risk assessment employs what have been termed worst-case or upper-bound statistical approaches in determining dietary risk. Basically, all components of the risk analysis are taken at their most conservative value to ensure that risk estimates are appropriately conservative. As such, carcinogenic risk estimates may be useful for regulatory purposes and, when adequate information is available, for comparing risks associated with various pesticides and other manufactured or natural chemicals. But the estimates do not predict actual human cancer incidence. This approach to risk assessment has been justified by these many uncertainties. It is quite possible, however, that priorities established on the basis of such analysis could result in a misallocation of resources.

NRC study

Concern over the degree to which pesticide residues in the food chain pose risks to consumers has prompted studies by consumer groups, research units, and government agencies. The most comprehensive study was performed by the National Research Council (NRC) of the National Academy of Sciences in 1987. The NRC study was requested by the U.S. Environmental Protection Agency (EPA) to examine the existing statutory basis for establishing legal levels (tolerances) for pesticide residues in food and assess the operation of the tolerance-setting process in practice. The NRC developed estimates of dietary cancer risks from pesticides currently in use and explored alternative regulatory approaches, evaluating the effects of these alternatives on health risks and pesticide use patterns. The NRC study has been critical in reforming existing pesticide policy.

The NRC risk analysis relied largely on the baseline of pesticides that have food tolerances using EPA's existing pesticide data base. The analysis largely followed EPA's current risk assessment techniques, employing the two-stage linear dose-response model and "potency factors" (slopes of the dose-response model estimated from animal studies) developed by EPA. These currently exist for 28 of the 53 pesticides identified by the EPA as suspected carcinogens. Assumed pesticide residue levels in foods were set equal to legal tolerance levels, with estimates of dietary exposure to residues derived from aggregate estimates of food consumption in the United States. Because of this approach, the NRC estimates are considered "legally allowable risk," which is quite different from actual risk. Risk was thus characterized as a person's probability of additional risk of cancer from a lifetime exposure to pesticide residues at levels legally allowed in food products under existing regulations.

Results of the NRC risk assessment indicate that the total legally allowable risk (the additional risk of cancer from 70 years of exposure to these 28 potentially carcinogenic pesticides at tolerance levels in food) was slightly less than 0.006 or 5.84×10^{-3}. (This is in addition to the current general cancer risk for the U.S. population of 0.25, or one in four.) The risk estimates were also separated into categories of pesticides. Fungicides made up the largest proportion (nearly 60%) of estimated risk; herbicides' share of the total was greater than that for insecticides (approximately 27% and 14%, respectively). Older (pre-1978) pesticides appeared to generate a larger share of risk.

Results suggest that in the case of both herbicides and insecticides, one or two chemicals explained a large portion of estimated risk, yet risk appeared to be more uniformly distributed among fungicide compounds. Twelve pesticides were identified by the NRC as contributing 96% of estimated dietary risk. According to the NRC, greater risk was associated with raw than with processed food products (80% and 20%, respectively). Fifteen foods accounted for nearly 80% of total dietary risk from pesticide residues with the greatest risks calculated from exposure to tomatoes, followed by beef, potatoes, oranges, lettuce, apples, peaches, pork, wheat, soybeans, beans, carrots, chicken, corn, and grapes. From this analysis, the NRC concluded that exposure to potentially carcinogenic pesticides was likely to be concentrated in a few foods and be derived from a relatively small number of pesticides, many of which were registered before 1978.

Bias in cancer risk estimates

Given the known gaps in the data and the compensating assumptions made in developing dietary risk estimates, the NRC figures are likely to be biased estimates of real risks. Therefore, the specific risk-benefit estimates and rankings of foods and pesticides presented in the NRC report should be viewed with considerable caution, rather than immediately used to guide regulatory action.

For example, in the absence of data on actual pesticide use patterns and residue levels, the NRC assumed that all materials registered for use on a specific crop are always used at maximum levels allowed and are always present on that crop at levels equal to the legal tolerance limit. This assumption surely leads to substantial upward bias in risk estimates.

Use varies by region and within a crop cycle in any given region. In California, for example, many pesticides are not used on specific commodities, although they may be registered for use. (See fig. 1, which compares registered and actual uses of 9 of the 12 riskiest pesticides identified by the NRC.) When pesticides are used on specific commodities, pesticides may not be applied to all of the commodity acreage (table 1). Therefore, the assumption that all materials registered for a crop are actually used may greatly overstate pesticide use. The assumption also can bias the ranking of foods by associated dietary risk, since more materials are registered for crops whose high value and market size provide economic incentives to pesticide manufacturers. If the 26 most frequently consumed fruits and vegetables are ranked by the number of pesticides registered for use on each, the list is almost identical to the NRC list of the 15 foods with the greatest dietary risk.

Setting residues at tolerance levels because it is difficult to obtain data on actual residue levels leads to additional upward bias. Despite a lack of consensus on estimates of actual food residues, historical data from the Food and Drug Administration (FDA) and the California Department of Food and Agriculture (CDFA) over the past two decades consistently show that residues in excess of established tolerance levels are encountered infrequently (generally in less than 1% of the samples). In California in 1987, for example, 1,839 lettuce samples and 259 tomato samples were analyzed by CDFA for residues of over 100 pesticides. No residues were detected in 78% of the lettuce samples and 81% of the tomato samples. In the majority of lettuce and tomato samples in which residues were detected, residue levels were within 10% of the established tolerances. These results are not surprising, considering that tolerances are established to exceed the maximum residues determined from field studies using the most severe application conditions, including maximum application rate, maximum number of applications per growing season, and minimum preharvest intervals. Typical, legal application of pesticides should therefore not result in residues approaching tolerance levels. The NRC's assumption that residues would always be present at tolerance levels biases risk estimates significantly upward, leading to distortions in risk rankings.

Other assumptions used in the analysis, however, may bias risk estimates downward, lending even greater uncertainty to the estimates. Risk estimates were based on data for only 28 of 53 suspected carcinogenic pesticides accounting for less than 10% of food-use pesticides. A second source of underestimation derives from the fact that many tolerances were set for pesticides with incomplete toxicological data. Of the active pesticide ingredients registered for use on food, most were registered before 1972. Also, estimates of dietary exposure to residues were based on the 1977-78 U.S. Department of Agriculture (USDA) Food Consumption Survey. Food consumption patterns have changed significantly over the past decade, with noticeable decreases in the quantities of processed foods consumed and increases in consumption of raw fruits and vegetables. Furthermore, NRC's use of aggregate averages ignores significant differences in dietary patterns in children, women, and the elderly, as well as regional differences. Average consumption estimates imply that the "average" Ameri-

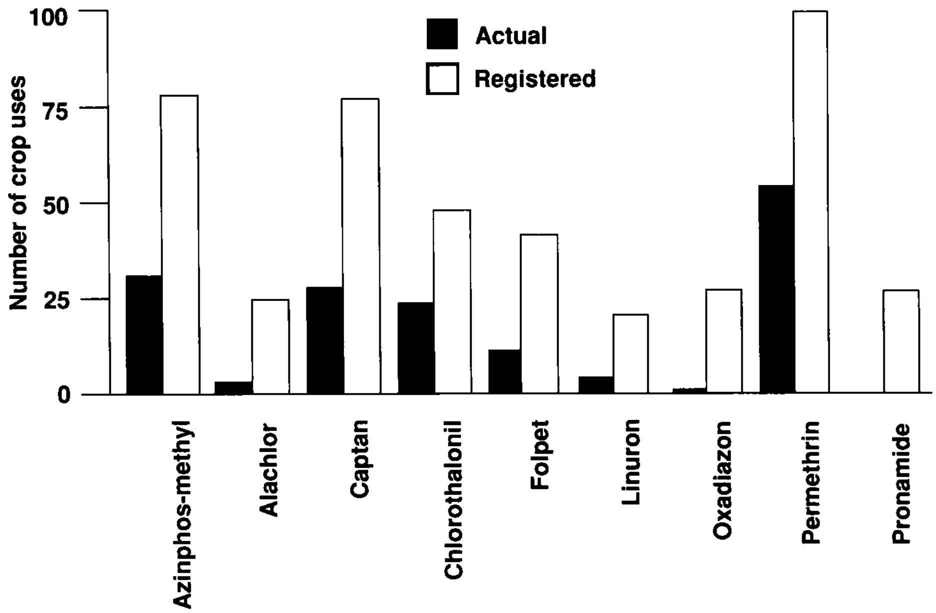

Fig. 1. Number of actual uses of selected pesticides in California in 1986, compared with their registered crop uses. (Sources: California Department of Food and Agriculture and National Research Council, 1987)

TABLE 1. Percentages of lettuce and tomato acreage treated with selected pesticides in California, 1986

Commodity, pesticide	Percent treated
LETTUCE	
Acephate	95.92
Captan	5.48
Dinoseb	33.79
Folpet	18.29
Mancozeb	1.64
Maneb	13.53
Methomyl	223.29*
Parathion	21.53
Permethrin	212.21*
Zineb	<1.00
TOMATOES	
Benomyl	1.86
Captafol	1.13
Chlorothalonil	26.42
Dicofol	2.28
Folpet	<1.00
Glyphosate	15.09
Lindane	1.17
Mancozeb	4.44
Maneb	4.16
Parathion	5.62
Permethrin	3.84
Trifluralin	9.53

* Percentages greater than 100 indicate that some acreage is treated more than once.

can would have to consume less than 7.5 ounces per year of 74 different foods, when many may consume more than this quantity of some foods such as almonds or mushrooms.

Recalculations of cancer risk

To highlight difficulties with NRC's underlying assumptions in their cancer risk estimates, we recalculated dietary risk in two ways. In both we held constant the cancer potency factor but used exposure estimates that differ from NRC's.

The first method recalculated the dietary risk of selected pesticides by basing exposure on results from FDA's 1987 Total Diet Study, in which inspectors purchased "market baskets" of selected food items, including meat and poultry, and had the food prepared "ready-to-eat" in institutional kitchens before analyzing for residues. A total of 234 food items were selected to represent the 5,000 foods identified in the 1977-78 USDA Nationwide Food Consumption Survey and the 1976-80 National Health and Nutrition Examination Survey. Samples of each food were purchased from retail stores in three cities in each of four U.S. geographical areas (northeastern, southern, north central, and western). This approach more accurately documents actual human exposure to pesticide residues, since it reflects the changes in residue levels that may result from transportation, handling, preparation, and processing, all of which have been shown to have the potential to dramatically alter pesticide residue levels.

The second method recalculated the dietary risk from pesticides on tomatoes and lettuce, basing exposure on actual residues found by FDA's Los Angeles laboratory.

First recalculation. Table 2 presents the NRC estimates of cancer risk for 7 pesticides (for which data were available) of the 28 analyzed by NRC. In the recalculation, instead of using NRC exposure estimates, we used data from the 1987 FDA Total Diet Study for population subgroups.

The risks calculated by the NRC for these seven pesticides ranged from 14.7 to 1,520 excess cancers per million. Five of the pesticides (linuron, captan, permethrin, folpet, and chlorothalonil) were ranked among the top 10 pesticides contributing to dietary cancer risk by the NRC. With our recalculation, these risks dropped by several orders of magnitude. Only one pesticide, permethrin, exceeded the EPA's "negligible risk standard" of one excess cancer per million. Risks posed by the other six pesticides were from 4,600 to nearly 100,000 times lower than NRC estimates. Although different results are obtained for the three population subgroups due to differences in food consumption patterns, more realistic calculations of cancer risk would require that the age-group data be combined, since risks are calculated assuming 70 years of exposure. It is not valid to consider that the risks of the 6- to 11-month-old subgroup are accurate for lifetime estimates, because this assumes that consumption patterns and body weight would remain constant for 70 years.

Even though we did not obtain data necessary to evaluate the other 21 potentially carcinogenic pesticides analyzed by NRC, monitoring data provide evidence about actual residue levels for many of these pesticides. We know that the FDA detected no residues of six potentially carcinogenic pesticides—chlordimeform, oxadiazon, alachlor, diclofop-methyl, metolachlor, and ortho-phenylphenol—and that residues were well below tolerances in other cases.

Second recalculation. The NRC assumption that all residues were always present at tolerance levels may also have severely distorted the estimated aggregate cancer risks from consumption of specific commodities. More pesticides are registered for use on high-value, high-volume commodities. Therefore, the assumption that all pesticides registered for use on a crop are actually used overstates pesticide use on these crops and the cancer risk these pesticides pose. Such logic does not take into account actual pesticide use practices on specific commodities.

Alternatively estimated cancer risks from pesticides used on tomatoes (the riskiest food identified by the NRC) and on lettuce (the fifth riskiest food) are shown in table 3. Risks reported by the NRC are compared with our recalculation using FDA residue data from its Los Angeles laboratory from 1982 to 1986. During this period, 3,179 tomato and 2,139 lettuce samples were analyzed for residues of over 200 pesticides, including all of the pesticides shown in table 3.

Large differences exist between NRC's calculated cancer risks using tolerance levels and ours using actual residue findings. The NRC, for example, found the major contributor to cancer risk for tomatoes was chlordimeform, but chlordimeform was not detected by the Los Angeles laboratory. Both the NRC and our recalculation found the main contributor to cancer risk on lettuce was permethrin, but the risks calculated using actual residue data were considerably lower.

Conclusions

Estimates of carcinogenic risk from the presence of pesticide residues have been provided. Such estimates differ greatly depending on the assumptions used in calculating them. The assumption by the NRC that all residues will always be present at the tolerance levels results in estimates of carcinogenic risk several orders of magnitude greater than the risks calculated using residue data. Our analysis clearly shows that tolerances do not equal exposure and demonstrates that the use of tolerance values to calculate risk is not appropriate. Such calculations should be used only as guides to more in-depth analysis. Even then, it may be critical to obtain more information on actual use and probability of exposure to ensure that relative risk rankings are accurate.

Additional uncertainty is associated with gaps in toxicological data for a large num-

TABLE 2. Comparison of estimated cancer risks from selected pesticides under alternative exposure assumptions

Chemical	Excess cancers per million: NRC estimates	Exposure assumptions based on FDA's total diet study: 6-11 months old	14-16 years, males	60-65 years, females
Acephate	37.3	0.01725	0.02139	0.03243
Linuron	1520	0.328	0.0984	0.1312
Captan	474	0.04462	0.02024	0.05612
Permethrin	421	2.13	0.9	1.215
Chlorothalonil	237	<0.0024	<0.0024	0.0024
Parathion	14.7	0.01116	0.00126	0.00288
Folpet	324	0.0273	0.01015	0.0336

TABLE 3. Comparison of estimated cancer risks under alternative residue assumptions

Commodity, pesticide	Excess cancers per million: NRC tolerance	FDA residue data*
TOMATOES		
Acephate	14	0.0017
Azinphos-methyl	0.00015	1.5×10^{-8}
Captafol	191	0.0033
Captan	29	0.0026
Chlordimeform	479	0
Chlorothalonil	61	0.23
Folpet	45	0.00017
o-Phenylphenol	8	0
Parathion	0.92	0.0002
Permethrin	31	0.088
Total	859	0.33
LETTUCE		
Acephate	16	0.025
Captan	55	0.011
Folpet	42	0.054
Parathion	0.43	0.00025
Permethrin	143.4	0.8
Pronamide	3.8	0.0044
Total	261	0.89

* Authors' recalculations are based on residue data from FDA Los Angeles laboratory, 1982-86.

ber of pesticides. Toxicology is an evolving science, and information that meets today's standards may be considered inadequate within a few years. If risk assessments are to guide regulatory policy, toxicology must be current and complete.

Concerns about the cancer risks posed by pesticides in the food chain have triggered calls for regulatory action and legislative reform. The choice of methods used to evaluate cancer risks and the criteria for establishing which risks are excessive should be made on the basis of the best scientific data available. Our analysis shows that lack of accurate data can impart great imprecision to the estimates of dietary risk. Probable risks based on likely pesticide use patterns and residues in foods indicate that the carcinogenic risks from pesticides may be well below earlier estimates. At the same time, it may be difficult to assess the effects on agriculture of modifying the use of specific pesticides. Eliminating a specific pesticide may increase pesticide expenditures by an estimated amount, as more expensive substitutes are employed, and yields and quality may be reduced, affecting supply and demand in a complex manner. In cases where no substitute chemicals are available, economic costs of use withdrawals would be higher. Economic impacts will depend on actual pesticide use patterns, benefits—including quality effects—from specific materials, and substitution possibilities.

Consideration should also be given to alternative risks to public health following removal of a specific pesticide. Elimination of specific fungicides, for example, could decrease the safety of the food supply by allowing the production of greater levels of naturally occurring fungal carcinogens. Better understanding of use patterns, benefits, and substitution possibilities remains critical to any reliable estimation of economic and health costs of pesticide withdrawals. Absence of actual data to estimate both risk and benefits of pesticides complicates and compromises the use of quantitative risk assessment as a regulatory tool.

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Water seepage from unlined ditches and reservoirs

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Seepage losses in the San Joaquin Valley's Westlands Water District were estimated at 27,000 acre-feet a year, or about 2% of the district's water supply. Ditch configuration and construction techniques appear to influence seepage rates.

Irrigation of agricultural land on the west side of the San Joaquin Valley since the mid-1960s has led to rising groundwater tables and an increased need for on-farm drainage to sustain productivity. The presence of naturally occurring trace elements in the shallow groundwater, the result of decades of soil leaching, has compounded the drainage problem. Drainage return flows contaminated with selenium, when concentrated in surface impoundments, have adverse effects on fish and waterfowl.

Control of drainage flows at the source has been advocated by the San Joaquin Valley Drainage Program (SJVDP) and others as the most promising short-term strategy for managing the drainage problem. Deep percolation loss to the shallow groundwater, resulting from excessive pre-season and seasonal irrigations, is the major contributor to drainage flow. Another source affected by on-farm management is seepage from unlined ditch and reservoir facilities. To develop comprehensive plans for long-term management of drainage and drainage-related problems, the SJVDP needs to be able to assess the relative importance of these losses compared with the groundwater recharge caused by inefficient irrigation and varying soil infiltration rates in agricultural fields.

Preliminary field studies of ditch seepage losses performed in 1987 by Westlands Water District indicated that seepage losses from unlined ditches and reservoirs in the district could be as great as 50,000 to 70,000 acre-feet a year. Until now, however, there has been no rigorous study of the magnitude of these losses on a regional scale. Although the region chosen for this survey was Westlands Water District, it was envisaged that conclusions drawn from the analysis would have transfer value to other regions and water districts.

Westlands Water District (WWD) applies 1.2 million acre-feet of irrigation water annually, obtained from U.S. Bureau of Reclamation project supplies and groundwater sources within the district. Water is delivered to more than 600 agricultural users through a 1,035-mile pressure and gravity pipeline distribution system. From the pipeline, the water often flows through conveyance ditches or directly to a head ditch for surface application to fields. Tailwater is commonly recycled by pumping directly out of small reservoirs or regulating ditches into which tailwater flows are directed.

Although there is some use of gated pipe or permanent lining to reduce seepage losses from irrigation head ditches, on most farms seepage occurs from head ditches, tailwater ditches, conveyance ditches, and tailwater reservoirs. This seepage contributes directly to shallow groundwater levels. During October 1987, about 303,000 acres of land had saline water tables within 20 feet below the ground surface. The water table was within 10 feet below the ground surface on about 222,000 acres. WWD staff estimate that about 300,000 acres in WWD will eventually need subsurface agricultural drainage.

Procedure

We selected 56 test sites, 18 of which were tested twice during the growing season (74 total tests). We also tested 19 reservoirs. Soil samples were collected from the top 1 foot in the bottom of each test ditch. Soil texture was determined by the standard particle size analysis (Bouyoucos hydrometer) procedure. Exchangeable sodium percentage (ESP) and salinity (electrical conductivity, $EC_e \times 10^3$) were also determined. The texture of the soil profile was determined through ribboning (manual evaluation) at 1-foot intervals from the surface to a depth of 6 feet adjacent to each ditch test site. If a shallow groundwater table was present in the top 6 feet of the soil profile, the depth was recorded.

Ditch dimensions were recorded for each test site. Before each test, the grower was interviewed to obtain additional information on ditch construction and management practices, such as the implement or implements used to construct each ditch, the machinery used to pull the implement and