# ENVIRONMENTAL EQUITY AND PESTICIDE EXPOSURE

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Toxicology and Industrial Health, Vol. 9, No. 5, pp. 913-959

ISSN: 0748-2337

*Although people of color and low-income groups bear a disproportionate share of the health risks from exposure to pesticides, research attention has been meager, and data on acute and chronic health effects related to their toxic exposures are generally lacking. Increased resources are needed both to study this issue and to mitigate problems already identified. People of color should be a major research focus, with priority on long-term effects, particularly cancer, neurodevelopmental and neurobehavioral effects, long-term neurological dysfunction, and reproductive outcome. Suitable populations at high risk that have not been studied include noncertified pesticide applicators and seasonal and migrant farm workers, including children.*

## INTRODUCTION

People of color and low-income groups bear a disproportionate share of the potential health risks from exposure to pesticides. Migrant and seasonal farm workers and their children, who cultivate and harvest crops sprayed heavily with pesticides, are the largest single group exposed. The majority of these workers are Latinos and blacks, as are most noncertified mixers, loaders, and applicators who handle agricultural pesticides. Many janitors, custodians, and maintenance workers who work with pesticides, including disinfectants, are people of color. People of color also suffer disproportionately from pesticide poisoning.

1. This manuscript has not been subjected to review by the authors' agencies and institutions. The views expressed are solely those of the authors and do not necessarily represent the policies of their respective organizations.

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3. Key Words: agriculture, cancer, neurological, pesticides, race, reproductive.

4. Abbreviations: 2,4-D, 2,4-dichlorophenoxyacetic acid; 2,4,5-T, 2,4,5-trichlorophenoxyacetic acid; ATSDR, Agency for Toxic Substances and Disease Registry; AAPCC, American Association of Poison Control Centers; BHC, benzene hexachloride; CDFA, California Department of Food and Agriculture; CRLA, California Rural Legal Assistance; DBCP, dibromochloropropane; DDE, dichlorodiphenylethylene; DDT, dichlorodiphenyltrichlorethane; DDVP, dichlorovos; EDB, ethylene dibromide; EEG, electroencephalogram; EPA, United States Environmental Protection Agency; FIFRA, Federal Insecticide, Fungicide, and Rodenticide Act; HCB, hexachlorobenzene; HDL, high density lipoprotein; HHANES, Hispanic Health and Nutrition Evaluation Survey; LD50, lethal dose in 50% of test animals; LDL, low density lipoprotein; MCS, multiple chemical sensitivity; NCHS, National Center for Health Statistics; NCTP, Neurobehavioral Core Test Battery; NEFOES, NCI/EPA Farm Occupational Exposure Study; NES, Neurobehavioral Evaluation System; NHANES, National Health and Nutrition Examination Survey; NHATS, National Human Adipose Tissue Survey; NTE, neuropathy target esterase; NIOSH, National Institute for Occupational Safety and Health; OPIDN, organophosphate pesticide-induced delayed neuropathy; OR, odds ratio; OSHA, Occupational Safety and Health Administration; PCB, polychlorinated biphenyl; PCMR, proportional cancer mortality ratio; PCO, pest-control operator; PMR, proportional mortality ratio; PPB, parts per billion; RR, risk ratio; SEER, surveillance, epidemiology and end results; SIR, standard incidence ratio; SMR, standard mortality ratio; TCDD, 2,3,7,8-tetrachlorodibenzo-*p*-dioxin; ULV, ultra-low volume; VLDL, very low density lipoprotein; VOC, volatile organic compound; WHO, World Health Organization.

Chlorinated hydrocarbon pesticide levels in serum, fat, and breast milk are higher in blacks compared to whites (Davies et al., 1972; Woodward et al., 1976; Martin et al., 1985; Mines et al., 1991; Moses, 1993; Rosenberg et al., 1993).

Recent immigrants, especially from Latin America (where pesticides are often misused and poorly regulated), native Americans, and children, especially children of agricultural workers, are other groups about whom there is great concern. Poor people (including whites) may have disproportionate pesticide exposures from subsistence farming, fishing, and food gathering (especially in the South); the poor are also more likely to have greater residential exposures from heavy spraying for severe pest problems in substandard housing. Data on health effects related to toxic exposures are, however, generally lacking for people of color.

People of color are more likely to have multiple simultaneous and sequential exposures to pesticides, which may be difficult to document and characterize. This problem of multiple exposures is characteristic of environmental inequity. There are remarkably few recent quantitative data, including simple descriptive data on duration, frequency, and intensity of exposure, that are specific for the race or ethnicity of persons who are occupationally or environmentally exposed.

Lack of access to and unavailability of adequate health care contribute significantly to the impact of environmental contamination, and constitute a major problem for farm workers (and for owner/operators of small farms and their families) who live in rural areas. Minorities as a group are most likely to be exposed to pesticides, and yet they have the least control over mitigation of their exposures or over proper assessment and treatment of potential health problems arising from the exposures.

The purpose of this article is to document the following conclusion: although research attention has been meager, sufficient evidence is available to show that people of color and low-income groups are disproportionately exposed to and affected by pesticides. As a result, increased resources are needed both to study this issue and to immediately mitigate the problems identified.

### *The Number and Kinds of Pesticides*

In 1939, there were 32 pesticide products registered with the U.S. Department of Agriculture. In 1989, there were 729 active-ingredient pesticide chemicals mixed with other ingredients and formulated into 22,000 commercial products (U.S. EPA, 1989). Synthetic chemical pest control began in the early 1940s with the introduction of the insecticides DDT and parathion, and the herbicides 2,4-D and 2,4,5-T. Current annual use in the United States is 1.5 billion pounds—2.5 billion pounds if wood preservatives are included, and even more if chlorine compounds used in water treatment are included (U.S. EPA, 1988).

"Pesticide" is a generic term that includes insecticides, herbicides, fungicides, rodenticides, nematicides, acaricides, molluscicides, pisicides, and avicides, named according to the pest against which they are active. Classification based on function includes defoliants, desiccants, disinfectants, repellents, attractants, chemosterilants, plant and insect growth regulators, and wood preservatives. "Fumigant" is a classification based on physical state (gas). The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) defines pesticides as economic poisons.

Commercial pesticides are formulations containing the active ingredient pesticide mixed or diluted with other ingredients, called "inert" because they are not active as pesticides. Inert ingredients include adjuvants, added to the formulation to improve the effectiveness of the pesticides, carriers (e.g., kaolin clays, diatomites), surfactants (primarily nonionic detergents and wetting agents), and solvents (e.g., toluene, xylene, 1,1,1-trichloroethane, mineral spirits, alkylated naphthalenes, and petroleum oils). Inert ingredients can be more toxic than the pesticide itself, and often pose a more significant potential chronic health hazard. The identity of most "inerts" in individual pesticide products is protected by trade-secret laws, even though they are highly toxic. Pesticide formulations also can contain undesirable process contaminants, including dibenzodioxins, dibenzofurans, nitrosamines, perchlorethylene, and hexachlorobenzene.

Pesticide formulations occur as powders, dusts, granules, emulsifiable concentrates, solutions, seed treatments, drenches, and baits. "Ultra-low volume" (ULV) refers to formulations in which the total volume of spray is one half gallon or less per acre applied undiluted. These formulations may be more hazardous to the handler, since the percentage of the active ingredient pesticide is very high.

*Pesticide Use in the United States*

The largest single area of use of pesticides in the United States is agriculture, which annually uses over one billion pounds of herbicides, insecticides, fungicides, fumigants, and other pesticides, or 80% of all pesticide use (U.S. EPA, 1988). Organic farms account for less than 2% of the two million farms in the United States. An additional one billion pounds of pesticides are used as wood preservatives, mainly creosote on railroad ties. The above figures may not include chlorine products used for water treatment.

Of the billion pounds used in agriculture, about 750 million pounds, or 75%, are used on three crops: corn, soybeans, and cotton. There has been a marked change in the pattern of pesticide use in American agriculture during the past 25 years. Herbicide use has increased 175%. Since 1972, there has also been increased use of the less persistent, but more acutely toxic, organophosphate and N-methyl carbamate insecticides, after the environmentally persistent chlorinated hydrocarbons such as DDT, aldrin, dieldrin, chlordane, heptachlor, and toxaphene were banned or restricted (Moses, 1992).

The use of highly toxic fumigants to sterilize soil and as nematocides, such as Telone II, methyl bromide, and metam-sodium, is markedly increasing. While fungicides represent a

small percentage of total volume of pesticide use, they are important because a large percentage are animal carcinogens and/or teratogens; they are used extensively on labor-intensive crops of fruits and vegetables; and they persist as residues in the marketed product, whether fresh or processed.

An enormous problem inherent in the current technology of pesticide application is the problem of drift, or dispersal of the pesticide away from the site of application (Akesson and Yates, 1964; University of California, 1981; Carman et al., 1982; Matthews, 1982; Morse et al., 1982; Haverty et al., 1983; Barnes et al., 1987; Goldman et al., 1987). Some studies show that as little as 10 - 15% of applied pesticides actually reaches the target pest, while the remaining 85 - 90% is dispersed off-target to air, soil, and water through drift, runoff, volatilization, and off-gassing. Significant concentrations of almost all pesticides applied aerially or by ground-rig sprayers can drift up to a mile or more from the site of application, even under the best of wind conditions, depending on particle size and method of application. Pesticide residues can be very persistent soil contaminants, a continuing source of contamination from runoff, and a widespread contaminant of surface water and ground water in the United States (Zaki et al., 1982; Cohen et al., 1984; Leistra et al., 1984; Miles and Delfina, 1985; State of California, 1985; Jones and Marquardt, 1987; Russell et al., 1987; Pimentel et al., 1992). Pesticides also concentrate in fog (Glotfelty et al., 1987).

Chemigation, or adding pesticides to irrigation water, is increasingly being practiced. Pesticides are also incorporated into soil (usually as granular formulations), or, as in the case of fumigants, injected into the soil and then covered with plastic sheeting to minimize loss from off-gassing. Animals are also treated with pesticides, externally through the use of "dips," or in their feed. Residues of pesticides from drift, animal feed, or treatment of animals can contaminate their meat, milk, eggs, gelatin, and other products (Skaftason and Johannesson, 1979; Stehr-Green et al., 1986).

Major nonagricultural uses of pesticides include structural pest control in homes and buildings; maintenance of lawns, turf, and rights-of-way on highways, railroads, and power transmission lines; industrial use in paint, textiles, and pulp and paper; public health use for rodent and mosquito control, and for water treatment; and in thousands of products sold over the counter for home, garden, and pet use. Table 1 lists selected pesticides widely used in the United States. With rare exceptions, most of the pesticides used for nonagricultural purposes are different formulations of the same active-ingredient pesticides used in agriculture.

Over the past several years, the U.S. Environmental Protection Agency (EPA) has carried out studies designed to assess residential exposure to pesticides. These studies focused on middle-class suburban communities or on farm owners and their residences (U.S. EPA, 1990). The EPA is currently embarking on a joint study with the National Institute of Environmental Health Sciences to study residential pesticide exposures of farm workers and their families.

**TABLE 1. Selected Pesticides Widely Used in the United States**

| Insecticides | Herbicides |
|---|---|
| Organophosphates | Alachlor (Lasso) |
| Azinphos-methyl (Guthion) | Atrazine (Aatrex) |
| Chlorpyrifos (Dursban, Lorsban) | 2-4-D |
| Diazinon (Spectracide) | Glyphosate (Roundup) |
| Dichlorvos (DDVP) | Paraquat (Gramoxone) |
| Dimethoate | Simazine (Princep) |
| Methamidophos (Monitor, Tamaron) | Trifluralin (Treflan) |
| Methidathion (Supracide) | |
| Methyl parathion | Fungicides |
| Mevinphos (Phosdrin) | |
| Parathion (ethyl) | Benomyl (Benlate) |
| | Captan |
| N-methyl carbamates | Chlorothalonil (Daconil, Bravo) |
| Aldicarb (Temik) | Hexachlorobenzene |
| Carbaryl (Sevin) | Mancozeb |
| Carbofuran (Furadan) | Maneb |
| Methomyl (Lannate) | Metiram |
| Oxamyl (Vydate) | Triadimefon (Bayleton) |
| Propoxur (Baygon) | |
| | Fumigants |
| Chlorinated Hydrocarbons | |
| Endosulfan (Thiodan) | Chloropicrin |
| Lindane | Ethylene oxide |
| Methoxychlor | Methyl bromide (Brom-O-Gas) |
| | Metam-sodium (Vapam) |
| Synthetic Pyrethroids | Sulfuryl fluoride (Vikane) |
| Cyfluthrin (Baythroid) | Telone II (Dichloropropene) |
| Cypermethrin | |
| Deltamethrin | Multiple Use |
| Fenvalerate (Pydrin) | |
| Flucythrinate | DNOC |
| | Dinocap |
| Acaracides | Pentachlorophenol |
| Dicofol (Kelthane) | |
| Propargite (Omite) | |

While the use of household pesticide products by the middle class may exceed that of low-income urban or rural residents, housekeeping and other behavioral differences may influence exposures. Pesticide residues have been shown to accumulate in house dust, frequently by tracking it in from outdoors. Ingestion of house dust from floors and other interior surfaces by young children may constitute a relatively important route of exposure, especially from discontinued pesticides such as chlordane and DDT (Lewis et al., 1991).

Table 2 lists the major agricultural sources of human exposure to pesticides, both occupational and nonoccupational. Table 3 lists the major nonagricultural sources of pesticides, both occupational and nonoccupational.

**TABLE 2. Source**

| Occupational |
|---|
| Pesticide formulators |
| Pesticide mixers/load |
| Pesticide applicators |
| Flaggers for cropdust |
| Cropduster pilots |
| Field workers |
| Pesticide manufactur |
| Packing house work |
| Commodity fumigati |
| Veterinarians |
| Truck drivers, wareh |

**TABLE 3. Sourc**

| Occupationa |
|---|
| Exterminators (PCOs*. |
| Wood preservation wo |
| Chemical lawn care wo |
| Golf course workers |
| Park maintenance worl |
| Pet groomers |
| Landscape maintenanc |
| Highway, railway bed. maintenance wor |
| Mosquito abatement v |
| Custodians who apply |
| Truck drivers, wareho |
| Textile workers |
| Pulp and paper worke |
| Paint manufacturing |
| Morticians |

*PCO = Pest control op
**OTC = Over-the-cou

Although the followi
developing countries
ethylene dibromide
(Moses, 1992).

*Rates of Exposure*

Pesticides are readil
tract. The eyes can

**TABLE 2. Sources of Human Pesticide Exposure—Agricultural**

| Occupational | Nonoccupational |
|---|---|
| Pesticide formulators | Drift, overspray |
| Pesticide mixers/loaders | Off-gassing, volatilization |
| Pesticide applicators | Food contamination |
| Flaggers for cropdusters | Ground water contamination |
| Cropduster pilots | Surface water contamination |
| Field workers | Soil contamination |
| Pesticide manufacturing workers | Air contamination (indoor, outdoor) |
| Packing house workers | Sports fishing |
| Commodity fumigation workers | Leaks, spills, accidents |
| Veterinarians | Disposal sites |
| Truck drivers, warehouse workers | |

**TABLE 3. Sources of Human Pesticide Exposure—Non-Agricultural**

| Occupational | Nonoccupational |
|---|---|
| Exterminators (PCOs*—structural) | Homeowner pest control—OTC** |
| Wood preservation workers | Homeowner garden pest control—OTC** |
| Chemical lawn care workers | Pet products—OTC** |
| Golf course workers | Drift from lawn care treatment |
| Park maintenance workers | Drift from municipal, county park maintenance, mosquito control |
| Pet groomers | Indoor air contamination—homes, schools, offices, aircraft, buildings |
| Landscape maintenance workers | Recreational—golf courses, parks |
| Highway, railway bed, right of way maintenance workers | Leaks, spills, accidents |
| Mosquito abatement workers | Disposal sites |
| Custodians who apply pesticides | |
| Truck drivers, warehouse workers | |
| Textile workers | |
| Pulp and paper workers | |
| Paint manufacturing workers | |
| Morticians | |

*PCO = Pest control operator
**OTC = Over-the-counter

Although the following pesticides are banned in the United States, they may be widely used in developing countries: DDT, aldrin, endrin, dieldrin, chlordane, heptachlor, BHC, toxaphene, ethylene dibromide (EDB), dibromochloropropane (DBCP), Folpet, and dinitro (Dinoseb) (Moses, 1992).

## EXPOSURE TO PESTICIDES

### *Rates of Exposure*

Pesticides are readily absorbed through the skin, the respiratory tract, and the gastrointestinal tract. The eyes can be a significant route of exposure in splashes and spills. The major route

of occupational exposure to pesticides is the skin, and not, as commonly believed, the respiratory system (Spear, 1991). Pesticides can persist on the skin for many months after exposure (Kazen et al., 1974). The respiratory tract is the major route of absorption for fumigants, which in part accounts for their great toxicity. It also is the main route for products formulated as aerosols, foggers, and smoke bombs, but the skin absorbs them as well. Diet, breast milk, and placental transfer are the nonoccupational routes of absorption. House dust can also be a significant source of pesticide exposure, especially to infants and toddlers. The rate of absorption of pesticides into the body is specific to the product and depends on the properties and concentration of the active-ingredient pesticides and the inert ingredients in a particular formulation.

*Exposure of Agricultural Workers*

Commercial agriculture in the United States has always been dependent on immigrant labor, beginning with Africans forced to work as slaves on plantations in the South, and continuing with the sharecropping system. Many farm laborers were compelled to travel great distances from their homes to find work in agriculture, becoming part of an East Coast migrant stream aptly described as "The Harvest of Shame" (CBS, 1962). African Americans, as well as Jamaicans, Haitians, and other Caribbean Islanders, continue to be a major part of this migrant stream, along with increasing numbers of Latinos from Puerto Rico, Mexico, and Central and South America.

Large-scale commercial agriculture in California, called "agribusiness," also depends on immigrant labor—exploiting in turn Chinese, Japanese, Filipino, and Mexican workers (McWilliams, 1971). The only large influx of white migrant workers, the dust bowl "Okies and Arkies," was siphoned by World War II into shipyards and defense plants. Beginning in 1942, workers began to come from Mexico in large numbers because of wartime labor shortages. In 1951, Public Law 78 authorized contractual agreements between the U.S. and Mexican governments, allowing growers to import Mexican nationals to pick crops, and then to send them back to Mexico after the harvest was complete. These workers, all men, were known as *braceros* (Spanish for "arms," or field hands). When the "Bracero Law" was repealed in 1963, approximately 350,000 braceros were working annually in the United States (Galarza, 1964).

The largest amount of farm acreage in the United States is in field crops such as corn, wheat, soybeans, and cotton. Cultivating and harvesting of these crops is almost completely mechanized, and white workers dominate the work force. Labor-intensive crops, primarily perishable fruits and vegetables, still require large numbers of workers for hand-cultivating and harvesting, which are the major jobs of the migrant and seasonal farm workers.

Ethnic minorities continue to harvest perishable food crops in the United States, and peak seasonal demand for workers and dependence on cheap labor has become a permanent feature of commercial agriculture. A 1990 national survey of farm workers by the Department of Labor

found that 77% identify themselves as members of a minority group. Two-thirds of the farm workers were foreign born—92% Mexican, 4% other Latinos, 3% Asian, and 1% Caribbean. Of the one-third who were born in the United States, 34% were Latinos, 5% were African Americans, 1% were from other ethnic groups such as native Americans and Asians, and the rest were non-Latino whites (Mines et al., 1991). In California, farm workers are primarily Latinos of Mexican origin, who may comprise over 90% of the agricultural work force (Martin et al., 1985). Latinos migrating from California, Texas, and Florida now predominate the West Coast and Midwest migrant streams.

Workers who handle the concentrated pesticides are at the highest risk: pesticide formulators, farmers, and agricultural workers who mix, load, and apply pesticides; flaggers of crop dusters; exterminators; and maintenance workers for lawns, golf courses, turf, highways, and other rights-of-way. Ethnic minorities are often exterminators and custodians, who use disinfectants as well as other pesticides, in some parts of the country. Pest-control operators (PCOs, exterminators) are the largest single group of pesticide applicators, but they might not be as heavily exposed as mixers, loaders, and flaggers for commercial firms that apply pesticides in agriculture. Exposure is generally lower in pesticide manufacturing, where batch processing and closed systems require almost no direct contact. Exposure could be higher in formulation plants. Field workers are exposed to pesticide residues from leaf surfaces, on the crop itself, in the soil, or in the duff (decaying plant and organic material that collects under vines and trees), as well as from drift from crop-duster aircraft and ground applicators, especially airblast sprayers.

The poor sanitary conditions in which farm workers must live, often without sufficient hot water or changes of work clothing, further intensify their exposures. This is a special problem because, even under the best conditions, laundering work clothes does not completely remove pesticide residues (Finley and Rogillio, 1969; Finley et al., 1974, 1979; Lillie et al., 1981, 1982; Kim et al., 1982; Easley et al., 1983; Easter and DeJonge, 1985; Chiao-Cheng et al., 1988).

The total number of farm workers in the United States is not known. The Department of Agriculture estimates that there are two million hired workers and three million farmer/owners and their unpaid families working on the two million farms in the United States. California, Florida, and Texas hire the most farm workers (U.S. Department of Agriculture, 1991).

*Exposure of Children*

Children bear greater risks in terms of exposure because of their higher respiratory rate, more exposed surface area, and greater caloric and fluid intake. The "occupation" of children is to explore, which results in extensive oral and hand-to-mouth contact with their environment.

Children may be at greater physiological risk from pesticides because of issues related to their growth and development, and these factors may increase their susceptibility to acute toxicants.

Children's greater susceptibility to chronic toxicants such as lead is well documented (Borowitz, 1988).

Children can comprise as much as 25% of the agricultural work force during the summer harvest. They are legally allowed to work in hazardous jobs in agriculture at a younger age than children in other industries, where the minimum age for such work is 18 years. In agriculture, 16-year-olds are permitted to operate hazardous farm machinery, such as tractors and harvesters; if the farm is owned or operated by their parents, a child of any age can do the hazardous work. The minimum age at which children can work in nonhazardous jobs in other industries is 14 to 16. In agriculture, children younger than 14 can work, and outside of school hours 12-year-olds can work with parental consent; a child of any age can work on a family farm.

Use of indoor pesticides puts infants and children at risk. Frequently, pesticides are used in substandard and inadequate housing afforded to the poor, for example, where spraying to control roaches can be excessive. Legal and directed use of pesticides for the home also may put children at risk. For example, indoor foggers containing the N-methyl carbamate propoxur could expose children to levels approaching one-tenth of the $LD_{50}$ (the median lethal dose, or the amount of toxicant necessary to kill 50% of the test animals). Calculations in a child's breathing zone after using home foggers according to directions on labels resulted in levels of pesticide exposure to children far exceeding equivalent work-place standards for adults (Lewis et al., 1991). In addition, children are at much greater risk of accidental ingestion than are adults, because many pesticides for home use are not in child-proof containers. Label directions, which are often difficult to comprehend even for English-speaking adults, are meaningless to children.

Very little monitoring or other data exist regarding exposure levels of herbicides and fungicides and their absorption in human beings (Coye et al., 1986). Almost all of the available data are measurements of herbicides in ground water and soil, and measurements of fungicide residues on marketed fruits, vegetables, and grain products, whether fresh and processed.

## HUMAN BODY BURDEN OF PERSISTENT CHLORINATED HYDROCARBONS

Almost all of the chlorinated hydrocarbon pesticides that biodegrade slowly and persist in human and animal tissue and the environment are no longer registered for use in the United States. These include DDT, aldrin, dieldrin, chlordane, heptachlor, BHC, and toxaphene. Lindane (gamma-hexachlorocyclohexane), widely used in structural pest-control and the major ingredient in the pediculicide/scabicide "Kwell," is an exception. Methoxychlor and endosulfan are nonpersistent chlorinated hydrocarbons still widely used on food crops in the United States.

Because the chlorinated hydrocarbons are highly lipophilic (reside in fatty tissue), with long biological half-lives, these pesticides and their metabolites can persist for many years in human tissues. The most commonly found residues are DDE, DDT, Beta-BHC, dieldrin, transnonachlor, hexachlorobenzene, heptachlor expoxide, and oxychlordane. Pesticides can be found in a wide variety of biological tissues and fluids, including blood, urine, fat, breast milk, autopsy and surgical specimens, products of conception, placenta, cord blood, and semen. The persistence of pesticide residues in and their recovery from other biological tissues such as hair, sweat, and saliva has not been rigorously studied. Published studies seem to indicate that minorities, particularly blacks, have higher levels of environmental pollutants, particularly those that are sequestered in lipid-rich tissue, than do whites. Whether these differences are attributable to occupation, diet, residence, or biological susceptibility as influenced by race, or some combination of these variables and race, is not known.

A population survey of 497 whites and 303 blacks in Dade County (Miami, Florida) found that, for both races, serum levels of DDT and DDE were significantly lower among members of the more affluent social classes I and II (as defined by the survey) than among members of the less affluent classes IV and V. Among whites the difference in serum levels between classes was statistically significant for DDT ($p < 0.001$) and DDE ($p < 0.001$); similar class-related differences were found among blacks for DDT ($p < 0.01$), and for DDE ($p < 0.001$). Among people of the same social class, blacks still had higher residues. Residues were greater among less affluent people whether they were classified by the Hollingshead Two-Factor Index, by census tract population density, or by median income of the census tract (Davies et al., 1972).

A similar relationship between the concentration levels of DDE and DDT in the plasma of blacks and whites was observed when 175 urban black, 199 urban white, 139 rural black, and 210 rural white volunteers in Charleston County, South Carolina, were evaluated for pesticides and polychlorinated biphenyls (PCBs). Both rural and urban blacks had higher levels of DDE and DDT than whites. The mean serum DDE level in rural and urban blacks was 10.5 parts per billion (ppb) and 8.2 ppb, respectively; in rural and urban whites, levels were 3.4 ppb and 2.6 ppb, respectively. The mean serum DDT level in rural and urban blacks was 8.8 ppb and 5.4 ppb, respectively; among rural and urban whites, levels were 1.6 ppb and 1.7 ppb, respectively. The difference between races was statistically significant for both pesticides ($p < 0.0001$). Urban and rural whites, however, had higher concentrations of PCBs than did their counterpart blacks. The mean serum PCB concentrations among rural and urban blacks were 0.3 ppb and 1.9 ppb, respectively, with the difference between races statistically significant ($p < 0.0001$) (Finklea et al., 1972).

A study compared human milk samples from 38 rural low-income black women in Mississippi and Arkansas with milk samples from 14 white women in Nashville. The mean DDT concentration was 447 ppb in blacks and 75 ppb in whites (Woodward et al., 1976). A study of 852 white, 51 black, and three Asian lactating women in North Carolina

found that 45% of the black women and 5% of the white women had milk-lipid concentrations of DDE greater than 8 parts per million (ppm). The concentration of PCBs in milk lipids was similar for both races (Rogan et al., 1986).

In a study of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) in Vietnam veterans ranging in age from 36 to 46 years, the geometric mean serum TCDD level for blacks at the high end of the range in age (44 to 46 years) of 5.2 parts per trillion (ppt) was 49% higher than the geometric mean of 3.5 ppt at the low end of the range in age (36 to 38 years). The serum TCDD levels of whites showed no difference in mean concentration for the same age ranges—3.7 ppt for the 44- to 46-year-olds and 3.6 ppt for the 36- to 38-year-olds. The increase in TCDD concentration for blacks was found to be significantly correlated with age ($p = 0.02$) (Devine et al., 1990).

An analysis of data from the National Health and Nutrition Examination Survey (NHANES) II showed that nonwhites had significantly more DDE in their serum than did whites (19.0 ppb versus 11.6 ppb ($p < 0.01$)) and that their serum was more likely to contain quantifiable amounts of three of the sixteen pesticides measured in NHANES II. Living below the national poverty level and residing in the South or West increased the likelihood of having measurable levels of pesticides in one's serum (Stehr-Green, 1989).

An analysis of fat samples from the EPA National Human Adipose Tissue Survey (NHATS) collected between 1970 and 1983 for residue trends in PCBs, hexachlorobenzene (HCB) and beta-benzene hexachloride (beta-BHC) found that nonwhites had median adipose tissue concentrations of beta-BHC that were only slightly higher than those of whites (0.16 ppm versus 0.14 ppm). Whites had median concentrations of HCB in adipose tissue that were slightly higher than those of nonwhites (0.037 ppm versus 0.033 ppm). The percentage of nonwhites, however, was higher among those whose PCB levels in adipose tissue exceeded 3 ppm (7.8% nonwhites vs. 4.7% white) (Robinson et al., 1990).

In two separate studies, researchers observed differences between nonwhites' and whites' body burden of the pesticide Mirex. EPA's National Human Monitoring Program, a component of the National Pesticides Monitoring Program, reported the presence of Mirex in only six specimens during the first year it was included in the testing program. Although Mirex was detected in only a small number of specimens, it was present in two nonwhites and in four whites. The average concentration was 3.74 ppm for nonwhites and 1.25 ppm for whites (Kutz, 1974). In a study designed to monitor specific body burdens of Mirex in the southeastern United States, the geometric mean in adipose tissue was 0.252 ppm for whites and 0.406 ppm for nonwhites, which was not statistically significant (Kutz et al., 1985).

In Triana, Alabama, members of a black community who consumed fish contaminated with DDT had a geometric mean serum level of total DDT of 76.2 ppb, five times greater than the national level of 15 ppb (Kreiss et al., 1981b). Mohawk Indians in upstate New York, who

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live along the Upper and Lower Peninsula in Michigan, and Alaskan natives consume seafood in quantities that could contribute to body burdens of environmental contaminants. Similarly, select populations of whites (e.g., sport fishermen) are unduly exposed to environmental contaminants because of diet. A study of human beings exposed to waterborne chemicals in the Great Lakes found that persons who eat fish had a median total serum PCB concentration of 21.4 ppb, compared with 6.6 ppb in control subjects who did not eat fish. A correlation of 0.45 was found between annual fish consumption and total PCB concentration in the serum ($p < 0.0001$) (Humphrey, 1983).

A community-based study of white and black men and women aged 40 years and older found median concentrations of total cholesterol, triglyceride, and LDL cholesterol to be similar for both races. However, the median level of HDL cholesterol among black men appears to have been higher than that among white men in all age-groups studied; and the level among black women was higher than that among white women in three of the four age-groups studied (Castelli, 1977). In a study of the distribution of two environmental contaminants, DDE and PCBs, among three lipid factions in serum, it was found that for analytes the concentration order in the lipids was HDL>LDL>VLDL (unpublished data, CDC). When mean concentrations are analyzed by three lipid fractions (HDL, LDL, and VLDL), the results imply that earlier studies showing higher body burdens of lipophilic environmental contaminants in blacks could be misleading (Castelli et al., 1977).

Some of the major causes of deaths among minorities that are excessive when compared with deaths among the white population may be at least in part a function of exposure to environmental contaminants. DDT exposure has been positively correlated with increased levels of serum cholesterol and triglycerides, and with data from certain liver function tests (Kimbrough, 1982). The relationship among lipophilic xenobiotics (biologically active substances foreign to the organism) for example, DDT, DDE, and PCBs to serum lipid concentrations, and certain enzymes is complex. The scientific question is to determine if serum lipids are elevated due to deviations in lipid metabolism caused by a xenobiotic insult to the liver, or whether the increased level of xenobiotic insult is due to the hyperlipidemia.

A pilot study of breast tissue taken from 50 white women in Hartford, Connecticut, found higher concentrations of PCBs, DDE, and DDT in samples taken from women with breast cancer than in samples from women with benign breast disease (Falck et al., 1992). Concentration levels of certain pesticides were significantly higher among stillborn fetuses than among neonates (Saxena et al., 1983). Certain chemicals have been found to play a significant role in the etiology of diabetes mellitus (Wilson and Ledoux, 1989). Serum PCBs have been found to be positively associated with increased blood pressure (Kreiss et al., 1981a).

If environmental contaminants play a significant role in the etiology of the health problems cited above, and if blacks have higher body burdens of certain xenobiotics, then environmental

factors may be contributing to an enhanced incidence of these health-related problems among blacks. There are as yet no similar data for Latino populations that compare them to whites or blacks.

## HEALTH EFFECTS IN POPULATIONS EXPOSED TO PESTICIDES

Pesticide-exposed populations are at risk for both acute and chronic health effects. The most serious acute problem is poisoning, which can result in death. Less serious acute problems include skin rashes and irritation to the eyes and upper respiratory tract. While some persons may have problems with allergic reactions, pesticides are not a frequent source of allergies, except for pyrethroids and pyrethrum pesticides. Pesticide exposure can exacerbate or precipitate bronchospasm and asthma. There are limited data on acute effects of pesticides for nonoccupational exposures. Multiple chemical sensitivity, which has not yet been well characterized in relation to pesticide exposure, is described in more detail below.

### *The Nervous System*

Most of the occupational and nonoccupational poisonings and deaths from pesticides in the United States are related to highly toxic organophosphate pesticides such as parathion, Phosdrin (mevinphos), methamidophos (Monitor), and azinphosmethyl (Guthion); and N-methyl carbamates such as aldicarb (Temik), methomyl (Lannate), and carbofuran (Furadan), which exert their toxic effects by inhibiting the neurotransmitter cholinesterase at synaptic sites in muscles, glands, autonomic ganglia, and the brain. Table 1 lists examples of organophosphate and N-methyl carbamate insecticides widely used in the United States.

*Acute Effects.* The acute toxic effects of exposure to organophosphates and N-methyl carbamates are well characterized and documented (Namba et al., 1971; Tafuri and Roberts, 1987; State of California, 1988b; Morgan, 1990; Osorio and Ames, 1990; Hayes and Laws, 1991; O'Malley, 1992a).

Measurements of levels of red blood cells and of plasma cholinesterase activity are excellent tools for diagnosing pesticide poisoning, and for monitoring exposures of workers to these compounds. Since the normal range of cholinesterase activity is very wide, and a variability of 10 - 15% can exist in the same individual, it is very important in the occupational setting that a baseline activity level be taken on all workers prior to exposing them to pesticides that inhibit cholinesterase (Morgan, 1990; Hayes and Laws, 1991). Cholinesterase testing has been widely and rather haphazardly used in surveys of pesticide-exposed workers, and a paucity of rigorous validation and standardization limits its results. Older research suggests there is great variability among laboratories (Serat and Mengle, 1973), and even variability within a single laboratory appears to be common over time. Different methods are also being used that are not comparable for regulatory purposes. The EPA convened a workshop to address these problems of monitoring cholinesterase in the blood and serum of workers (U.S. EPA, 1992). For research on exposure, cholinesterase testing should be considered a supplemental test to more

sensitive indicators of exposure, including dermal-patch testing and testing for urinary alkyl phosphates (Richter et al., 1986).

Even though some organophosphates may reactivate *in vitro* in reagent solution, there is virtually no research on the effects of transport on cholinesterase reactivation *in vitro*. A new cholinesterase test kit attempts to obviate the issue of reactivation by conducting the assay in the field, but it has yet to be adequately validated. Red cell mass may account for much of the variability among individuals in red blood cell cholinesterase. Appropriate adjustment for hemoglobin concentration, hematocrit, or red cell mass might substantially improve the utility of cholinesterase measurement for assessing exposure in epidemiologic studies (McConnell et al., 1992).

A large variability in the activity of the enzyme paraoxonase, which metabolizes paraoxon and chlorpyrifos-oxon, and perhaps other organophosphate insecticides, has been identified among individuals as well as among species (Costa et al., 1990). There appear to be marked ethnic differences in the frequency of the homozygous alleles for low metabolic activity against paraoxon (Hassett et al., 1991). Data are lacking on the relationship between enzyme activity and the rate at which humans excrete organophosphate metabolites. Nor has the activity of paraoxonase been examined as a potential modifier of the effects of organophosphate exposure on physiological effects, such as cholinesterase activity, and on acute and chronic neurological outcomes.

Chlorinated hydrocarbon pesticides including DDT, dieldrin, chlordane, toxaphene, and lindane, are central nervous system stimulants. In toxic doses, they can cause anxiety, tremor, hyperexcitability, and generalized seizures that can result in death.

*Chronic Effects.* Much less is known about the delayed or chronic neuropathological and neurobehavioral effects of pesticides in humans, whether potential long-term effects from low-level exposures that are insufficient to cause acute poisoning, or long-term sequelae of acute poisoning.

Several early cases of mental illness or severe psychological disturbances were reported in workers who applied pesticides. Behavioral changes such as anxiety, difficulty in concentrating, memory deficits, and other more subtle effects have also been widely reported (Bowers et al., 1964; Dille and Smith, 1964; Durham et al., 1965; Brown, 1971; Rodnitzky et al., 1975; Levin and Rodnitzky, 1976; Duffy et al., 1979). Chronic EEG disturbances, especially an increase in beta wave activity, have been reported among individuals previously poisoned with organophosphates (Gershon and Shaw, 1961; Namba et al., 1971). Few follow-up studies are available on persons poisoned by pesticides to determine whether any long-term or delayed effects occurred. One such study examined 117 of 235 individuals three years after they were occupationally poisoned by organophosphate pesticides, mainly parathion and Phosdrin. Thirty-three persons still had complaints, ten of the cases involving the central

nervous system, mainly visual disturbances. No major psychiatric or neurological sequelae were found (Tabershaw and Clark, 1966). Another study compared the neuropsychological status of 100 persons poisoned by organophosphate pesticides (mainly parathion) an average of nine years earlier with the status of 100 nonpoisoned controls; poisoned subjects were found to have significant differences in measures of memory, abstraction, and mood. Twice as many had scores consistent with cerebral damage or dysfunction, and personality scores showed greater distress and complaints of disability, although the statistical analyses maximized the potential for finding effects (Savage et al., 1988).

The percentage of acutely poisoned individuals who develop clinically significant chronic neuropsychological sequelae is not known. Some studies suggest that even single episodes of severe organophosphate poisoning may be associated with a persistent decrement in neuropsychological function (Savage et al., 1988; Rosenstock et al., 1991). Auditory attention, visual memory, visual-motor speed, sequencing and problem solving, motor steadiness, reaction time, and dexterity were significantly poorer among the poisoned cohort. In these studies, individual exposure was not quantified, nor was it possible to examine dose-response relationships.

An association between organophosphate pesticide exposure and Parkinson's disease was suggested in a case report (Davis et al., 1978), and an association with choreoathetosis was suggested in another (Joubert et al., 1984). There are reports of increased incidence of Parkinson's disease in agricultural areas of Quebec that use pesticides heavily (Barbeau et al., 1987), and in workers who apply pesticides (Bocchetta and Corsini, 1986; Sanchez-Ramos et al., 1987). Herbicide exposure was suggested as a possible risk factor for the disease because MPP, a metabolite of the street drug MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine), which was found to cause Parkinsonian syndrome in humans, is similar in structure to paraquat (Langston et al., 1982, 1983; Langston and Ballards, 1983; Lewin, 1985, 1987). There is a report of two young agricultural workers with a Parkinsonian syndrome who had been exposed to the magnesium-containing fungicide maneb (Ferraz et al., 1988), and an earlier report that early-onset Parkinson's disease was more prevalent in rural areas (Rajput et al., 1986).

There have been many reports of severe neurotoxic and neuropsychological effects, including toxic psychoses that are related to methyl bromide exposure. Such mental and behavioral changes can occur after acute overexposures or from low-level chronic exposures, and these changes appear to be progressive and irreversible (Hine, 1969; Greenberg, 1971; Anger et al., 1981, 1986; Chavez et al., 1985; Prockop and Smith, 1986; Bishop, 1992).

Certain organophosphate pesticides induce delayed neuropathy (OPIDN), a distal "dying back" axonopathy, with muscle weakness that may progress to paralysis; the lesion occurs ten days to three weeks after an episode of unusually severe acute poisoning (Johnson, 1974, 1980). Currently registered organophosphates known to cause OPIDN include trichlorfon (Dipterex),

DDVP (dichlorvos), DEF, and isofenphos (Oftanol). EPN and leptophos (Phosvel) cause OPIDN, but they are not registered in the United States. Leptophos is thought to have caused severe neurological disease in twelve workers at a pesticide plant in Texas in the early 1970s (Xintaras et al., 1978). In humans, OPIDN has been reported to occur after poisoning with methamidophos (Monitor), chlorpyrifos (Lorsban, Dursban), and perhaps fenthion (Lotti et al., 1984; Metcalf et al., 1985). Further laboratory and field research are needed to characterize this disease clinically and as a public health problem. Although case reports suggest that OPIDN is an uncommon sequela to acute poisoning, unpublished data suggest that mild cases of OPIDN after severe cholinergic poisoning with methamidophos (Monitor, Tamaron) may be much more common than previously suspected (McConnell et al., 1990).

Further studies are needed to elucidate the mechanism involved in OPIDN. The pathophysiology probably requires the inhibition and subsequent aging of a poorly characterized esterase known as "neuropathy target esterase" (NTE), which is distinct from acetylcholinesterase. The hen brain NTE inhibition assay has been used as a tool for screening new organophosphate insecticides for delayed neuropathic effects. In a patient poisoned with chlorpyrifos (Dursban, Lorsban), the inhibition and aging of NTE activity in human lymphocytes were shown to predict the onset of OPIDN (Lotti et al., 1986). Preliminary studies are currently underway to validate the presence of NTE in lymphocytes as a potential biomarker for the development of human disease. Neurobehavioral effects of pesticides were discussed in a review of delayed effects of pesticides (Sharp et al., 1986).

*Neurobehavioral Testing of Pesticide-exposed Populations.* During the 1940s, adverse effects of work-place chemicals on the human nervous system were discovered in workers by alert clinicians, and were identified as well in animal research in industry. Objective behavioral methods to study the effects of neurotoxicants in humans in the work place began in the middle 1960s, using noninvasive measures of motor, sensory, and cognitive capabilities. Although these tests are appropriate for the many pesticides that are neurotoxic by design, research in pesticide-exposed populations is extremely limited.

By the end of 1989, 250 unique behavioral test methods had been used in the 185 cross-sectional studies done worldwide, as described in a comprehensive review (Anger, 1990). As behavioral methods used in this research continue to proliferate, over the past decade two major influences have led to a growing interest in developing standardized tests. The first influence was a 1983 meeting in Cincinnati, Ohio, sponsored by the World Health Organization (WHO) and the National Institute for Occupational Safety and Health (NIOSH). At this meeting, experienced field researchers recommended that seven field-proven behavioral tests with established sensitivity to neurotoxic chemicals be used for worksite research on neurotoxic chemicals. The researchers named these tests the Neurobehavioral Core Test Battery, which has since become known as the WHO-NCTB (Johnson, 1990).

The second major influence is the Neurobehavioral Evaluation System (NES), consisting of 22 clinically useful and field-proven behavioral tests implemented on a personal computer (Baker et al., 1985). The major advantage of the NES is that it can be readily administered in a more reliable and efficient manner than the NCTB, which requires a person to administer the test verbally to the subject. The major advantages of the NCTB are that it includes field-proven motor tests, that it can be administered in nonindustrialized settings (computers require service), and that it offers a greater potential for testing poorly educated subjects (since, unlike the NES, it does not require the ability to read instructions that appear on the computer screen).

Baker, Letz, and others (1985) began using the NES in diverse settings to study neurotoxic or potentially neurotoxic chemicals. The on-screen instructions for the NES tests have been translated into several languages, and the NES has been widely used in industrialized countries, particularly in the United States and Europe. The NCTB followed a different course. WHO sponsored a feasibility study prior to using the NCTB to study chemically exposed persons, because of increasing world interest in using the NCTB in developing countries.

Data from the NCTB feasibility study have now been collected from 2,300 subjects in ten countries on three continents. When viewed across age categories, data from some tests demonstrate a relative consistency in findings between countries and a greater degree of consistency within countries. Subjects differing significantly in level of education (three years vs. eight to thirteen years in other countries) and living in a rural setting, revealed much poorer performance on most NCTB tests, versus those living in an urban setting.

These findings raise important questions regarding the impact of education, especially very poor education, on cognitive tests used to assess work site exposures. There are more Latinos and blacks with five or fewer years of education than whites (U.S. Department of Commerce, 1991). Alternatively, some cultural groups may not be able to perform adequately the cognitive tests, developed by western Europeans, that are used in the NCTB and NES.

The use of computerized tests raises a practical issue. The computerized NES can be given to illiterate people by presenting the instructions orally, while the subjects are sitting at the console looking at the monitor. However, some groups, with no exposure to computers and very poor education, may be quite uncomfortable responding to prompts on a computer monitor, and this could compromise the value of computer-implemented tests for persons in those groups. Thus, issues of culture and education are effectively intertwined and raise concerns about the ability of the existing test batteries to assess performance in pesticide-exposed people of color. These limitations of the tests themselves have a direct impact on environmental equity.

*Cancer*

Cancer is another chronic effect of pesticide exposure. Data on long-term effects of pesticide exposure on the liver, lungs, kidneys, and immune system, including autoimmune disorders,

are limited. An outbreak of hemorrhagic cystitis in workers who formulated the carcinogenic insecticide chlordimeform (Galecron, Fundal) was an unusual early indication of potential chronic toxicity (Folland et al., 1978). The pesticide was withdrawn from the market because of the increased bladder cancer risk in exposed workers.

Little is known about the extent or magnitude of pesticide-related cancer in ethnic minority farm workers, because appropriate studies have not been done. Most cancer epidemiologic research has focused on farm owner/operators. The few studies that have evaluated cancer in adult farm workers suggest that, like farm owner/operators, they may experience excessive multiple myeloma and cancers of the stomach, prostate, and testis. Farm workers may differ from farm owners by experiencing excessive cancers of the buccal cavity and pharynx, lung, and liver. Cervical cancer was elevated in female farm workers in one study (Stubbs et al., 1984).

Difficulties in documenting cancer include not knowing the period of clinical latency, which can range from ten to twenty years or longer, and the low level of awareness among workers of the pesticides to which they are exposed, let alone their understanding of the potential risks to their health. Adults and children are potentially exposed to a variety of mutagenic and carcinogenic pesticides during planting, weeding, thinning, and harvesting crops over a working lifetime. Field conditions that provide little opportunity to wash skin or clothing to minimize absorption may intensify their exposure.

Cancer epidemiologic studies of migrant and seasonal farm workers are needed and would be scientifically valuable, because farm workers are almost constantly exposed to potential carcinogens, often starting at an early age. The present lack of such research may be partly due to concern over anticipated feasibility difficulties. Feasibility investigations whose results would help researchers plan successful etiologic studies should be conducted. Some existing studies of adults and children occupationally or environmentally exposed to pesticides are, however, relevant to minority workers, especially farm workers. These studies are summarized below.

*Cancer in Adults.*

*Lymphoma.* Statistically significant increased risk for malignant lymphoma has been reported in California farmers, Proportional Cancer Mortality Rate (PCMR) = 109 (Stubbs et al., 1984); Iowa farmers, Standard Mortality Ratio (SMR) = 129, Odds Ratio (OR) = 1.3 (Burmeister, 1981; Burmeister et al., 1983); Kansas farmers, OR = 1.6, with increased risk in those exposed to herbicides more than 20 days a year, OR = 6.0, and a risk for farmers who mixed or applied herbicides themselves of OR = 8 (Hoar et al., 1986); Minnesota farmers, Risk Ratio (RR) = 1.35 (Cantor et al., 1985), Utah farmers, OR = 6.6 for those diagnosed between 1952 and 1956, and OR = 3.1 for those diagnosed between 1966 and 1971 (Schumacher, 1985); Washington state farmers, OR = 1.33, and forestry herbicide applicators, OR = 4.80 (Woods et al., 1987); Wisconsin farmers, Proportionate Mortality Ratio (PMR) =

123, PCMR = 110 (Saftlas et al., 1987); New Zealand farmers, OR = 1.76 (Pearce et al., 1985); agricultural extension agents, OR = 1.21, PMR = 2.32 (Alavanja et al., 1988); United States grain workers, PMR = 272, PCMR = 249 (Alavanja et al., 1987); and Swedish grain workers, Standard Incidence Ratio (SIR) = 137 (Alavanja et al., 1987a). There is a case report of two firemen in California who died of malignant lymphoma six years after cleaning up a tank-truck spill of the fumigant 1,3-dichloropropene (Markovitz and Crosby, 1984).

*Leukemia.* Statistically significant increased risk for leukemia has been reported in British Columbia farmers, PCMR = 122 (Gallagher et al., 1984a); Iowa farmers, SMR = 135, OR = 1.24, with OR = 1.39 for those who died between 1971 and 1978, and OR = 1.6 for counties with high herbicide use (Burmeister, 1981; Burmeister and Morgan, 1982); in Iowa and Minnesota farmers associated with insecticide exposure, OR = 1.5, and exposure to herbicides OR = 1.86 (Everett et al., 1985); Nebraska farmers, OR = 1.25 (Blair and Thomas, 1979); nonwhite farmers in North Carolina, PMR = 190 (Delzell and Grufferman, 1985); Oregon and Washington farmers, based on chi-square analyses of frequencies (Milham, 1971); and agricultural extension agents, PMR = 1.8, OR = 1.92 (Alavanja et al., 1988).

*Multiple Myeloma.* Statistically significant increased risk for multiple myeloma has been reported in Iowa farmers, SMR = 147, OR = 1.5 (Burmeister, 1981; Burmeister et al., 1983); Oregon and Washington farmers, based on chi-square analyses of frequencies (Milham, 1971); Wisconsin farmers, PMR = 123 (Saftlas et al., 1987), OR = 1.4 (Cantor and Blair, 1984); Swedish agricultural workers, SMR = 120 (Wiklund, 1986b); New England farmers, OR = 2.22 (Pearce et al., 1985); and agricultural extension agents, PMR = 1.97 (Alavanja et al., 1988). A study in Washington state; Utah; Atlanta, Georgia; and Detroit, Michigan, found OR = 2.6 in those with past exposure to pesticides (Morris et al., 1986).

*Testicular Cancer.* Statistically significant increased risk of testicular cancer has been reported in southern farmers, OR = 1.4 (Brown and Pottem, 1984); farm managers in England and Wales, OR = 1.85 (McDowall and Balarajan, 1984); and Texas agricultural workers, OR = 4.18, and farmers, OR = 6.27 (Mills et al., 1984). There is a report from Illinois of testicular cancer in two 30-year-old workers at the same canning plant diagnosed within a year of each other; both had occupational exposure to pesticides (Prabhakar, 1978); and another report concerning pesticide manufacturing workers in Michigan and Arkansas, SMR = 1799, based on two cases in workers whose only common exposure was methyl bromide (Wong et al., 1984). A nonsignificant trend for increasing risk of testicular cancer over time was found in Swedish men employed in agriculture. The SMR = 83 between 1961 and 1966 increased to SMR = 94 in 1967 and 1973 and to SMR = 135 between 1974 and 1979. Eighteen cases of testicular cancer were found in a cohort of 20,245 pest control operators; 11.6 cases were expected, SMR = 144, which was not significant (Wiklund, 1986a).

*Liver Cancer.* Statistically significant increased risk for liver cancer has been reported in New Jersey agricultural production and service workers, RR = 2.08, and farm laborers,

RR = 1.89 (Stemhagen et al., 1983); and in Swedish grain workers, SIR = 238 (Alavanja et al., 1987a). A study of Swedish agricultural workers reported a trend for increasing risk over time between 1967 and 1979 (Wiklund, 1986b). There are case reports from Egypt of increased prevalence of hepatic angiosarcoma in farmers (El Zayadi et al., 1986).

*Stomach Cancer.* Statistically increased risk of stomach cancer has been reported in British Columbia farmers, PCMR = 119 (Gallagher et al., 1984); California farm workers, PCMR = 134, and farm owner/managers, PCMR = 202 (Stubbs et al., 1984); Iowa farmers, SMR = 135, OR = 1.3 (Burmeister, 1981; Burmeister et al., 1983); Wisconsin farmers, PMR = 124, PCMR = 113 (Saftlas et al., 1987); and Swedish agricultural workers, SMR = 107 (Wiklund, 1986b).

*Pancreatic Cancer.* Statistically significant increased risk of pancreatic cancer has been reported in British Columbia farmers, PMR = 112 (Gallagher et al., 1984b); Iowa farmers, SMR = 123 (Burmeister, 1981); Wisconsin farmers, PMR = 110 (Saftlas et al., 1987); United States grain workers, PMR = 191 (Alavanja et al., 1987b); and DDT manufacturing workers, RR = 4.8, increasing to RR = 7 for those exposed for a mean of 47 months (Garabrandt et al., 1992).

*Lung Cancer.* Statistically significant increased risk of lung cancer has been reported in Florida pest control operators, SMR = 289 (Blair et al., 1983); Maryland pesticide manufacturing workers, SMR = 265 (Mabuchi et al., 1980); and East German pesticide sprayers, PCMR = 180 (Barthel, 1981).

*Brain Cancer.* Statistically significant increased risk of brain cancer has been reported in California farm workers, PCMR = 155 (Stubbs et al., 1984), and Italian farmers, OR = 5.0 (Musicco et al., 1982). Nonsignificant increased risk has been reported in Iowa farmers, SMR = 111 (Burmeister, 1981); nonwhite North Carolina farmers, PMR = 230 (Delzell and Grufferman, 1985); Wisconsin farmers, PMR = 110 (Saftlas et al., 1987); Florida pest-control operators, SMR = 200 (Blair et al., 1983); and pesticide manufacturing workers, SMR = 132 (Wong et al., 1984).

*Cancer in Children.* Five children were diagnosed with neuroblastoma at the same Ohio hospital in the same year. All the mothers of the children had prenatal exposure to chlordane (Infante et al., 1978). These reports were among the first suggesting an association between pesticide exposure and cancer in children. Nine cases of colorectal cancer, which is very rare in children, were diagnosed at the same hospital in the South within a two-year period; eight of the children were from rural areas in Mississippi, Arkansas, or Tennessee, and had insecticide exposure (Pratt et al., 1977). This same investigator reported a case of colon cancer in a child who had lived in Times Beach, Missouri, where the child had potentially been exposed to dioxin (Pratt et al., 1987). There also are case reports of hematopoietic disorders in children,

including leukemia, as possibly associated with household pesticide use (Infante et al., 1978; Reeves et al., 1981).

A study of Baltimore, Maryland children with primary brain cancer found the risk for brain cancer was more than two times greater if the children had pesticide exposure in the home (Gold et al., 1979). A study of children in Los Angeles with acute lymphocytic leukemia found that the risk for leukemia was almost four times greater if their parents used pesticides in the home, and over six times greater if the pesticides were used in the lawn and garden (Lowengart et al., 1987).

A cluster of childhood cancer has been reported from several agricultural communities. In the San Joaquin Valley of California, in McFarland, between 1982 and 1985, eight children were diagnosed with cancer when two cases would have been expected. The types of cancer were two cases of Wilms' tumor, and one case each of non-Hodgkin lymphoma, neuroblastoma, astrocytoma, osteogenic sarcoma, fibrosarcoma, and rhabdomyosarcoma (Kern County Health Department, 1986; State of California, 1988a). Since this report, two additional cases of cancer have occurred in children in McFarland; a 14-year-old boy died of hepatoblastoma in 1988, and a 7-year-old boy was diagnosed with non-Hodgkin lymphoma in 1989.

In 1989 another cluster of childhood cancer was found in Earlimart, California, an agricultural town 14 miles north of McFarland. From 1984 to 1989, six cases of childhood cancer have been diagnosed. The types of cancer found were acute lymphocytic leukemia in three children (all of whom have died), and one case each of rhabdomyosarcoma, non-Hodgkin lymphoma (Burkitt's), and Wilm's tumor (State of California, 1993). Several children of farm workers in the town of Delano, which is equally distant from McFarland and Earlimart, were also recently diagnosed with cancer.

A statistically significant increased risk of cancer in children in Finland was associated with the mother being a farm wife, OR = 2.2, and the father's occupation being agriculture, gardening, or forestry, OR = 1.42 (Hemminki et al., 1981). Another study found acute nonlymphocytic leukemia in children to be related to parental exposure to pesticides, and to paternal pesticide exposures in jobs held for longer than 1,000 days, OR = 2.7 (Buckley et al., 1989).

*Effects on Reproduction*

Many of the pesticides widely used in agriculture are known to affect reproductive outcome in laboratory animals, and pesticide exposure can be a risk factor for sterility, spontaneous abortion, stillbirth, and birth defects in humans. Most reports and studies of reproductive toxicity and pesticides are of occupational or environmental exposure to a variety of pesticides in unknown quantities. Many are ecological studies in which the actual exposure of the individuals studied is not known, and not all studies find increased risk or deal adequately with potential confounders. Much of the research in pesticides and reproductive outcome is the

testing of hypotheses, and, with the exception of the fumigant DBCP discussed at length below, most findings are not definitive. The following discussion summarizes the results of some of these studies.

*Birth Defects.* Pesticide exposure has been studied as a risk factor for birth defects in farmers, farm workers, and in persons living in areas with heavy use of agricultural chemicals. Limb reduction defects were associated with parental occupation as a farm worker and living in an agricultural area, with the risk being greater with pesticide exposure during the first trimester, and with repeated exposure (Kricker et al., 1986; Schwartz et al., 1986; Schwartz and Logerfo, 1988). An interview study of crop-duster pilots and their sibling controls showed no difference between them in the number of birth defects in their offspring (Roan et al., 1984).

While not all studies report increased risk, associations have been found for facial clefts, spina bifida, anencephaly, neural tube defects, and other malformations (Balarajan and McDowall, 1988; Sever et al., 1988; White et al., 1988; Brender and Suarez, 1990; Restrepo et al., 1990a; Roeleveld et al., 1990). There is a case report in which a farm worker exposed to the insecticides Metasystox-R (oxydemeton-methyl), Phosdrin (mevinphos), and Lannate (methomyl) during her first trimester delivered a chromosomally normal child with multiple severe defects who died two weeks later (Romero et al., 1989). In another case report, a couple heavily exposed to 2,4-D for six months prior to conception and up to five weeks after the last menstrual period had a chromosomally normal child with severe mental retardation and multiple anomalies, who survived (Casey and Collie, 1984).

Controversy continues to surround Agent Orange, a 50/50 combination of the phenoxy herbicides 2,4-D and 2,4,5-T used by the United States military in Vietnam from 1962 to 1970. The EPA suspended the registration of most uses of 2,4,5-T in 1979, and banned it in 1985. 2,4-D is still widely used in hundreds of different formulations and mixtures with other herbicides and fertilizers. Other widely used phenoxy herbicides include 2,4-DP, 2,4-DB, 2,4,5-TP, MCPP, and Dicamba. Some studies of agricultural sprayers of 2,4,5-T, and of populations living in areas of heavy agricultural use of 2,4,5-T, reported a possible association between herbicide exposure and facial clefts and neural tube defects, but other studies did not. The studies were done in the United States, Canada, England, Australia, and New Zealand; most were ecological studies in which birth records were looked at, but no attempt was made to document actual exposures (Field and Kerr, 1979; Nelson et al., 1979; Lowe et al., 1981; Smith et al., 1982; Golding and Sladden, 1983). Well-conducted studies of Vietnam veterans from the United States and Australia found no significant increased risk that might father children with birth defects (Australian Government, 1983; Erickson et al., 1984).

Teratogenesis. Many chemical pesticides are embryotoxic and fetotoxic in laboratory animals. One reason more birth defects are not found in pesticide-exposed farm workers may be that exposures cause early fetal death that results in spontaneous abortion. In the few studies

available on humans exposed to pesticides in agriculture, increased risk for spontaneous abortion and stillbirth have been reported. Female farm workers in Washington state and in agriculture and horticulture in Denmark and Finland were at increased risk for spontaneous abortion or stillbirth (Hemminki et al., 1980; Heidam, 1984; Vaughan et al., 1984). One study found substantially increased risk for second trimester but not first trimester spontaneous abortion (McDonald et al., 1988). In a large United States study of 6,386 stillbirths, self-reported pesticide exposure of either parent increased the risk for stillbirth in their offspring (Savitz et al., 1989). A study in India of couples who worked in the vineyards as sprayers and also lived there found a much higher prevalence of spontaneous abortion and stillbirth than in a comparison group who did not work and live in the vineyards. The pesticides to which the couples were exposed included DDT, lindane, Dithane M45, metasystox, parathion, copper sulfate, dichlorvos, and dieldrin (Rita et al., 1987). A study of 314 pilots of crop dusters and 178 of their siblings who were not exposed to pesticides showed no difference in the prevalence of spontaneous abortion in their wives (Roan et al., 1984).

*Sterility/Infertility.* Two pesticides are known to cause sterility and infertility in male workers: the fumigants DBCP (dibromochloropropane) and EDB (ethylene dibromide). In 1977, several men working in a chemical plant in northern California that manufactured and formulated DBCP realized that they had not recently fathered children. Five of the men were found to have complete absence of sperm (azoospermia), or an abnormally low sperm count of less than 20 million/dl (oligospermia). All five had exposure to DBCP (Whorton et al., 1977). Further study of other workers at the plant exposed to DBCP found that almost half had abnormal sperm counts: 13% were azoospermic, 16.8% were oligospermic, and 15.8% had low-normal sperm counts (20 to 39 million/dl). Two of the sterile workers had not had any exposure to DBCP for nine and thirteen years respectively, and both had fathered children prior to their exposure. None of the workers studied was acutely poisoned or had any symptoms of clinical illness related to their exposure to DBCP, and all were otherwise healthy (Whorton et al., 1979).

Pesticide workers exposed to DBCP in other parts of the United States and in Israel were also found to be azoospermic or oligospermic (Glass et al., 1979; Potashnik et al., 1979; Sandifer et al., 1979; Wong et al., 1979; Potashnik, 1983). Eight years later, none of the American azoospermics showed any improvement, and five of eight men in Israel showed no improvement (Eaton et al., 1986; Potashnik and Yanai-Inbar, 1987).

The sterile or infertile men exposed to DBCP in Israel who recovered sperm function and subsequently fathered children were found to have no increase in birth defects or spontaneous abortion in their offspring; however, a significantly altered sex ratio (more girls than boys) was found (Goldsmith et al., 1984). A study of ten of these children, whose ages ranged from 1 to 16 years of age, found that they were normal when given physical examinations, and had no abnormalities in chromosomes in blood lymphocytes (Potashnik and Abiliovich, 1985).

DBCP was banned for agricultural use in the United States in 1979, but Hawaii permitted its use for pineapples until it was fully banned in 1985. Ethylene dibromide (EDB), a very similar fumigant, was substituted for many of DBCP's uses after the 1979 ban. Low sperm counts and decreased fertility were found in workers exposed to EDB in manufacturing and in commodity fumigation (Wong et al., 1979; Ratcliffe et al., 1987). EDB was banned in agriculture in the United States in 1984, but it is still widely used in third-world countries. DBCP's use as a soil fumigant in agriculture in the United States began in the early 1950s, and millions of pounds were injected into the soil. DBCP is the most widespread contaminant of groundwater and drinking water wells in California. There is no evidence that the levels found cause adverse reproductive outcomes in those drinking the water. EDB is also a widespread groundwater contaminant, especially in the state of Florida. Both DBCP and EDB are potent animal carcinogens.

*Multiple Chemical Sensitivity*

For more than three decades, clinical evaluations of individuals with pesticide poisoning have reported a syndrome of acquired intolerance to pesticides that can sometimes spread to other odorous inhalants. This syndrome is known as the "multiple chemical sensitivity syndrome" (MCS). A case definition has been formulated (Cullen, 1987), a National Academy of Sciences subcommittee on immunotoxicology has called for research to clarify this disorder, and a workshop of some 100 experts concurred with the need for scientific clarification of this syndrome and its mechanism (National Research Council, 1992). The syndrome is probably uncommon, representing 1.8% of the patients treated at the Yale Occupational and Environmental Medicine Clinics since 1986 (Cullen, 1991).

There are two categories of environmental exposure involved with this syndrome. An acute high-dose exposure to a chemical leads to an induction of the illness, and subsequent low-dose exposures trigger symptoms. In one study, pesticides triggered the illness in 40% of cases, and organic solvents induced the syndrome in 60% of cases (Meggs et al., 1992). Since pesticides are commonly dissolved in organic solvents, it is not clear whether the active ingredient or the solvent is responsible for inducing the syndrome. Subsequent reactions are triggered by common environmental inhalants such as perfumes, solvents, and tobacco smoke.

Opinion about the mechanism of this disorder is divided into two camps: those who favor a psychogenic mechanism such as somatization or hysteria, and those who favor a physiological mechanism. Clinical experience does not support the view that this disorder is more prevalent in upper-income whites; low-income ethnic minorities may be equally affected.

In one physician's practice, severe rhinitis was observed in 100% of MCS patients. Upper airway symptoms are not always present. A controlled study of nasal pathology in individuals with MCS, including subjects without regard to race, sex, or income, is currently in progress (Meggs and Cleveland, 1992). Preliminary findings show lymphocytic infiltrates in the nasal submucosa, with basement-membrane thickening and epithelial desquamation on electron-

microscopy. Further study is needed to delineate the pathophysiology of MCS and to determine the incidence in ethnic minorities and low-income individuals.

## REPORTING OF PESTICIDE-RELATED ILLNESS

*Underreporting of Pesticide-Related Illness*

There are no reliable data on the extent of pesticide-related illness in farm workers in the entire United States. EPA estimates 20,000 to 300,000 acute poisonings annually in agricultural workers, but this wide range attests to the need for a national reporting system that will document pesticide-related illnesses. California, with about 10% of the United States population, estimates about 1,500 occupational and 17,000 nonoccupational exposure incidents per year (Litovitz, et al., 1988; Maddy et al., 1990). Efforts to mandate such a reporting system have repeatedly failed because it requires amending the federal pesticide law (FIFRA), and because of powerful resistance to changes in the law by farm and chemical interests. There are reports that death from nonintentional acute pesticide poisoning is three times higher among blacks than among whites (Hayes and Laws, 1991). WHO estimates that there are one million poisonings and 20,000 deaths worldwide annually from pesticides, mostly in developing countries (World Health Organization, 1989; Jeyaratnam, 1990).

Since many physicians fail to recognize pesticide poisoning, or to even consider the diagnosis, the potential for underreporting is large. Furthermore, in mild and moderate poisoning, the signs and symptoms are nonspecific and may be confused with common illnesses such as gastroenteritis, upper respiratory disease, and other flu-like illness. Workers ill from pesticide exposure may never see a doctor. There are strong disincentives to report illness, both for the employer and the worker. The employer does not want the harvesting of a perishable crop to be disrupted, and does not want to pay increased premiums for Workers' Compensation insurance. Many workers justifiably fear the loss of their jobs if they complain, or if they ask to be sent to a doctor. The workers must maximize income and cannot afford to take time off from work or to pay for medical care themselves. Since there is usually only one vehicle per family and the whole family works, driving one person to a medical facility may mean that no member of the family earns any money that day (Moses, 1993).

Many workers are unaware of their rights under the law, and they may not report the illness or do not realize that they may see a doctor at their employer's expense (Kahn, 1976; Wasserstrom and Wiles, 1985). Undocumented workers are especially vulnerable since many do not know that they are covered by the law and are fearful of contact with authorities. Another factor that contributes to the underreporting of pesticide-related illness is the number of workers who return to Mexico for diagnosis and treatment if they become ill. There is almost no information on the extent or nature of these illnesses and their relationship to pesticide exposure.

The lack of affordable, accessible, and appropriate health care relates to potential pesticide-related health problems, since workers who have no access to a doctor also are usually without financial or legal recourse to document a suspected pesticide-related illness, or to have it diagnosed and treated. The problems with health care for minorities are especially severe for farm workers in rural areas; they rarely receive health benefits from their employers, and, even if health benefits are offered, they are extremely limited and may not fully cover dependents. State eligibility requirements for Medicaid vary enormously, and coverage is not transferable between states (Wilk, 1988; American Academy of Pediatrics, 1989; Rust, 1990; Moses, 1993).

*The California Reporting System*

Most of the information on pesticide poisoning of farm workers in the United States comes from California. The state's pesticide-illness reporting system, often said to be the best in the country, merits this reputation in part because other systems are so dismal. While there are good features in the California system, its deficiencies and inadequacies will be discussed in some detail since it is so often looked to as a model and is heavily relied on by the EPA.

About 80% of the approximately 2,500 poisonings in California reported by physicians directly to the state annually are occupational, and most of the serious poisonings are in workers who handle the technical formulations: mixers, loaders, and applicators (Maddy et al., 1990). A large percentage of these workers who have the greatest exposures and highest rate of illness is noncertified Latinos who work under the supervision of a certified pesticide applicator.

A Workers' Compensation medical report (called the Doctor's First Report of Work Injury) triggers entry into the California reporting system as a pesticide-related illness. The worker must see a doctor, the doctor must recognize the illness as pesticide-related, the doctor must file a Workers' Compensation claim relating the illness to pesticides, and the California Environmental Protection Agency must agree with the physician that the illness is related to pesticides. California counties have an agricultural commissioner whose office is responsible for the initial field investigation and report of any suspected pesticide incident or illness. These employees are not trained in public health, occupational health and safety, or toxicology, yet they often make decisions that require expertise in these disciplines. Their reports are used in conjunction with the doctor's medical report for Workers' Compensation to determine whether an illness is pesticide-related and eligible for listing in the annual pesticide-illness report. The cases that are rejected are classified as unrelated to pesticides, unlikely to be related, or inadequately investigated to determine the relationship to pesticide exposure.

An investigation by California Rural Legal Assistance (CRLA) reported that, between 1982 and 1988, 58% of doctors' reports of field-worker pesticide-illness cases were discounted by the California Department of Food and Agriculture (CDFA): 25% as unrelated, 13% as unlikely to be related, and 20% as unclassifiable. In 21% of the field-worker illness investigations by the

county agricultural commissioner's office, either the name of the pesticide, the date of application, or both were missing, yet the CDFA classified the investigation as "adequate" 75% of the time. CRLA concluded that the high number of field-worker cases reported by physicians but discounted by CDFA as unlikely or unclassifiable may in part be a result of incomplete investigations by county agricultural commissioners (Lightstone, 1990).

The CRLA investigation also found that law enforcement actions are infrequent and weak. After a watermelon poisoning episode in 1985, agricultural commissioners were given the authority to fine violators of pesticide laws. But commissioners rarely exercise this new authority; most violations of pesticide laws do not result in fines or sanctions. In 1988 and 1989, there were 5,766 warnings and notices of violations of pesticide laws; 8% of the agricultural and 3% of the nonagricultural violations resulted in fines. In the rural county of Kern, which leads the state in reported pesticide illnesses, only 4% of violations resulted in fines, while in the urban county of Alameda, 25% of the violations resulted in fines (Lightstone, 1990).

All of these problems contribute to under-reporting of pesticide-related illness in the state reputed to have the best reporting system. And this system is only for acute, observable, immediate illness. There is no attempt in any state to document or monitor chronic health effects from pesticide exposure. No other state has a reporting system even similar to California's. Texas, Florida, Oregon, and Washington have reporting systems, but they are rudimentary and/or poorly enforced.

*Workers' Compensation*

One of the most important state laws that has relevance for pesticide-related illness is Workers' Compensation Insurance, but this law excludes farm workers or denies them equal protection. Farm workers are specifically excluded from coverage in 24 states; in six others, they are effectively excluded since coverage is elective, depending on voluntary choice by the employer. Twelve states partially cover farm workers, which usually means exclusion of migrant workers. In general, partial coverage means that a very small number of year-round employees are covered but migrant workers are not. Farm workers are fully covered in only 8 states. In some states, the law requires the person to work for the same employer for a specified amount of time in order to qualify for benefits. This period of time is usually set to be longer than the harvest season for the crops that migrant workers pick. Since migrant workers often work for more than one employer, and for a very short period of time, they are effectively denied coverage.

Farm workers are caught in a no-win situation. There are no comprehensive and reliable pesticide-illness reporting systems anywhere in the country, yet the low number of reported pesticide-related illnesses in farm workers is used to claim that no serious problem with pesticide-related illnesses exists.

## METHODOLOGICAL ISSUES

General methodological issues are summarized first, then design issues appropriate to epidemiological studies of cancer and of neurotoxicology are discussed.

*General*

Some areas especially relevant in environmental quality include time of sampling, sample size, low incidence, confounding exposures, place of residence and of biological sampling/monitoring, use of national sampling data, use of vital and medical records, underreporting, biological monitoring, follow-up studies, research on human activity patterns, exposure assessment, and surveillance methods.

1. *Time of sampling* must be clearly, logically, and temporally related to correspond to the time of maximum exposure.

2. The issue of *sample size* is raised by the following fact: farm workers are 1/20th to 1/40th of the population of the state of California. Studies based on random sampling therefore will need a size 40 times that judged as adequate at a state level in order to obtain comparable data among farm workers. At the national level, this sampling problem would be even worse. A recent study reported that the Surveillance, Epidemiology, and End Results (SEER) program data for cancer mortality in the black population tended to show variable results because of the smaller sample size (Frey et al., 1992).

3. There is a *low incidence* of pesticide-related disease and deaths. In California, only 4% of 38,000 occupational diseases reported in 1987 were potentially pesticide-related. Of the 17,000 human exposure incidents, almost all were nonoccupational. The number of pesticide deaths in 1983 was 22, and therefore, there is only limited coding of deaths as pesticide-related.

4. *Confounding exposures* can alter results, particularly when there are multiple exposures to multiple pesticides, with specific exposures changing over time.

5. Data on *place of residence* and *biological sampling/monitoring* are necessary for adequately interpreting results. For pesticides with a long half-life in adipose tissue, for example, the design of cross-sectional sampling must include measures for addressing time of exposure, decay life of the pesticide, trends in exposure, and so on. For example, presumed high levels in certain urban populations may be due to immigration of persons with initially high levels acquired in rural areas; this might explain why DDE levels in urban blacks are higher than in rural whites. Thus, place of exposure may be different from place of health effect.

6. *Use of national sampling data* is currently problematic. For example, a new study shows that SEER may not be representative of the United States population (Frey et al., 1992). There also are disadvantages in using national sampling databases such as NHATS (National Human Adipose Tissue Survey), which use composite samples. Problems arise particularly when the target population for the study constitutes only a small fraction of the general population.

7. *Vital records and hospital and other medical records* are seriously inadequate. Diagnoses on death certificates are likely to be of poor quality because the deceased lacked access to good medical care, and the physician who certifies death is likely to do so without knowledge of the deceased's medical and occupational history. Foreign migrants may return to their home country when seriously ill to die there; hence their mortality and morbidity will be underreported in the United States. Use of hospital records to study morbidity is also likely to be of limited value if migrant workers do not have full access to medical care.

8. *Underreporting*, discussed above, will continue to bias research results unless the underlying economic reasons can somehow be removed.

9. Reliable, standardized, low-cost, analytical methods of *biological monitoring* must be developed for the many pesticides that do not have approved and/or adequate laboratory methods for detection and quantification in biological and environmental samples.

10. The need for *follow-up* studies raises the issue of the feasibility of tracing farm workers over extended periods of time, and of reconstructing lifetime histories of multiple exposures, with special attention to farm workers, pesticide handlers, and recent immigrants.

11. *Human activity pattern research* needs to be emphasized in both farm and nonfarm situations. Studies such as the recently initiated NCI/EPA Farm Occupation Exposure Study (NEFOES) should include migrant and minority workers and their families. Additional studies are needed to assess residential exposures of low-income families to pesticides.

12. Toxic "inert" ingredients must be included in the *exposure assessment* of toxicity from pesticides, both in handlers and field-workers exposed to crop residues, as well as in residential and dietary exposures.

13. *Methods to establish surveillance* of pesticide exposures, incidents, and health effects must be developed for areas where large numbers of people of color are exposed to agricultural pesticides.

*Cancer Epidemiology*

Descriptive data and etiologic research on cancer among farm worker and family members are urgently needed. Some issues related to the feasibility of methods proposed for studies of cancer in migrant and seasonal farm worker follow.

1. Death certificate data may have limitations because of possible inaccuracies in statements about the deceased's occupation, race, ethnicity, and cause of death. As a result, death certificate information for a sample of farm workers needs to be assessed in order to judge the value of existing and proposed cohort and proportionate mortality studies that use such data. A sample of farm workers from sources such as the Third National Cancer Survey, population-based cancer registries that collect occupational information, hospital records, or farm worker unions could be studied to determine current vital status. Death certificates for deceased farm workers can then be obtained. Information on occupation, race, ethnicity, and cause of death on the death certificate can then be compared with "true" information recorded by the cancer registries, hospitals, or other sources.

2. Tracing farm workers over extended periods of time would be critical to determine whether, and how, cohort studies of farm workers could be conducted to evaluate risk of cancer, which can have a latency of 10 to 30 years. It would be useful to identify a sample of farm workers from at least ten years earlier, using sources such as union records, parents and children identified in the Migrant Student Record Transfer System, or migrant health clinic patients, to determine current vital status, percent successfully traced, percent lost to follow-up, percent thought to have left the country, and other parameters.

3. It is important to determine whether current or former farm workers are diagnosed and treated for cancer and entered into cancer registries or other relevant databases with the same accuracy as the general population. A sample of members of older generations who developed cancer could be studied for the type of medical care, the provider who diagnosed their cancer, their residence at the time, where they were treated, and the type of treatment.

4. The accuracy with which current and former farm workers can provide lifetime histories of states in which they were employed, crops, and activities by month and year needs to be assessed. Histories from workers and from next-of-kin could be compared to evaluate the quality of data from surrogate respondents. In addition, the ability of agricultural experts to determine possible and probable exposures to pesticides and other substances based on such histories, and their reliability and validity would be evaluated.

5. Since it may be logistically easier to conduct epidemiologic studies of seasonal farm workers than of migrant workers, quantitative studies on levels of pesticide exposure (biological monitoring of absorbed dose) need to be conducted in locations where both migrant and seasonal farm workers are employed. This information can help researchers to evaluate whether the risks of one group are likely to be shared by the other. Migrant and seasonal farm workers usually perform similar tasks and presumably have the same exposures, but their housing, access to bathtubs or showers, and laundry facilities may vary significantly.

6. The role of different classes of pesticides in the development of lymphoma and leukemia can fruitfully be investigated. For pesticides having hormonal effects, the relationship, if any, to the development of hormonally related cancers in women is another important area for research.

*Neurotoxicology*

The lack of health effects research on individual pesticides or combinations of pesticides argues for the use in epidemiological studies of a wide variety of potential nervous system effects to confirm research on established effects, to generate hypotheses for further research, and to obtain control data by sex and age.

1. Existing neurobehavioral evaluation methods, including questionnaires, need to be revalidated and perhaps modified for use in populations with low literacy and from different cultural backgrounds, especially for those who do not speak English or for whom English is a second language.

2. A strategy is needed to study single chemicals, even in workers with multiple exposures. Statistical power would be optimized because there is less inherent variability in neuropsychological parameters within each individual over time than between individuals.

3. In studies of persons with neurological disease (e.g., Parkinson's disease and Alzheimer's disease), persons of color should be oversampled. Questions on occupational and environmental exposures, especially pesticides, should always be included.

4. An appropriate public institution (e.g., the Centers for Disease Control) should make available an effective, low-cost, standardized method of testing red blood cell and plasma (serum) cholinesterase. The test should be capable of rapid turnaround, and be applicable to the field situation. Further research on the methodology of chemical sampling, transport, storage and correction for hemoglobin or red cell mass, including development of new methods, is needed.

5. If problems with exposure assessment and follow-up can be overcome, research on chronic neurological effects of pesticide exposure is best done among highly exposed groups, such as mixers/loaders/applicators.

6. The most sensitive neuropsychological tests for examination of never-poisoned but chronically exposed cohorts must be identified to determine whether repeated episodes of acute organophosphate intoxications cause chronic long-term neurological dysfunction.

7. Prospective studies of poisoned workers are needed to verify the suspected relationship between organophosphate poisoning and chronic neuropsychological effects. Severity of poisoning measured at the time of poisoning, perhaps in a multi-center study, would

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allow evaluation of a dose-response relationship to subsequent neurologic outcome, as measured with neurobehavioral and neuropsychological test batteries.

8. The correlation of recoverable urinary organophosphate metabolites with acute symptoms and cholinesterase inhibition needs to be determined.

9. Pesticides that are not organophosphates but that nonetheless offer fruitful potential areas for neurotoxicological research include methyl bromide (central effects), N-methyl carbamates (central and peripheral effects), and perhaps paraquat and maneb (movement disorders).

10. Researchers should consider undertaking collaborative studies in third-world countries where repeated pesticide intoxication of farm worker populations is much more common than in the United States.

## RECOMMENDATIONS

Our recommendations fall into three categories: those for mitigating exposures, those for using existing data and systems, and those for undertaking new research.

*For Mitigating Exposures*

Extensive and cumulative exposure to toxic pesticides should be considered presumptive evidence of probable health impact that requires the intervention of public health authorities. The most protective remedial measures should be determined, prioritized, and implemented to reduce exposures immediately, even with the limited knowledge available. Any plan for correcting environmental inequities must include community-based organizations, as well as providing for funding to implement the plan. Some monies should be allocated to organizations that represent at-risk minorities, for technical assistance in making their environmental concerns known and addressed.

- Determine the number of children who are working in agriculture, their work practices, and their potential for differential exposure.
- Require mandatory reporting of all pesticide use, not just of pesticides classified for restricted use.
- Require mandatory reporting of occupational pesticide-related incidents and illness.
- Implement baseline and serial monitoring of red blood cell and plasma cholinesterase as standard procedures for all pesticide handlers (mixers/loaders/applicators/flaggers) exposed to Toxicity Category I and II organophosphate and N-methyl carbamate pesticides.

- Implement serial monitoring of red blood cell and plasma cholinesterase in suspected or actual poisoning incidents for all field workers exposed to Toxicity Category I and II organophosphates and N-methyl carbamates.

- There must be better assessment of the intervals when a treated field can safely be entered for certain jobs. These intervals need to be specified on the basis of the hazard and characteristics of the specific pesticide under actual field conditions. Until the intervals are established scientifically, interim intervals should be set with the view to making the workplace as safe as possible on the basis of already existing data.

- Provide workers with access to relevant and understandable information on exposure to pesticides and the means of minimizing exposure through the use of work practices, protective equipment, and simple hygiene procedures, including soap and water. Enforce already existing regulations and require additional provisions for basic levels of personal protection and washing facilities for all agricultural workers.

- Develop more innovative methods of delivering information to both employers and workers to promote the use of protective equipment and safer work practices. The language, format, and distribution of basic written information should assure that the materials are culturally relevant and appropriate. Heavy reliance on conventional written materials as the primary educational tool in populations with limited reading skills is not particularly effective.

- Evaluate the effectiveness of the many and often costly training programs that promote personal protective equipment and personal hygiene in the agricultural setting. Evaluate the cultural factors that may affect the usefulness of such programs among different minority groups, especially immigrant workers.

- Extend the Occupational Safety and Health Act (OSHA) coverage to farm workers. The exclusion of farm workers from OSHA regulations is particularly unfair with respect to pesticides. OSHA coverage would be an important step in insuring that well-established industrial hygiene procedures that are standard in other sectors are implemented and enforced in agriculture.

- Set stronger national standards and regulations to protect farm workers and field workers, whether enforced by the state, EPA, or OSHA. Programs for mitigating risk need to be put into place and evaluated.

- The state of California, which has mandatory reporting of pesticide use and pesticide-related illness, needs to continue studies to mitigate previously unrecognized hazards and to find any new hazards from changes in pesticide application practices and changes in farm-cropping practices. Other states could use much of the information developed in California for their
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California for their own safety programs. New studies are also needed in other states for different application practices as well as different harvesting practices.

- Identify the specific obstacles and constraints on the EPA, the Department of Health and Human Services, and the Department of Labor (OSHA) that prevent them from conducting research, providing health services, and enforcing regulations to alleviate environmental inequities in exposure to toxic pesticides.

*For Using Existing Data or Systems*

- Maximize the use of routinely collected data, such as doctors' reports for Workers' Compensation, to supplement descriptive studies. The medical community needs to be better informed, so that clinicians are more alert to pesticide-related illness.

- Release exposure and health effects data to the public on public-use computer data tapes. Such data should also be transferred between and among government agencies, including EPA, the National Center for Health Statistics, the OSHA, the National Cancer Institute, the National Institute of Occupational Safety and Health, the National Institute of Environmental Health Sciences, and the Department of Health and Human Services.

- Evaluate and compare data on blood pesticide levels from the Hispanic Health and Nutrition Examination Survey (HHANES) with corresponding data from the NHANES II data set for whites and blacks. (Note: interpreters will need to allow for the time lag between the two studies). Currently, NHANES blood specimens are being collected and will be continuously collected through fiscal year 1994. Analysis of these specimens for pesticides, PCBs, and other environmental contaminants by using state-of-the-art techniques and correcting for the lipid content of the sample would be a positive step toward quantifying possible differences in exposure levels among blacks, Latinos, and whites.

- Analyze data currently being generated at the Centers for Disease Control in a reference range study of phenolic type metabolites in urine and of volatile organic compounds (VOCs) in blood. These specimens are from NHANES II, and researchers have access to demographic information (e.g., age, race, sex, and occupation) on the donors. These data would be useful in determining whether racial differences in exposure levels exist for those compounds not generally found in lipids.

- Obtain data from poison control centers, including social history from their computer records of calls. Education about resources for dealing with exposure needs to be disseminated through all communities, including phone numbers of poison control centers and recognition that poison control centers deal with all routes of exposure, not just ingestion.

- Support the development of a network of occupational and environmental health clinics which has been undertaken by the Agency of Toxic Substances and Disease Registry (ATSDR), emphasizing that access to physicians with environmental health expertise should be available for all citizens.

- Assess the quality of information on people of color in routinely collected vital and medical records, census, and other data.

- Modify and use national surveys of acute health effects (including the National Center for Health Statistics (NCHS) hospital survey, emergency room surveys, and the American Association of Poison Control Centers (AAPCC) poisoning survey) so that they include standardized information on occupation, race, ethnicity, income, education, and circumstances of pesticide-related incidents. This information can then be used as indicators to characterize the extent and trends of acute adverse effects in people of color.

- Collect information on occupation in emergency rooms at the time of the initial visit for a specific problem.

- The Department of Labor should collect and publish regional and local information on occupation between census years, especially for native Americans and Asian Americans.

*For Undertaking New Research*

People of color should be a major research focus, in addition to being included as subgroups in other research efforts. Studies must include children, pregnant women, and women of childbearing potential, as well as adult men and women. The focus must be on the most highly exposed populations for all health outcomes of interest, whether it be acute poisoning, cancer, central and peripheral nervous system effects, birth defects, allergic sensitization, immunotoxicity, or other effects on the liver, lung, kidneys, and other body systems. The following research recommendations are listed in priority order.

- Investigate cancer among children of farm workers, including leukemia, lymphoma, and primary brain cancer.

- Investigate the potential neurodevelopmental and neurobehavioral effects of pesticide exposure among children of farm workers.

- Conduct studies of cancer among pesticide-exposed farm workers, making sure to include noncertified mixers, loaders, applicators, and flaggers, who have the highest exposures and are primarily people of color.

- Conduct studies of nervous system integrity among pesticide-exposed farm workers, making sure to include noncertified mixers, loaders, applicators, and flaggers. These

people are in immediate need of epidemiological assessment, including determining whether exposures to organophosphate, N-methyl carbamate, and other neurotoxic pesticides that are insufficient to cause acute effects can cause long-term neurological dysfunction. Cohorts of workers poisoned by acute and/or repeated exposure to organophosphates and N-methyl carbamates should be prospectively identified to measure severity of poisoning; they should be studied with sufficient follow-up to determine potential neuropsychological and peripheral neuropathic outcome. Case control studies of specific neurological diseases should be undertaken, including dementia (from organophosphates and methyl bromide); peripheral neuropathy (from certain organophosphates); and parkinsonism (from paraquat, maneb).

Design and carry out studies that address reproductive outcomes in male and female farm workers and their offspring who are exposed to pesticides.

Investigate the association, if any, between pesticide exposure and autoimmune disorders, with emphasis on determining the role of specific classes and types of pesticides.

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