■INSECTICIDE FACTSHEET

CHLORPYRIFOS, PART 1: TOXICOLOGY

The broad spectrum organophosphate insecticide chlorpyrifos is the most widely used insecticide in the U.S. Total use is estimated at almost 30 million pounds per year.

Like all organophosphate insecticides, chlorpyrifos affects the nervous system by inhibiting an enzyme that is important in the transmission of nerve impulses. Symptoms of acute poisoning include headache, nausea, muscle twitching, and convulsions. Chlorpyrifos poisonings are reported to state and federal agencies more often than poisonings of almost every other insecticide. In both laboratory animals and humans, chlorpyrifos can also cause delayed effects on the nervous system. Some effects have been measured years after exposure.

Human birth defects have been associated with exposure to chlorpyrifos products. In pregnant laboratory animals, chlorpyrifos exposure caused fetal death. Pups that did survive were smaller pups and did not survive as well as pups from unexposed mothers. Chlorpyrifos also affects the male reproductive system; exposure to a chlorpyrifos product has caused death of cells in male rat testes and a decrease in sperm production in cattle.

Chlorpyrifos has caused genetic damage in human blood and lymph cells, mice spleen cells, and hamster bone marrow cells.

Immune system abnormalities have been reported from patients exposed to chlorpyrifos. Many individuals report developing sensitivities to a broad array of substances following chlorpyrifos exposure.

The second part of this factsheet will discuss human exposure to chlorpyrifos and the ecological effects of chlorpyrifos.

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Chlorpyrifos (see Figure 1) is the most widely used insecticide in the United States, both in crop production and in nonagricultural applications.[1] Its non-agricultural use in the United States is estimated at between 9 and 12 million pounds per year.[1] Agricultural use estimates vary: the U.S. Environmental Protection Agency (EPA) estimates that between 10 and 15 million pounds are used annually,[1] while the U.S. Department of Agriculture (USDA) estimates agricultural uses at 21 million pounds per year.[2] (See Figure 2 for details.)

Chlorpyrifos is a broad spectrum insecticide[3] and has many uses. Nationwide, USDA estimates show that the primary agricultural uses are on corn, alfalfa, and cotton.[2] (See Figure 3 for details.) In California, where pesticide use reporting is more comprehensive than in other states, the pri-

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Caroline Cox is JPR's editor.

mary agricultural uses are for oranges, almonds, and walnuts.[4] Structural pest control uses much more chlorpyrifos than does any single agricultural crop. (See Figure 4.)

In American homes, lawns, and gardens, over two hundred million chlorpyrifos ap-

Figure 1
Chlorpyrifos and Chlorpyrifos-oxon

chlorpyrifos

chlorpyrifos-oxon

Chlorpyrifos is transformed in animals to chlorpyrifos-oxon, a much more potent neurotoxin.

plications are made annually. Over 17 percent of U.S. households use chlorpyrifos. Most of the chlorpyrifos products are used in the kitchen, bathroom, and other living spaces.[5] (See Figure 5.)
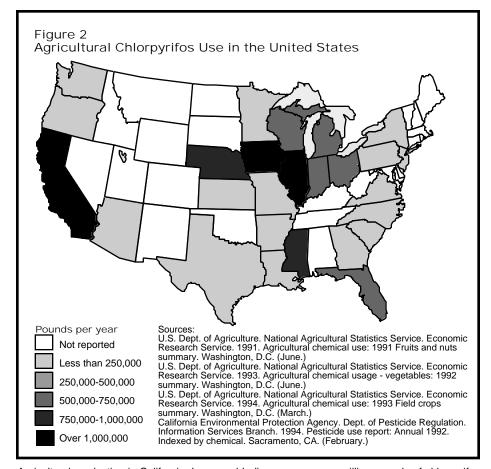
Chlorpyrifos has been registered in the U.S. since 1965,[6] and is manufactured by DowElanco, formerly the Dow Chemical Company. Common brand names are Dursban (for household products) and Lorsban (for agricultural products).[3]

Mode of Action

Chlorpyrifos is an organophosphate insecticide. Investigations of this family of chemicals began during World War II when chemists studied their use as nerve gases.[7]

Chlorpyrifos is directly toxic to the nervous system. In addition, it is transformed inside animals to chlorpyrifos-oxon[8,9] (see Figure 1) which is about 3000 times as potent against the nervous system as chlorpyrifos itself.[10] Like all organophosphates, chlorpyrifos and chlorpyrifos-oxon kill insects and other animals, including humans, because of this toxicity to the ner-

Figure 2
Agricultural Chlorpyrifos Use in the United States

Pounds per year

Not reported

Less than 250,000

250,000-500,000

500,000-750,000

750,000-1,000,000

Over 1,000,000

Sources:
U.S. Dept. of Agriculture. National Agricultural Statistics Service. Economic Research Service. 1991. Agricultural chemical use: 1991 Fruits and nuts summary. Washington, D.C. (June.)
U.S. Dept. of Agriculture. National Agricultural Statistics Service. Economic Research Service. 1993. Agricultural chemical usage - vegetables: 1992 summary. Washington, D.C. (June.)
U.S. Dept. of Agriculture. National Agricultural Statistics Service. Economic Research Service. 1994. Agricultural chemical use: 1993 Field crops summary. Washington, D.C. (March.)
California Environmental Protection Agency. Dept. of Pesticide Regulation. Information Services Branch. 1994. Pesticide use report: Annual 1992. Indexed by chemical. Sacramento, CA. (February.)

Agricultural production in California, Iowa, and Indiana uses over a million pounds of chlorpyrifos annually.

Figure 3
Crops on which Chlorpyrifos Is Used in the U.S.

wheat
1.0 million pounds

citrus
0.9 million pounds

soybeans
1.1 million pounds

other
4.1 million pounds

peanuts
1.1 million pounds

cotton
1.4 million pounds

alfalfa
1.8 million pounds

field corn
9.6 million pounds

Source: U.S. Dept. of Agriculture. National Agricultural Pesticide Impact Assessment Program. 1994. The biologic and economic assessment of the field crop usage of chlorpyrifos: Briefing paper. Washington, D.C. (April.)

Almost half of the chlorpyrifos used in U.S. agriculture is used on corn.

vous system. They inhibit an enzyme, acetylcholinesterase (AChE), that breaks down acetylcholine, a chemical involves in transmitting nerve impulses across the junctions between nerves. Without functioning AChE, acetylcholine accumulates, producing rapid twitching of involuntary muscles, convulsions, paralysis, and ultimately death.[7]

Chlorpyrifos exposure has also been shown to inhibit enzymes other than AChE. It impedes respiration (production of energy within a cell) in the livers of laboratory animals. This results from the effect of chlorpyrifos on the activity of ATPase, an enzyme important in cellular respiration.[11] Chlorpyrifos-oxon inhibits the enzyme cholesterol ester hydrolase; inhibition of this enzyme in rats eliminates one of their normal reactions to stress.[12]

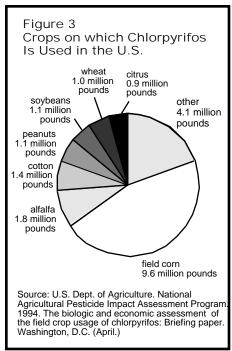## Acute Toxicity

Symptoms of acute chlorpyrifos poison-ing in humans include headache, nausea, dizziness, muscle twitching, weakness, increased sweating and salivation, and fluid-filled lungs. These symptoms are common to all organophosphate insecticides. Unconsciousness, convulsions, and death can result with sufficient exposure.[13]

A variety of different kinds of exposure to chlorpyrifos can cause acute toxicity. Direct skin contact with the insecticide, either as a solid or in water can be toxic. Ingestion, breathing of vapors, or contact with chlorpyrifos-treated soil is also toxic.[3]

The acute oral median lethal dose (LD$_{50}$; the dose required to kill half of a population of laboratory test animals) for chlorpyrifos is between 82 and 270 milligrams per kilogram (mg/kg) of body weight in rats.[14] If it is assumed that humans are equally as sensitive as rats (usually a more conservative assumption should b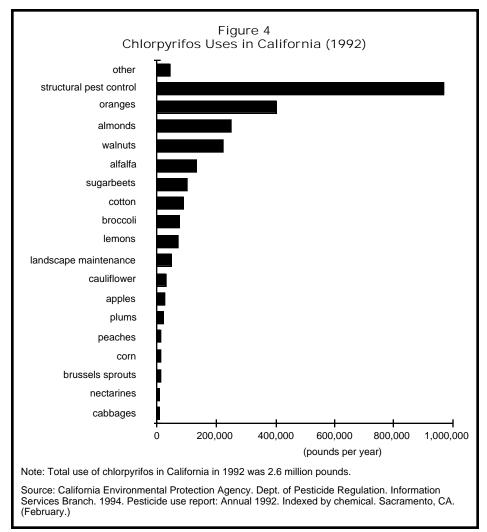e made), then a dose of less than one-fifth of a ounce could be sufficient to kill an average-sized (60 kg) adult human.

Based on the LD$_{50}$, inhalation of formulated chlorpyrifos is more toxic to mice and rats than is oral ingestion.[15] Dermal (skin) exposure in laboratory animals is less toxic than ingestion.[14] However, dermal exposure causes skin irritation, and also allows the body to absorb chlorpyrifos. This is especially true if the skin is cut or scratched. Therefore, the Cooperative Extension Service warns that "dermal contact should be avoided."[14]

Inhibition of AChE activity has been measured at doses that are much smaller than the LD$_{50}$. For example, AChE inhibition in female rats was measured at doses of 0.1 mg/kg/day (less than 1 percent of the LD$_{50}$) and in beagle dogs at 3.3 mg/kg/day (less than 5 percent of the LD$_{50}$).[14]

The inhibition of AChE activity caused by chlorpyrifos is more persistent than that caused by other organophosphates, with measurable inhibition two weeks after exposure in one study,[8] one month after exposure in another study,[16] and six weeks in other studies.[17-18] Researchers believe that this is because chlorpyrifos is lipophilic (at-

Figure 4
Chlorpyrifos Uses in California (1992)

other	
structural pest control	
oranges	
almonds	
walnuts	
alfalfa	
sugarbeets	
cotton	
broccoli	
lemons	
landscape maintenance	
cauliflower	
apples	
plums	
peaches	
corn	
brussels sprouts	
nectarines	
cabbages	

0   200,000   400,000   600,000   800,000   1,000,000

(pounds per year)

Note: Total use of chlorpyrifos in California in 1992 was 2.6 million pounds.

Source: California Environmental Protection Agency. Dept. of Pesticide Regulation. Information Services Branch. 1994. Pesticide use report: Annual 1992. Indexed by chemical. Sacramento, CA. (February.)

More chlorpyrifos is used for structural pest control in California than is used in any single agricultural crop.

Figure 5
Use of Chlorpyrifos by U.S. Households

pets (1.5 million uses annually)

other outdoor uses (5.0 million uses)

kitchens (5.5 million uses annually)

lawns (2.5 million uses)

bathrooms (3.5 million uses annually)

other indoor uses (3.8 million uses)

bedrooms, living rooms (3.8 millions uses annually)

Source: Whitmore, R.W., J.E. Kelly, and P.L. Reading. 1992. National home and garden pesticide use survey. Final report, Vol. 1: Executive summary, results, and recommendations. Research Triangle Park, NC: Research Triangle Institute.

Household use of chlorpyrifos is divided approximately equally between indoor and outdoor applications.

tracted to the non-water soluble, fatty, parts of body tissues). This means the chlorpyrifos is stored but then released and transformed to chlorpyrifos-oxon so that effects occur over a long interval.[8] Along with the AChE inhibition, EPA researchers measured behavioral changes, including a reduction in working memory and a slowing of motor activity, 2 to 3 weeks following exposure.[18] One response was altered for 12 weeks after exposure.[17] Weekly injections of smaller amounts of chlorpyrifos caused similar changes.[19] Researchers caution that "subtle, long-term changes in behavior may be induced" by acute exposure to chlorpyrifos.[17]

Acute poisoning of humans by chlorpyrifos is alarmingly frequent. For example, in California (where pesticide illness reporting is more comprehensive than in other states), physicians reported over 400 illnesses caused by chlorpyrifos from 1984 to 1990, more than were caused by any other insecticide except propargite.[20,21] Almost 40 cases of chlorpyrifos poisoning were reported in 1991, more incidents than were reported for any insecticide except propoxur.[22] EPA's pesticide information hotline reported several hundred calls about chlorpyrifos-related incidents each year; only the organochlorine insecticide chlordane received more calls.[23]

Delayed Neuropathy

In addition to inhibition of AChE ac-

tivity, some organophosphates cause a "less common but potentially more devastating syndrome" called delayed neuropathy. Symptoms of this nervous system disorder include cramps, weakness, tingling and numbing of the extremities, a high stepping gait,[24] paralysis of the lower limbs,[25] and (in severe cases) quadriplegia.[24] The syndrome typically occurs one to three weeks after exposure to an organophosphate. It is caused by the inhibition of an enzyme (called neuropathy target enzyme) whose function in the nervous system is not yet understood. Degeneration of nerves in the spinal cord, as well as in limbs, is visible at the same time that the physical symptoms occur.[25] Typical delayed neuropathy is not reversible; victims do not recover.[24]

Tests submitted to EPA in support of chlorpyrifos's registration showed that it did not cause delayed neuropathy.[26] However, subsequent studies have shown that single doses of chlorpyrifos can cause delayed neuropathy in chickens[27-29] and cats.[24] A high dose was required to induce delayed neuropathy in all these studies.

Perhaps of greater concern are studies of

delayed polyneuropathy caused by repeated exposure to chlorpyrifos. In hens, relatively low daily exposures (either through the skin or ingested) for a period of between 1 and 4 months induced delayed neuropathy. One hen became paraplegic after 145 days of chlorpyrifos exposure.[30]

Both the study of delayed neuropathy in cats, and the study using repeated exposures of hens found that the neuropathy caused by chlorpyrifos was "atypical" when compared to that caused by other organophosphates.[24,30] In cats, the symptoms were less severe, but more persistent than is typical.[24] In hens, the delay before the onset of symptoms was longer than expected, and some symptoms were reversible.[30]

Chlorpyrifos-induced delayed neuropathy has also occurred in humans. In 1986, physicians reported the development of delayed neuropathy in a man who had intentionally consumed a large amount of a chlorpyrifos-containing insecticide. Neuropathic symptoms were noted 43 days following ingestion.[25] In 1993, "life-threatening" delayed neuropathy, including paralysis of the vocal cords and a loss of normal reflexes, occurred in a three-year old boy about two weeks after he was found playing with a bottle of Dursban roach poison.[31] In 1993, physicians described eight patients who developed delayed neuropathy after exposure to Dursban. Two of the patients were themselves physicians, a third was a professional exterminator, and all except the exterminator were exposed through routine Dursban treatments of their home or office.[32] A recent (1994) study measured the neurological functioning of over 25 patients who had been treated for chlorpyrifos poisoning between 1982 and 1990. The speed at which nerves in the arms and legs conducted impulses was reduced, and there was evidence of nerve degeneration in fingers.[33] Both of these effects are consistent with delayed neuropathy, and are striking given the length of time between exposure and the follow-up study.

Effects on Reproduction

Chlorpyrifos-related problems with reproduction made headlines in 1993 in a McCall's article which featured the Burke family from Suffolk County, New York. When their oldest daughter was a toddler, the Burkes began regularly treating their carpets with Dursban to kill Lyme-disease carrying ticks that their dog might have brought in. Their second child was born with cerebral palsy, cataracts, and suffered from seizures. When their third child was born with similar problems, doctors agreed that the children might have been damaged prenatally by the Dursban treatments.[34]

> **" When their oldest daughter was a toddler, the Burkes began regularly treating their carpets with Dursban.... Their second child was born with cerebral palsy, cataracts, and suffered from seizures. When their third child was born with similar problems, doctors agreed that the children might have been damaged prenatally by the Dursban treatments."**

Chlorpyrifos has also caused reproductive problems in laboratory tests. In tests conducted by Dow Chemical, feeding chlorpyrifos at high doses caused pregnant mice to give birth to small pups with an increased incidence of skeletal abnormalities. At a lower dose, the same study found an increase in skull defects that allowed the brain to be exposed.[35] Others tests, also conducted by Dow, showed that chlorpyrifos reduced pup weight and pup survival in studies of pregnant rats.[26]

Other types of exposures to chlorpyrifos also cause reproductive problems. Injection of pregnant female rats with low doses of Dursban (less than 1/1000 of the LD_{50}) caused increased fetal mortality as well as decreased body weight and neurotoxicity in the pups that survived.[36] Injection of male rats with Dursban caused death of the cells that make up the semen-producing tubules (small tubes) in the testes.[37] Dermal exposure of mice to a Lorsban-bran mixture resulted in high mortality of parents, particularly females who have a large skin area relative to their weight. Surviving mothers gave birth to fewer litters, smaller litters, and litters with smaller pups. Almost half of the pups died as newborns.[38]

Reproductive effects were dramatically illustrated when Dursban 44 was applied to the skin of 185 Holstein bulls to kill lice at an artificial insemination facility in New York. All became ill, and seven of the bulls died. The bulls were carefully monitored following this illness and estimates of sperm production showed that the sperm production was reduced during the following six months to between 57 and 88 percent of pretreatment production. The sickest bulls had sperm production that was the most reduced.[39] A second farm that made a similar Dursban treatment, but then washed the bulls thoroughly when the first farm warned them of their sick and dying bulls, measured a 7 percent drop in sperm production. Experiments conducted later to confirm that chlorpyrifos was the cause of the bulls' illness found that sperm production of bulls exposed experimentally was reduced by 16 percent.[40]

Concerns about chlorpyrifos's effects on human reproduction are increased by analysis of tissues important in reproduction. A study by German researchers found chlorpyrifos in cervical mucus, sperm fluid, and human milk.[41]

Carcinogenicity

EPA has evaluated the carcinogenicity tests submitted in support of chlorpyrifos's registration and classifies them evidence of noncarcinogenicity.[42] These tests showed that feeding of chlorpyrifos to rats and mice over a two year period resulted in "no in-
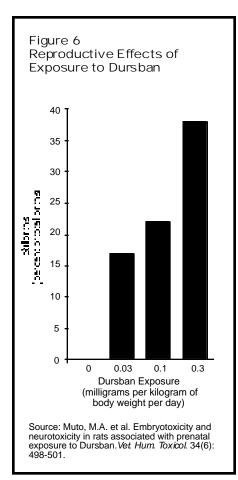
crease in the incidence of tumors."[14] However, xylenes, used as solvents in some chlorpyrifos-containing products,[43] have caused increased rates of leukemia in workers who inhaled xylenes on the job. Xylenes also seem to be cocarcinogens and increase the number of skin cancers caused by other carcinogens in laboratory animals.[44]

Mutagenicity

Most of the tests for potential genetic damage submitted in support of the registration of chlorpyrifos have been negative.[26] However, a variety of other tests show that chlorpyrifos, in fact, can cause genetic damage. Tests using cells from human lymph nodes showed that Dursban causes an increase in the frequency of sister chromatid exchanges (SCE; exchange of genetic material within a chromosome pair during cell division).[45] A test using human white blood cells showed a similar increase in SCEs.[46]

Tests with laboratory animals have also shown that chorpyrifos has the potential to cause genetic damage. In spleen cells from mice, chlorpyrifos caused an increase in chromosomal aberrations as well as an increased frequency of SCEs.[47] In live mice, injection, ingestion, or skin absorption of Dursban caused an increase in the number of polychromatic (young or degenerating) red blood cells in the bone marrow. Oral and dermal exposure to chlorpyrifos also increased the number of micronuclei in the red blood cells. These are small pieces of genetic material formed when preceding cell divisions have been abnormal.[48] Micronuclei were also found after chlorpyrifos exposure in bone marrow cells from Chinese hamsters. These tests were conducted both on live hamsters and on cell cultures.[49]

Chlorpyrifos can also cause genetic damage in organisms other than mammals. In fruitflies, an agricultural chlorpyrifos product caused an increase in mutations of the wing primordia cells as well as an increase in the frequency of recessive sex-linked lethal mutations.[50] Chlorpyrifos has also caused chromosome aberrations in barley pollen mother and root-tip cells,[51,52] chromosome aberrations in vetch root-tip cells,[53] micronuclei in onion root-tip cells,[54] and DNA damage in three species of bacteria.[55]

Figure 6
Reproductive Effects of Exposure to Dursban

Source: Muto, M.A. et al. Embryotoxicity and neurotoxicity in rats associated with prenatal exposure to Dursban. *Vet. Hum. Toxicol.* 34(6): 498-501.

Low doses of Dursban caused an increase in the frequency of stillbirths in rats.

Effects on the Immune System

Recent research has identified immune system abnormalities in individuals following chlorpyrifos exposure. Higher than usual frequencies of allergies and sensitivities to antibiotics together with atypical abundances of certain types of lymphocytes (decreases in T cells and increases in CD26 cells) were found in patients one to five years following chlorpyrifos exposure. Increased expression of CD26 cells is associated with autoimmunity, where an individual's immune system acts against itself, rather than against infections.[56]

The link between immune system problems and chlorpyrifos exposure was widely publicized in 1988 when *The New Yorker* profiled a physician who had suffered prolonged illness, including delayed neuropathy, and the development of sensi-

tivities to many insecticides following exposure to Dursban. She was exposed in her vacation cabin which had been recently treated with bendiocarb (a carbamate insecticide) and Dursban to kill carpenter ants.[57] Another widely publicized incident involved a woman who was exposed both at work and at home to chlorpyrifos-containing flea sprays who developed multiple sensitivities and has since suffered from a variety of life-threatening symptoms.[58]

This type of illness, in which a particular exposure incident triggers sensitivities to multiple chemicals (often called multiple chemical sensitivity or MCS) is a subject of strenuous debate within the medical community.[59,60] From the patients' perspectives, however, chlorpyrifos is clearly responsible for many sensitization cases. A statistician who works at EPA reports that individuals "who have become sensitized to this chemical," have made "many reports of serious allergic-type reactions to chlorpyrifos."[23]

The potential for an individual's immune system to be particularly affected by chlorpyrifos exposure is increased if detoxification mechanisms are not functioning at normal rates. Researchers have discovered that one of the enzymes involved in the detoxification of chlorpyrifos-oxon inside the human body exists in several forms. Individuals who have the low-activity form of this enzyme will detoxify chlorpyrifos at low rates, as much as 13 times slower than individuals with the fastest detoxification systems.[61] Note that this also has implications for all types of toxicity, not just immune system problems.

Other Toxicological Problems

Results of a two-year study in which rats were fed chlorpyrifos showed some degeneration of the exposed rats' retinas.[26] Effects on eyes were also found in a study that involved injecting chlorpyrifos into rats. Recordings of the electrical activity of the retina found dose-dependent abnormalities up to two days after chlorpyrifos exposure.[62]

The two year rat study also found that chronic exposure to chlorpyrifos caused rats to gain less weight than was gained by unexposed rats.[26] ❧

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■**INSECTICIDE FACTSHEET**

CHLORPYRIFOS, PART 2: HUMAN EXPOSURE

Americans are widely exposed to chlorpyrifos. Typical diets, particularly those of children, contain significant chlorpyrifos residues. About 10 percent of the food items tested by the U.S. Food and Drug Administration contained chlorpyrifos residues, and illegal residues occur on many foods.

In addition people are exposed when their homes or workplaces are treated with chlorpyrifos. When homes are surveyed for pesticide residues, typically chlorpyrifos is found in all residences tested.

Chlorpyrifos contaminates air, ground water, rivers, lakes, rainwater, and fogwater. Chlorpyrifos contamination has been found up to 15 miles from the site of application.

Chlorpyrifos residues have been found in soil up to eight years after termiticide treatments under a house, and in indoor air up to 6 weeks after "crack and crevice" treatment (a treatment aimed at areas favored by household insect pests). In most studies, residues persist until the end of the study so that establishing a definite persistence time is difficult.

Children appear to be more susceptible to chlorpyrifos poisoning than adults, and are often exposed to more residues. The U.S. Environmental Protection Agency estimates children consume (after adjusting for their size) between 2 and 2.5 times as much chlorpyrifos on their food as do adults. When houses are treated with chlorpyrifos, carpets can serve as a source of chlorpyrifos vapors when residents return. Infants, who crawl and sit on the carpet, will breathe much higher concentrations than adults.
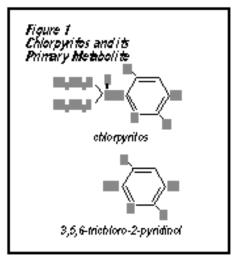
BY CAROLINE COX

Chlorpyrifos, an organophosphate insecticide, is the most widely used insecticide in the U.S. It is used both in agriculture and for pest control in houses and other buildings. The toxicology of chlorpyrifos was discussed in the first part of this factsheet. (JPR 14(4):15-20). This part of the factsheet focuses on human exposure to chlorpyrifos through contamination of air, water, soil, and food. Part 3 will discuss its ecological effects.

Exposure to Chlorpyrifos in Food

A national survey of pesticides and their metabolites in Americans found that the primary chlorpyrifos breakdown product, 3,5,6-trichloro-2-pyridinol (see Figure 1), was the second most commonly detected chemical.[1] Over 16 percent of urine samples contained the pyridinol. How are so many Americans exposed to chlorpyrifos? One

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Caroline Cox is JPR's editor.

important route is through food. Food testing carried out by the U.S. Food and Drug Administration (FDA) found that chlorpyrifos was the fifth most commonly detected pesticide and was found in ten percent of the samples tested.[2] Between 1990 and 1992, FDA found chlorpyrifos on tomatoes, oranges, peaches, cherries, bananas, and apples.[3] (See Figure 2.) Other
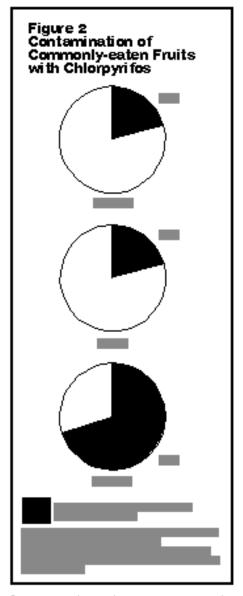
Figure 1
Chlorpyrifos and its
Primary Metabolite

chlorpyrifos

3,5,6-trichloro-2-pyridinol

3,5,6-trichloro-2-pyridinol is the primary breakdown product of chlorpyrifos.

food items on which chlorpyrifos residues have been found include broccoli, grapes,[4] orange juice,[5] tea[6], and several types of processed oriental foods including noodle soup.[7] A recent analysis of FDA's tests of commonly-eaten produce items for pesticide residues during 1992 and 1993 found illegal chlorpyrifos residues on 16 of the 42 foods. Only one other insecticide, the organophosphate insecticide methamidophos, had illegal residues on more types of food than did chlorpyrifos.[8]

Chlorpyrifos residues have also been found in meat and dairy products. For example, residues were found in mutton following a pour-on treatment to kill flies,[9] in beef following dipping to kill ticks,[10] and in pork following a pour-on treatment to kill lice.[11] In all cases fat appeared to have higher chlorpyrifos concentrations than other tissues. Chlorpyrifos was also found in milk and cream from cows experimentally fed chlorpyrifos.[12]

Under certain conditions, chlorpyrifos residues on food can be very persistent. Treatment of rice storage sacks with chlorpyrifos resulted in the rice grains absorbing the chlorpyrifos; residues were

**Figure 2
Contamination of
Commonly-eaten Fruits
with Chlorpyrifos**

Bananas, apples, and oranges are among the foods that are contaminated with chlorpyrifos.

measured for six months following treatment.[13]

The U.S. Environmental Protection Agency's (EPA) estimates of how much chlorpyrifos the average American consumes vary from 36 percent to 274 percent of the reference dose, the dose EPA believes will not cause any adverse effect.[14] The variation in the estimates comes from different assumptions made about how much of a food crop is treated with chlorpyrifos and how much residue remains on the food when it is eaten. However, regardless of assumptions made, it is clear that Americans can consume a significant amount of chlorpyrifos on a daily basis.

Indoor Exposure

Another source of widespread chlorpyrifos exposure is applications made to homes and other buildings. Chlorpyrifos exposures occur frequently. Over 10,000 adults and over 11,000 children reported chlorpyrifos exposures to poison control centers between 1985 and 1992.[15]

Americans spend about 90 percent of their time indoors, so that the potential for exposure to any residues is high. Surveys of homes throughout the U.S. have shown that chlorpyrifos residues are nearly ubiquitous. For example, a study of 9 houses in the south-eastern U.S. found chlorpyrifos in air samples from in all 9.[16] A survey of 12 houses in Indiana found chlorpyrifos in air samples from all 12; 2 out of the 3 houses that had recently been treated with chlorpyrifos had concentrations 10 to a 100 times greater than the others.[17] A study of 9 houses in Jacksonville, Florida found chlorpyrifos in dust samples from all 9, while a similar study in Seattle found chlorpyrifos in all 4 houses sampled.[18,19]

Occupational Exposure

Another source of exposure to chlorpyrifos is through workplace exposures. Over 1300 occupational exposures to chlorpyrifos were reported to poison control centers between 1985 and 1992.[15] Given the diversity of chlorpyrifos uses, it is not surprising that a diversity of workplace exposures occur. Nonagricultural workplace exposures have been documented for pest control operators doing termite treatments[20,21] and treatments for other insects,[22,23] pet handlers applying flea control products,[24,25] and lawn care workers.[26] For agricultural workers, chlorpyrifos exposure has been documented for greenhouse hand and tractor pesticide applicators,[27,28] field scouts for pest control consultants,[29] field workers,[30] and mixer-loaders.[31]

Workplace exposures can also occur in "unexpected settings"[32] where chlorpyrifos exposure is not typical, making diagnosis and treatment difficult. For example, five office workers in Pennsylvania became ill after their workplace was treated with Dursban and bendiocarb (a carbamate insecticide) to kill termites. Although treatment by a physician was delayed because the five were told by the exterminator that their symptoms were "most likely due to a viral illness,"[32] diagnosis of insecticide poisoning was made several days later.[32,33]

In another example, a postal worker was exposed to chlorpyrifos when a hose on a lawn care truck broke as she was delivering mail, causing the postal worker to be soaked with the insecticide. In this case, the exposed worker could not be properly treated for the exposure because the ChemLawn Services Corporation, owner of the truck, misled her about the actual contents of the truck for a period of a year and a half, until litigation over the incident was well underway.[34]
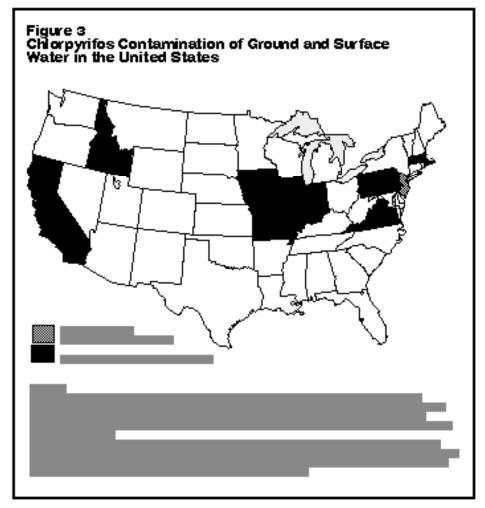
A special concern about occupational exposure is the effectiveness of protective clothing. One study showed that while disposable polypropylene coveralls were relatively effective, allowing only three percent of the chlorpyrifos reaching the outside of the coveralls to pass through, cotton/polyester overalls were much less protective, allowing almost twenty percent of the chlorpyrifos to pass.[35]

Researchers at Iowa State University intensively studied a pair of coveralls used during four growing seasons by a farmer who applied Lorsban. Although the coveralls had been washed after every wearing in a home washing machine, they contained significant residues of chlorpyrifos. The researcher found the results "discouraging" and recommended that any coveralls used as protection from pesticides be replaced every year.[36]
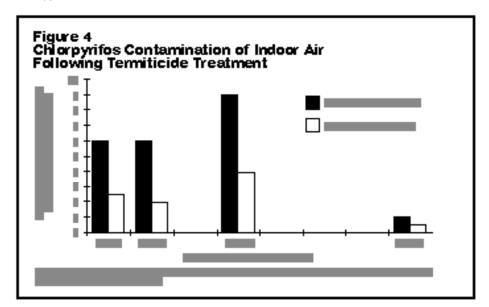
Contamination of Water and Air

Other exposure to chlorpyrifos comes from drinking contaminated water or breathing contaminated air. Because of its widespread use, chlorpyrifos has been found widely in air and water.

Water: Because it adsorbs readily to soil particles, chlorpyrifos is not highly mobile in soil;[37] in fact, some researchers have clas-

Figure 3
Chlorpyrifos Contamination of Ground and Surface Water in the United States

Chlorpyrifos-contamination of water has been measured in nine states and a lake.

Figure 4
Chlorpyrifos Contamination of Indoor Air Following Termiticide Treatment

Chlorpyrifos residues inside houses increased for four years following underslab or underfloor applications of chlorpyrifos. Residues were still present eight years after chlorpyrifos application.

sified it as "immobile."[38] Therefore, it is considered to have a low potential for contaminating ground and surface water. However, chlorpyrifos residues have been found in the groundwater of nine states (California, Illinois,[39] Idaho,[40] Iowa,[41] Indiana, Massachusetts, Missouri, Virginia,[39] and Pennsylvania[42] and in surface water in New Jersey[43] and Lake Erie.[44] (See Figure 3.)

Outside of the U.S., chlorpyrifos contamination of groundwater has been measured in Argentina, Canada, France, Italy,[38] and the Philipines.[45] Contamination of surface water in South Australia[46] and Spain,[47] lagoon sediments in Mexico,[48] and shallow ocean sediments in Costa Rica and Panama[48] has also been measured.

Chlorpyrifos contamination of rainwater and fogwater has been measured in California.[49,50] Chlorpyrifos-oxon, a potent transformation product of chlorpyrifos, has also been found in California fog.[49,51]

Contamination of fog may be especially significant because chlorpyrifos and other organophosphate insecticides concentrate in fogwater. Residues in fog are "two to three orders of magnitude greater than commonly reported … in rain …."[49]

Such contamination can lead to the insecticide being transported long distances.[49] For example, rain collected in California Sierra Nevada Mountains contained chlorpyrifos that had been carried almost 25 miles from the site of application.[50]

Air: Chlorpyrifos contamination of air close to agricultural applications has been measured. For example, one study found that up to one-half of the chlorpyrifos applied to a Maryland cornfield was volatilized (vaporized) and detected in air samples taken about three feet above the field during a 26 day period.[52] Volatilization from foliage is even more rapid: almost 80 percent of chlorpyrifos volatilized from corn foliage in a 2 day period.[38] Chlorpyrifos applied to a Nebraska cornfield via an irrigation system was measured in the air between 300 and 450 feet from the application site.[53]

Chlorpyrifos can also travel in the air away from the site of application: one study found chlorpyrifos in air samples collected

about a half-mile from the application site;[51] another study measured chlorpyrifos in air 15 miles from the application site.[50]

Indoor Persistence

Individuals who are concerned about their exposure to a chlorpyrifos treatment of their food, home, or workplace often want to know how long residues can be expected to persist. Although it is common to estimate a half-life, the time required for half of a chemical to break down or move elsewhere, a simple answer to the question of persistence is not possible because it varies with many factors.

The estimated half-life for chlorpyrifos indoors is 30 days.[54] However, studies of persistence of chlorpyrifos indoors following a variety of treatment methods show the insecticide can persist much longer than a month.

Termite treatments: These treatments involve application of a large amount (several hundred gallons) of chlorpyrifos-containing insecticide adjacent to a foundation or concrete slab. A series of studies looked at chlorpyrifos residues in the indoor air of sixteen North Carolina houses treated with chlorpyrifos for termites. Residues were consistently found whenever samples were taken during the first two years after treatments were made. Surprisingly, concentrations inside many of the houses were higher one year after treatment than they were immediately after treatment or 24 weeks after treatment.[55] Concentrations were even higher four years after treatment[56] and were still detectable eight years after treatment.[57,58] (See Figure 4.)

Crack and crevice treatments: These chlorpyrifos treatments are typically made to kill cockroaches inside buildings. Applications are directed to "cracks and crevices" where the insects are most likely to be found. A series of studies has looked at air concentrations of chlorpyrifos following crack and crevice treatments. These studies show that chlorpyrifos residues were present for as long as samples were taken: two of the studies collected air samples for 3 days,[59,60] one for 8 days,[61] and one collected samples from horizontal surfaces for 42 days after application.[62] Concentrations in the air fol-

lowing crack and crevice applications were high enough to kill flies, even when caged near the ceiling 2 days after application.[63] A study of food-handling establishments found chlorpyrifos residues two months after application in a hotel kitchen and a supermarket; residues were also found six months after application in a restaurant kitchen.[64]

> **"Use of chlorpyrifos pest control strips (designed to kill via direct contact so that'manufacturers believe that there is little if any vaporizationsof theseinsecticides into the air') also resulted in air residues for as long as samples were collected, 30 days."**

Fogging: Pesticide foggers are aerosol-type applicators which deposit their contents primarily on the floor of the treated room. Two studies of carpet residues following fogging showed that residues can be transferred from the carpet to people who contact the carpet. In the two studies, one that used human subjects and one that used a roller device to simulate human contact, residues persisted for as long as the study lasted (12 hours).[65,66]

Other application methods: Measurements of residues following broadcast applications of chlorpyrifos in seven office buildings showed that air concentrations of chlorpyrifos persisted until the end of the study, 6 to 10 days following treatment. Horizontal surfaces were also contaminated at both times that the samples were taken (2 and 24 hours after treatment).[67] In treated apartments, air and carpet residues were present for 4 days.[68] Air residues were

also measured for as long as samples were collected (15 hours) following application of a paint-on formulation of chlorpyrifos.[69] Use of chlorpyrifos pest control strips (designed to kill via direct contact so that "manufacturers believe that there is little if any vaporizations of these insecticides into the air") also resulted in air residues for as long as samples were collected, 30 days.[70]

Soil Persistence

Like persistence indoors, persistence in soil varies depending on the particular situation being studied. Most studies have been made in agricultural soils. Typical soil persistence is reported to be between 60 and 120 days,[44] although it can be longer under appropriate conditions. One Canadian study found residues of chlorpyrifos in carrot and radish plots 2 years after application;[71] a second found residues in soil from onion fields a year after application.[72] In both a western Oregon clay loam and a Canadian corn field, chlorpyrifos persisted about 160 days.[73,74] It is interesting to note that of 8 soil persistence studies collected by NCAP, not a single one lasted long enough to measure complete disappearance from the soil.[71-78] This means that no definite answer can be given to questions about persistence.

Long persistence times have also been measured for chlorpyrifos in forestry soils. In a Florida sand pine forest, chlorpyrifos persisted at least one year,[79] while in a loblolly pine forest in Georgia, up to 18 percent of the chlorpyrifos applied persisted for 15 months.[38] In a shortleaf pine forest in North Carolina, both a microencapsulated and an emulsifiable formulation persisted over 18 months. Almost 40 percent of the microencapsulated chlorpyrifos persisted for that time.[38]

Laboratory studies have identified some of the factors which cause variability in chlorpyrifos persistence.[38] Chlorpyrifos persists longer at low temperatures: each decrease in temperature of 10 degrees doubles its persistence. Some formulations are more persistent than others: granular and microencapsulated formulations persist in soil longer than any of the liquid formulations of chlorpyrifos. In addition, persis-

tence increases with application rate, so that chlorpyrifos used at high rates (termiticide applications, for example) have slower degradation rates than uses with lower rates (agricultural applications, for example).[38] Long-term (seven year) manuring of soil also increases chlorpyrifos persistence.[80]
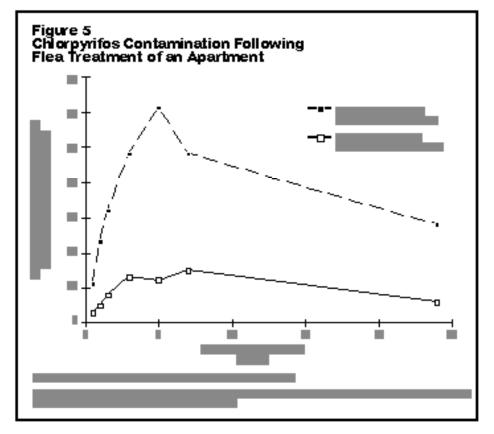
One study looked at persistence of chlorpyrifos in compost made from grass clippings. Chlorpyrifos residues persisted for six weeks in compost made during the summer and 16 weeks in compost made during the fall.[81]

Persistence in Water

DowElanco, manufacturer of chlorpyrifos, states that chlorpyrifos "dissipates very rapidly from the water column" while dissipation from sediments in streams, rivers, lakes, or ponds is "similar to that observed for soils."[38] However, as with soil persistence, persistence in water can vary depending on the particular conditions. Longest persistence has been measured in laboratory studies (between 35 and 140 days)[82-84] while shorter persistence has been measured under outdoor conditions (between 17 and 24 days).[85-86]

Special Susceptibility of Children

Laboratory tests have suggested that infants are more susceptible to chlorpyrifos than adults. In newborn rats, the highest dose of chlorpyrifos without visible effects was only one-sixth that measured in adult rats.[87] The dose required to inhibit half of their acetylcholinesterase activity was two to three times less in the newborn rats than in adults.[88] A laboratory test using rats showed that chlorpyrifos is more easily absorbed through the skin of young rats than that of adult rats. Penetration by chlorpyrifos was up to 50 percent higher in young rats.[89] If human skin has similar absorption patterns, this means that children who contact chlorpyrifos residues will absorb more of the insecticide into their bodies than would similarly exposed adults. Also, laboratory studies in young rats indicates that chlorpyrifos increased their susceptibility to convulsions. This susceptibility occurred at doses too low to cause "overt behavioral

Figure 5
Chlorpyrifos Contamination Following Flea Treatment of an Apartment

Air residues of chlorpyrifos following flea treatment are 3 to 5 times higher in the air close to the floor, where infants typically breathe, than in air further up in the room, where adults typically breathe.

signs of toxicity.[90]

In addition, infants and children may be more heavily exposed to chlorpyrifos in the home than are adults. EPA has recently compiled a list of reasons why this increased exposure occurs. Children "spend a significant amount of time … "on the floor," "spend more time at home than adults," "wear less clothing than adults while at home," and "may have more direct contact with pets that have been treated."[91]

A study of typical indoor application techniques showed that carpets act as a source of chlorpyrifos vapors following application, particularly for children. Air concentrations did not reach their maximum until 3 to 7 hours after application, when residents are likely to have returned home, and were up to 5 times higher in the infant breathing zone (1 foot above the carpet) than in the adult breathing zone (3 1/2 feet above the carpet). (See Figure 5.) Estimates of exposure to an infant in these

conditions showed that the child could be exposed to chlorpyrifos in amounts that were up to five times greater than the dose EPA believes not to cause any adverse effects.[92]

The California Department of Health Services made a similar estimate of the amount of chlorpyrifos to which a child would be exposed in one day following an indoor application of chlorpyrifos. The estimate was based on the amount that the child would breathe in added to the amount the child would absorb through his or her skin. The estimate was over 1700 times the acceptable daily intake established by the World Health Organization.[93] Children are also exposed to chlorpyrifos-contaminated house dust. Because of their low body weight and high dust intake, children appear to be at higher risk than adults from this kind of exposure.[19]

Children are also more exposed to chlorpyrifos in food than are adults because

children consume (for their size) more of the fruits and vegetables that contain chlorpyrifos residues. EPA estimates that infants consume about 2.5 times as much chlorpyrifos (again, for their size) as do adults. Children under 6 years of age consume about 2 times as much.[14]

Concerns about the effects on children are well illustrated by an incident that occurred in San Francisco, California. A newborn infant was brought to a hospital because he was not breathing, and successfully treated with atropine, an antidote to organophosphate poisoning. His house had been treated with Dursban to kill termites and roaches about the time of his birth. His parents were concerned about his possible exposure and kept him at a relative's house for several days. When they returned him to his own home he began vomiting, was lethargic, and then suffered from the breathing problems that brought him to the hospital. A subsequent investigation found chlorpyrifos on dish towels and food preparation surfaces in his home; his clothing was also contaminated.[94]

Metabolites

Chlorpyrifos degrades (breaks down) into a variety of compounds. A primary metabolite (breakdown product) in water, air, soil, plants, and animals is 3,5,6,-trichloro-2-pyridinol (TCP; See Figure 1).[38] TCP is more readily taken up by plants than is chlorpyrifos;[38] it is also more mobile in soil.[37] TCP is 2 to 3 times more toxic to developing chick embryos than is chlorpyrifos itself.[95] Analysis of chlorpyrifos-containing products has found they also contain between 0.1 and 0.6 percent TCP, with highest concentrations if they are at least two years old.[96]

One product, implicated in the death of 50 dairy bulls treated for lice, contained TCP at concentrations about 100 times over typical levels.[96] Chlorpyrifos-containing products also contain the impurity sulfotep,[96] an acutely toxic organophosphate insecticide.[97] The concentrations of sulfotep were 3 times higher than typical levels in the product involved in the bull deaths. However, the researchers stated that the TCP was the chemical that was "significant from a toxicological standpoint."[96]

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● INSECTICIDE FACTSHEET

CHLORPYRIFOS, PART 3: ECOLOGICAL EFFECTS

The organophosphate insecticide chlorpyrifos is toxic to a wide variety of beneficial arthropods including bees, ladybugs, and parasitic wasps.

Chlorpyrifos kills fish at concentrations as low as a few parts per trillion. It has other effects on fish as well: reduced growth and abnormal growth have been observed in fish exposed to chlorpyrifos. In addition, chlorpyrifos kills a wide variety of other aquatic organisms. When aquatic organisms are experimentally exposed to chlorpyrifos, some species disappear completely and populations of other species take months to recover. Chlorpyrifos bioconcentrates in many aquatic organisms.

Birds are also susceptible to chlorpyrifos poisoning. In addition to death, reduced weight gain and deformities in nestlings have resulted from chlorpyrifos exposure.
Cats, newborn calves, adult bulls, newborn pigs, and monkeys are known to have been poisoned or killed by chlorpyrifos.

Surprisingly, plants are damaged by exposure to chlorpyrifos. Delayed seedling emergence, fruit deformities, and abnormal cell division have all resulted from chlorpyrifos exposure.

If an entire ecosystem is exposed to chlorpyrifos, significant changes in the abundance of a number of species, even those not directly killed by chlorpyrifos, can result. This has been well-documented in aquatic ecosystems.

Chlorpyrifos interacts synergistically with several chemicals, including an herbicide. Synergism between three pesticides (including chlorpyrifos) and an anti-nerve gas drug may be the cause of the "Gulf War syndrome," a disease affecting combat veterans from the Persian Gulf war.
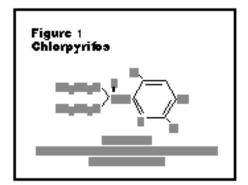
Chlorpyrifos products contain a number of hazardous unidentified "inert" ingredients. One common "inert" is xylene, which can cause nausea, vomiting, hearing and memory loss, reduced fertility, and leukemia.

BY CAROLINE COX

Chlorpyrifos (see Figure 1) is the most widely used insecticide in the U.S. Along with many other common insecticides, it belongs to the organophosphate chemical family. Chlorpyrifos has both agricultural and urban uses. Structural pest control, corn, alfalfa, and cotton are among its largest uses. The toxicology of chlorpyrifos was discussed in the first part of this factsheet (JPR 14(4):15-20). The second part of the factsheet focused on human exposure to chlorpyrifos, with a brief discussion of the hazards of its metabolites (JPR 15(1): 14-20). This part of the factsheet summarizes the effects of chlorpyrifos on plants, fish, birds, domestic animals, and other animals. In addition there are summaries of synergistic effects of chlorpyrifos with other chemicals and the hazards of the secret "inert" ingredients in chlorpyrifos products.

Ecological Effects

Chlorpyrifos adversely affects many more living things than the pests it is designed to

Figure 1
Chlorpyrifos

kill. Effects on non-target organisms include both acute and chronic hazards. Important problems include the following:

Beneficial insects: A common ecological problem with broad spectrum insecticides is that they kill beneficial insects: predators, parasites, and parasitoids of the targeted insect pests. This often results in an increase in the abundance of and damage caused by the pest. Chlorpyrifos is no exception; a review of toxicity to beneficial organisms done by the International Organization for Biological Control showed that, of 23 beneficial species tested, chlorpyrifos caused over 80 percent mortality to 17. Mortality of only 4 species was less than 50 percent.[1] Table 1 gives examples of beneficial insects affected by chlorpyrifos.

Fish: Chlorpyrifos is "very highly toxic to freshwater fish … and estuarine and ma-

Table 1
Examples of beneficial insects harmed by chlorpyrifos

Beneficial Species	Pest Species	Crop	Reference
Parasitoids and Parasites			
Encarsia perniciosi	San Jose scale	apple	1
Teleonemus remus	*Spodoptera litura*	tobacco, cabbage, cotton, cauliflower	2
Aphytis melinus	California red scale	citrus	3
Eucelatoria bryani	*Heliothis armigera*	tomato, bean	4
Aphelinus perpallidus	pecan aphid	pecan	5
Predators			
spider	bollworm	peanut	6
spider	many	turf	7
spider	many	grapefruit	8
carabid beetle	black cutworm	corn	9
carabid beetle	wheat midge	wheat	10
ant	fall armyworm, corn leafhopper	corn	11
Chrysoperla rufilabris	pecan aphid	pecan	5
Hippodamia convergens	pecan aphid	pecan	5
Cycloneda sanguinea	pecan aphid	pecan	5
Olla v-nigrum	pecan aphid	pecan	5
Pollinators			
Honey bee	NA	many	12,13,14
alkali bee	NA	seed alfalfa	13,14
leafcutting bee	NA	seed alfalfa	13,14

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rine organisms."[2] Application rates as low as 0.01 pounds per acre can cause fish deaths.[2] Typically, exposures of about 3 parts per million (ppm) are lethal to fish.[3] Some fish are killed by very much lower concentrations of chlorpyrifos. For example, the median lethal dose for grunion and silversides varies between 0.4 and 6.7 parts per billion (ppb).[4]

As expected because of the mode of action of chlorpyrifos, a symptom observed at low concentrations is inhibition of acetylcholinesterase (AChE) activity. (Acetylcholinesterase is an enzyme in the nervous system which is inhibited by all organophosphate insecticides.) For example, AChE inhibition in fathead minnows was measured at a concentration of less than 1 ppb, about 1/10 of the concentration that caused mortality of the fish.[5] In guppies, concentrations of 1 ppb significantly inhibited AChe activity, which then did not return to normal after two weeks of keeping the test fish in uncontaminated water.[6] In mummichogs, 1 ppb of chlorpyrifos also inhibited AChE, and inhibition was measured for 69 days following application of chlorpyrifos granules.[7]

Growth of fish is also reduced by low concentrations of chlorpyrifos. For example, less than 2 ppb of chlorpyrifos is sufficient to reduce the weight of grunion fry,[8,9] and less than 1 ppb reduced length and weight in fathead minnows.[10] The effects on fathead minnows were associated with decreases in the abundance of their typical prey, so that the growth reduction was probably due to changes in diet.[10] Abnormal growth (spinal deformities) occurred at concentrations of 5 ppb in juvenile rainbow trout and at 3 ppb in fathead minnows.[11] Exposure periods of 5 hours were sufficient to cause these deformities.[12] In tests lasting more for more than one generation, effects of chlorpyrifos on growth occur at even lower doses; in fathead minnows, the growth of the second generation was reduced at concentrations of 0.1 ppb.[5]

Low concentrations of chlorpyrifos also cause a variety of other adverse effects. For example, in fathead minnows, doses of 0.1
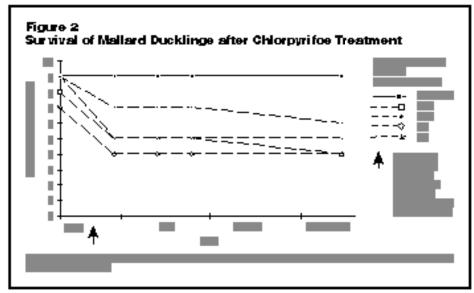
ppb caused a reduction in the number of sexually mature fish.[5] In catfish, concentrations of 2 ppb caused kidney damage.[13] In mosquito fish, concentrations of 5 ppb caused reduced thermal tolerance and reduced activity.[14]

Other aquatic organisms : Chlorpyrifos is acutely toxic to a wide variety of aquatic organisms from freshwater, estuarine, and marine habitats. Examples include freshwater algae[15,16]; rotifers[17,18]; water fleas[19]; copepod,[19,20] isopod, amphipod,[19] and ostracod[21] crustaceans; tadpole shrimp[22]; freshwater crabs[23]; stoneflies[24]; mayflies; damselflies; caddisflies[25]; larval reef coral[26]; fiddler crabs[27]; grass shrimp[28]; and marine diatoms.[29] Typical lethal exposures for these organisms range from less than 1 ppb to several parts per million (ppm).[3]
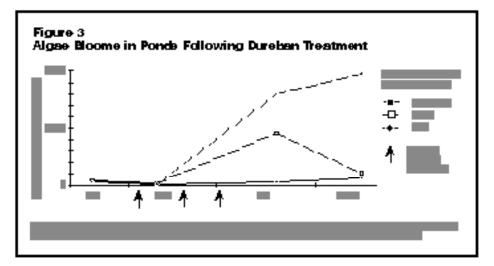
Effects on aquatic organisms can be both persistent and severe. In California lakes treated with chlorpyrifos, one amphipod crustacean was completely eliminated and did not reestablish in some areas for eight months.[21] In experimental drainage ditches, one isopod crustacean disappeared completely following chlorpyrifos treatment, and populations of other species required up to 16 weeks to recover.[19] The conclusions of U.S. Environmental Protection Agency researchers in Florida are revealing: "Less than 0.1 parts per billion of chlorpyrifos in water could be hazardous to saltwater ecosystems by their impacts on individual species, on communities of organisms, and on a wide variety of ecological relationships...."[30]

Accidental discharges of chlorpyrifos can also be devastating to aquatic organisms. In 1985 about 500 liters of Dursban 4E spilled into a British river when a truck carrying the chemical overturned. Virtually all aquatic invertebrates were killed. While chlorpyrifos-contaminated water moved downstream and was degraded relatively quickly, contaminated sediments persisted for at least and a year and populations of aquatic invertebrates required two years to return to normal levels.[31]

Bioconcentration : Chlorpyrifos bioconcentrates in aquatic organisms: this means that the insecticide moves from the water into biological tissues. In tissues, it is often more concentrated than in water.

Figure 2
Survival of Mallard Ducklings after Chlorpyrifos Treatment

In a 1968 experiment, about 40 percent of mallard ducklings died in ponds treated with chlorpyrifos.

Figure 3
Algae Blooms in Ponds Following Dursban Treatment

Algae blooms were observed in ponds experimentally treated with chlorpyrifos. The algae blooms were more intense, and lasted longer, when chlorpyrifos was applied at higher rates.

The extent of bioconcentration is measured by the bioconcentration factor (BCF), calculated by dividing the concentration in the living tissue (usually expressed as mg/kg) by the concentration in the water (usually expressed as mg/L). BCFs for fish exposed to chlorpyrifos range from 220 to 5000 in the laboratory, and 100 to 4667 under field conditions.[32] Bioconcentration has also been observed in yeast, isopod crustaceans, and protozoa.[33-35] This means that small amounts of chlorpyrifos can have a significant impact on living things.

Birds: Chlorpyrifos is acutely toxic to birds: the LD_{50} (the dose that kills half of a population of test organisms) for ring necked pheasants is 19 milligrams per kilogram (mg/kg) of body weight, 32 for bobwhite quail,[36] and 77 for mallard ducks.[3] Chicks whose drinking water contained 80 ppm of Dursban died within a three-week period.[37] Thus, it is not surprising that adverse effects on birds have been observed following agricultural, urban, and aquatic uses of chlorpyrifos. For example, 200 greenfinches and linnets were killed in the United Kingdom by a chlorpyrifos treatment of a brassica field.[38] Inhibition of AChE activity

in horned larks was measured following treatment of the wheat fields in which the larks fed.[39] In residential parts of Quebec, the number of robin young produced was negatively correlated with the number of nearby lawns treated with chlorpyrifos in preceding years. Researchers believed that chlorpyrifos killed earthworms, resulting in less food for robin nestlings.[40] Chlorpyrifos treatment of ponds to kill mosquitoes caused 40 percent mortality of mallard ducklings, even at the lowest rate applied.[41] (See Figure 2.)

Among the factors that influence the toxicity of chlorpyrifos to birds are age (juveniles are typically more susceptible than adult birds)[42] and stress (cold temperatures augment chlorpyrifos toxicity).[43]

Sublethal effects of chlorpyrifos exposure in birds include anorexia,[37] reduced efficiency of converting feed into body weight,[44] and reduced body weight gain.[45] In Japanese quail, exposure of eggs to chlorpyrifos resulted in an increase in the number of certain deformities (scoliosis and foot malformations) as well as an increase in the incubation period.[46]

Domestic Animals : The domestic animals most sensitive to chlorpyrifos exposure appear to be cats, newborn calves, adult bulls, and newborn pigs.

Cats have been poisoned or killed following treatments of their owners' homes with chlorpyrifos.[47,48] Cats appear to be particularly sensitive to chlorpyrifos-induced delayed neuropathy. (See JPR 14(4):17-18) for a description of this problem.) In addition, a single contact with chlorpyrifos can cause continuous exposure because chlorpyrifos is deposited in fat and then slowly released.[49]

Newborn calves are about 30 times more sensitive to chlorpyrifos than older calves.[50] Bulls have been killed by chlorpyrifos exposure, as well as exhibiting poisoning symptoms and a decline in sperm production.[51-55]

Pigs have been poisoned and killed after a chlorpyrifos-containing aerosol spray was used to treat wounds formed where the umbilical cord and the tail were removed.[56,57]

Monkeys: In 1978 a monkey rearing fa-

cility was treated with chlorpyrifos by a pest control operator who disregarded the facility manager's instructions to use a different product. Of the 98 monkeys in the facility, 19 died and many became ill. Among ill monkeys, two aborted pregnancies, and two became infertile. In addition, two retarded offspring were born.[58]

Plants: As an insecticide, chlorpyrifos is not expected to be toxic to plants. Surprisingly, it has been shown to be toxic to a number of different plants. Emergence of

> "In 1978 a monkey rearing facility was treated with chlorpyrifos by a pest control operator who disregarded the facility manager's instructions to use a different product. Of the 98 monkeys in the facilty, 19 died and many became ill. Among ill monkeys, two aborted pregnancies, and two became infertile. In addition, two retarded offspring were born."

both carrot and onion seedlings was delayed by chlorpyrifos treatment; seedlings were also reduced in size.[59] In grapefruit, chlorpyrifos treatment during bud break leads to damage to the fruit known as ridging.[60] Chlorpyrifos has also caused abnormal pollen mother cells and abnormal cell division in vetch,[61,62] and chlorophyll-deficient mutants in barley.[63]

Soil Organisms : Earthworms are suscep-

tible to chlorpyrifos poisoning, although the amount of exposure required to cause death varies widely among species. *Lumbricus rubellus*, a commercially available species, is about ten times more susceptible than *Eisenia foetida*, another commercially available species.[64,65]

Chlorpyrifos inhibits the growth of a variety of species of soil fungi[66,67] as well as nitrogen-fixing blue-green algae[68] and nitrogen-fixing bacteria.[69] Researchers state that these "negative effects … on the nitrogen economy of agricultural soils could be of primary importance."[69]

Ecosystem-level Effects : Treatment with chlorpyrifos can affect entire ecosystems when the mortality of sensitive species has a ripple effect on other species.

These kinds of interactions have most often been studied in aquatic ecosystems. As early as 1968, biologists noticed these kinds of effects when looking at the effects of chlorpyrifos used to control mosquitoes. Application of Dursban to eight experimental ponds in California resulted in reductions of both predaceous and herbivorous insects; populations of predaceous insects were reduced more, and for a longer time than were populations of herbivorous insects. Populations of several herbivorous crustaceans as well as an herbivorous rotifer increased because their insect predators had been killed. As a result, phytoplankton (specifically several species of blue-green algae and a diatom) then increased dramatically, resulting in an algae bloom. (See Figure 3.) The ecological effects can spread past the boundaries of the pond, because livestock and wildlife have been killed after drinking water affected by such algae blooms. The researchers also point out that "by stimulating algal blooms and reducing predaceous insect populations, Dursban created an ecological imbalance apparently favorable to the very insects it was meant to control."[70]

A more recent study used experimental pond enclosures in Minnesota in 1986 and 1987.[71,72] Researchers measured decreases in most species of invertebrates, an increase in algae abundance (resulting from the mortality of the invertebrates that usually fed on the algae), decreases in insect abundance,

and decreases in the growth of fish (fathead minnows) as they had to make changes in their diet because populations of their prey were killed by chlorpyrifos. Effects were measured at a concentration of 0.5 ppb.[71,72]

Effects can be even more complicated, as was illustrated by an experimental system designed to mimic drainage ditches. In this experiment, small algae and rotifers increased as their usual predators (aquatic invertebrates) were killed by chlorpyrifos treatment. Large colony-forming algae, on the other hand, decreased due to the competition from the smaller algae. Increases in small algae led to increases in snails and clams while predaceous worms declined as their invertebrate prey declined. The predaceous worms then switched to less favored prey, sediment-dwelling worms, which then decreased in abundance.[73] A second study of drainage ditches found that chlorpyrifos treatment caused a significant increase in the acidity of the water, resulting in (up to 200-fold) slower degradation of chlorpyrifos. Some parameters were not restored to their normal values for 130 days following chlorpyrifos application.[74]

Ecosystem-level effects have also been measured in terrestrial ecosystems. A four-year study of effects on plant communities of chlorpyrifos used to kill soil insects in a pasture and on disturbed soil found that chlorpyrifos treatment changed the competitive balance among plant species. On the disturbed soil, broadleaf plants increased following chlorpyrifos treatment, while grasses decreased. In the pasture, grasses increased while broadleaf plants decreased. The researchers note the "dramatic consequences" that elimination of the insects has on the "establishment and subsequent development of natural plant communities."[75]

Synergism

Synergistic interactions between chlorpyrifos and a variety of other chemicals have been observed. This means that chlorpyrifos either enhances the potency of another chemical, or its own potency is enhanced. For example, adding vitamin C (ascorbic acid) to the diet of rats almost doubled the acute toxicity of chlorpyrifos.[76] Pretreatment of partridges with the fungi-

Figure 4
"Inert" Ingredients in Chlorpyrifos-containing Products

All of these chemicals are used as "inert" ingredients in chlorpyrifos-containing products.

cide prochloraz increased the inhibition of acetylcholinesterase by chlorpyrifos about 80 percent.[77] Pretreatment of mice with the organophosphate insecticide phosfolan increased the acute toxicity of chlorpyrifos about 10 percent.[78] Ingestion of chlorpyrifos (accidental) by a child prolonged paralysis induced by the drug succinylcholine.[79]

Synergism has also been observed in the agricultural use of chlorpyrifos. Thifensulfuron is a sulfonylurea herbicide used to kill weeds in soybeans, a crop that is relatively tolerant of the herbicide. When applied in combination with chlorpyrifos (as well as certain other insecticides), damage to the soybean crop results. Researchers found that thifensulfuron in soybean leaves was detoxified by an esterase, an enzyme related chemically to acetylcholinesterase, the enzyme inhibited by chlorpyrifos. Chlorpyrifos also inhibited the esterase responsible for detoxifying thifensulfuron in soybeans, resulting in the crop damage.[80]

Synergistic interactions with chlorpyrifos were headline news recently, as Duke University researchers documented synergistic nervous system damage when laboratory animals were exposed to chlorpyrifos, the synthetic pyrethroid insecticide permethrin, the insect repellent N, N-diethyl-m-toluamide (DEET), and the anti-nerve gas drug pyridostigmine bromide. The same research also found synergistic effects when the three pesticides, without the drug, were tested. This particular combination of chemicals is of interest because it may be responsible for the "Gulf War syndrome," illnesses suffered by U.S. soldiers after returning from military service in the Persian Gulf.[81]

Since there is no systematic screening of pesticides for synergistic effects, it is impossible to estimate how many chemicals are likely to interact synergistically with chlorpyrifos.

"Inert" Ingredients

Almost all chlorpyrifos-containing pesticide products contain ingredients other than chlorpyrifos. These are publicly identified only as "inert" ingredients and are called trade secrets by the manufacturers of the products. The limited information available about "inert" ingredients used in chlorpyrifos products indicates that these "inerts" include xylene, 1,2,4-trimethylbenzene (used in Dursban L.O.[82]), cumene, ethyltoluene (all 4 used in both Dursban 2E and Dursban 4E[83,84]), propylene glycol (used in Dursban Pro[85]), and

1,1,1-trichloroethane (used in Lorsban 4E[86]). (See Figure 4.) Adverse health effects of these "inerts" include the following:

Xylenes are solvents. They cause nose and throat irritation, eye irritation, labored breathing, lung inflammation, nausea, vomiting, mild liver toxicity, impaired short-term memory, and hearing loss in exposed humans and/or laboratory animals. In laboratory tests, xylene exposure has also caused reduced fertility, increased number of fetal resorptions, increased incidence of cleft palate, and decreased fetal weight. Xylene inhalation has been associated with an increased frequency of leukemia in solvent-exposed workers. In addition, it may be a cocarcinogen; exposure to xylenes enhanced the number of skin cancers caused by other carcinogens. It also "has the potential for bioaccumulation in human adipose [fat] tissue."[87]

Trimethylbenzenes are highly volatile solvents that can cause skin and eye irritation, nervousness, tension, bronchitis, disruptions of the ability of blood to clot, headaches, fatigue, dizziness, and loss of consciousness.[88]

Propylene glycol is a widely-used colorless, odorless liquid. It causes damage to red blood cells, skin irritation, adverse neurological reactions, and (in rabbits) degeneration of lung cells.[89]

1,1,1-trichloroethane is a solvent. Exposure to 1,1,1-trichloroethane has caused respiratory depression, irregular heart beat, nausea, diarrhea, central nervous system depression and degeneration of peripheral nerves, behavioral changes, some evidence of an increase in the frequency of leukemia in rats, and skin irritation.[90]

Cumene is another solvent. It causes skin irritation, a narcotic effect, gastrointestinal disturbances, damage to the lungs, liver, and kidneys, and depression of the central nervous system.[91]

Ethyltoluene is also a solvent. It "may be harmful by inhalation, ingestion, or skin absorption." Unfortunately, "toxicological properties have not been thoroughly investigated."[92]

Interactions of "inerts" and chlorpyrifos: Interactions between chlorpyrifos and xylene may result in important health haz-ards. A recent neurotoxicology study looked at the ability of chlorpyrifos and xylene to affect the susceptibility of young rats to electrically-stimulated seizures. Chlorpyrifos alone is a proconvulsant: it decreases the number of electrical stimulations required to initiate a seizure. Xylene and chlorpyrifos together causes "a potentiation of the proconvulsant action." While more research will be required to establish what implications this might have outside of the laboratory, it is clear that chlorpyrifos and xylene work together to affect the nervous system.[93]

The interaction between the "inerts" in chlorpyrifos-containing products and the chlorpyrifos itself can also lead to unexpected environmental problems. In 1989, an "operational error" caused a small tank in a pesticide manufacturing facility in Cartagena, Columbia to overflow into a diked area. The xylene in the chlorpyrifos formulation dissolved the asphalt dike expansion joints. As a result, the chlorpyrifos escaped into Cartagena Bay and killed 17 tons of fish.[94] ❧

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