Aldicarb

By Caroline Cox

In 1966, four years before the insecticide aldicarb was registered for use in the United States, researchers were using the chemical on an experimental basis.[1] One researcher brought a small amount home and his wife applied it to the soil under a backyard rose bush. Over three weeks later she ate a sprig of mint from a plant growing nearby. Within half an hour she was suffering from vomiting, diarrhea, and involuntary urination. Her pupils closed to pinpoints, her muscles twitched, and her breathing was difficult. After hospitalization and treatment with the antidote atropine, she recovered. However, three grams of the same mint plant was sufficient to kill a rabbit.[1] While it might seem that a pesticide that caused this kind of incident is a poor candidate for managing pests on food crops, aldicarb has been extensively used for over 20 years on both food and nonfood crops.

Aldicarb, 2-methyl-2-(methylthio)-propionaldehyde *O*-methylcarbamoyloxime (see Figure 1), is currently manufactured in the U.S. by Rhone-Poulenc Company and sold under the trade name Temik. It is registered for use on citrus, cotton, beans, sorghum, soybeans, sugarbeets, and sweet potatoes.[2,3] The U.S. Environmental Protection Agency (EPA) estimated that between 5.2 and 5.6 million pounds of aldicarb were used nationwide in 1988.[4] Use of aldicarb during 1990 (totalling almost half a million pounds) in California is shown in Figure 2.

Mode of Action

Aldicarb is a carbamate insecticide and acaricide (pesticide used to kill mites). Like all members of this chemical family, it inhibits the action of an enzyme that is an essential component of both insect and mammal nervous systems. The enzyme, acetylcholinesterase (AChE), controls the chemical reaction that transforms acetylcholine, a neurotransmitter, into choline.[5] (Aldicarb and acetylcholine have similar chemical structures.[6] See Figure 1.) Without functioning AChE, acetylcholine accumulates and prevents the smooth transmission of nerve impulses across the junctions between nerves. This causes loss of muscular coordination, convulsions, and ultimately death.[5] The AChE inhibition is said to be reversible because the aldicarb disassociates from the AChE within several hours. This occurs even if death has occurred. Organophosphate insecticides (malathion and diazinon, for example) have the same mode of action except that the AChE inhibition is not as readily reversible.[7]

Aldicarb is a systemic insecticide. It is applied as granules below the soil surface and is then absorbed by plant roots and translocated throughout the plant, killing insects and mites that feed on the plant.[8]

Acute Toxicity

Aldicarb is "one of the most acutely toxic pesticides registered" according to EPA.[4] The oral LD_{50} (the dose required to kill 50 percent of a population of test animals) is between 0.3 and 0.9 milligrams per kilogram (mg/kg) of body weight.[9] If humans are equally sensitive, less than a thousandth of an ounce of aldicarb would be sufficient to kill a typical (60 kg) adult.

In humans, signs of aldicarb poisoning include dizziness, salivation, excessive sweating, nausea, abdominal cramps, vomiting, diarrhea, blurred vision, pinpoint pupils, difficult breathing, and muscle twitching. Death follows if exposure has been high enough.[10]

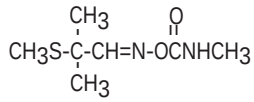
A sensitive sign of aldicarb poisoning is measurement of AChE activity. This can be done by laboratory analysis of blood and other tissue samples. In laboratory animals (beagles), AChE inhibition has been observed at doses as low as 0.05 mg/kg/day (given over a one-year period). The highest dose at which no adverse effects were observed (called the NOEL) was 0.02 mg/kg/day, about one-tenth of the LD_{50}.[11]

There is evidence that people may suffer acute symptoms when exposed to even lower levels of aldicarb. In humans who consumed aldicarb-contaminated watermelons, clinical signs of aldicarb poisoning were found in individuals consuming as little as 0.002 mg/kg of the aldicarb metabolite aldicarb sulfoxide. This amount is one-tenth the NOEL in the beagle study.[12]

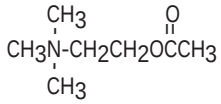
Chronic Neurotoxicity

In addition to its acute toxicity to animals' nervous systems, aldicarb can also have long-term delayed behavioral effects. Two studies of aldicarb-exposed chicks, one in which chicks were exposed during the first week after hatching and one in which chicks were exposed before hatching, showed that aldicarb caused changes in the chicks' gait.[13,14] The

Figure 1
Aldicarb and Acetylcholine

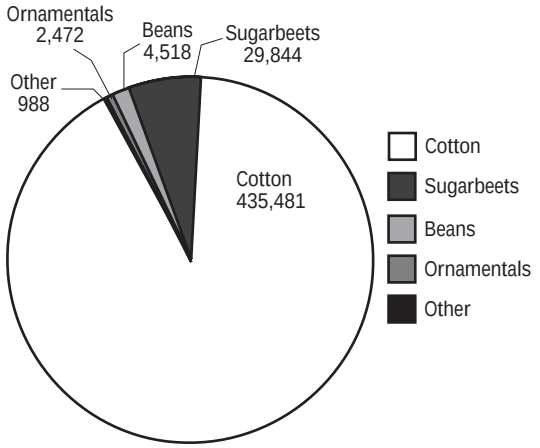


aldicarb



acetylcholine: the neurotransmitter mimicked by aldicarb

Figure 2
Use of Aldicarb in California During 1990 (pounds)



Source: State of California. Environmental Protection Agency. Department of Pesticide Regulation. Information Services Branch. 1990. Pesticide use report. Sacramento, CA.

Caroline Cox is JPR's editor.

changes in locomotion persisted after AChE inhibition could no longer be measured, over 40 days after treatment.[13,14]

Suppression of the Immune System

In 1986, epidemiologists in Wisconsin studied how well the immune system was functioning in women who were drinking water from wells that were contaminated by low levels of aldicarb. They found that consumption of aldicarb-contaminated water was associated with one immune system abnormality (an increase in the number of T8 cells). This abnormality could not be correlated with any clinical evidence of adverse health effects (self reported doctor visits, drug prescriptions, illnesses, etc.). The researchers concluded that "the public health implications of continuing to expose large populations to potential immuno–modulating environmental contaminants warrants careful review."[15]

The epidemiological study was prompted by a study of the effects of aldicarb on the immune system of mice.[16] In this study, consumption of water contaminated with as little as 1 part per billion (ppb) of aldicarb affected one parameter of immune function, the plaque forming cell response. Interestingly, the effect was strongest at the lowest concentration (1 ppb). Three subsequent mouse studies found effects of aldicarb (at doses as low as 0.0001 micrograms of aldicarb per mouse) on another immune system component, macrophage activity.[17-19] (See Figure 3.)

A recent follow-up study to the Wisconsin epidemiology study found that immune system abnormalities continued in women whose exposure to aldicarb continued.[20]

Mutagenicity and Carcinogenicity

In human cells, aldicarb causes an increase in the number of three different kinds of chromosome abnormalities: sister-chromatid exchanges, chromatid breaks, and chromosome breaks.[21,22]

In other mammal cells, no evidence was found linking aldicarb exposure to three types of genetic damage: mutation frequency of Chinese hamster ovary cells, chromosome aberrations in mouse bone marrow cells, and unscheduled DNA synthesis in rat liver cells. [23]

Aldicarb damages DNA in cells of *Salmonella typhimurium*, a bacteria.[24]

While chemicals that damage genes often also cause cancer, aldicarb exposure has not been associated with an increase in cancer incidence in tests conducted by the National Toxicology Program.[25] Even though carcinogenicity tests submitted in support of aldicarb's registration do not meet current standards, California's Department of Pesticide Regulation concluded in 1987, "Although no one study is unacceptable, the collective data from the several studies provide sufficient evidence on the lack of an oncogenic effect." Several unexpected tumors were observed in a reproduction study in rats completed in 1991; Rhone-Poulenc has reported to EPA that the tumor findings "might possibly reflect an adverse effect…."[23] Because very small doses of aldicarb cause death, it may be very difficult to detect a carcinogenic effect in laboratory tests.

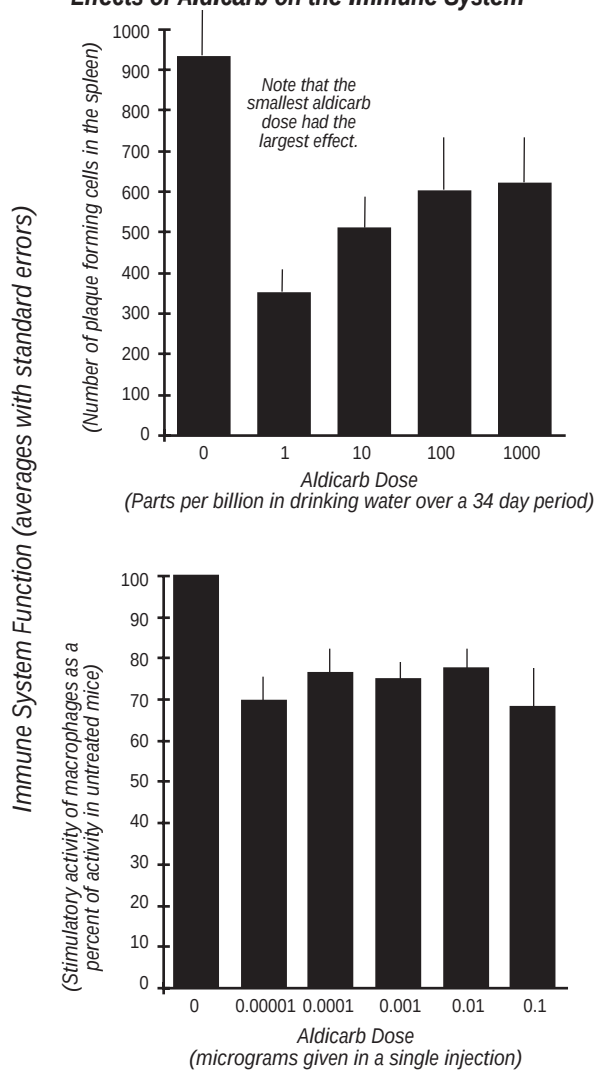
N-Nitrosoaldicarb, formed by a reaction between aldicarb and sodium nitrite (see Figure 4), is also mutagenic in *Salmonella*[26] and causes sister-chromatid exchanges in human cells.[27] In rats, consumption of N-nitrosoaldicarb has been associated with an increased incidence of stomach cancers.[28]

Effects on Reproduction and Development

After over 1000 consumers of aldicarb-contaminated watermelon became ill in July 1985, stillbirths were reported by two women who had suffered acute symptoms.[29] In addition, epidemiological studies of New York residents found an increase in the frequency of miscarriages associated with high aldicarb contamination levels in drinking water wells, although the study was not sufficient to conclude that aldicarb was the cause.[30]

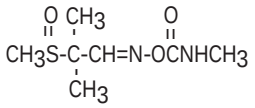
Aldicarb has also caused reproductive problems in laboratory rats. Doses of aldicarb as low as 0.001 mg/kg caused inhibition of AChE in fetal brains and livers. This dose is a thousand times lower than the adult LD_{50}. Doses of 0.01 mg/kg caused inhibition that continued for 24 hours following exposure.[31] Fetuses were more sensitive than their mothers to aldicarb's effects. In addition, aldicarb exposure of rats during pregnancy caused mothers' food consumption and body weights to decrease. The weight of their

Figure 3
Effects of Aldicarb on the Immune System

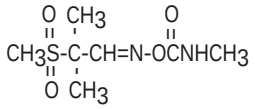


Sources:
Olson, L.J. et al. 1987. Aldicarb immunomodulation in mice: an inverse dose-response to parts per billion levels in drinking water. *Arch. Environ. Contam. Toxicol*. 16:433-439.
Dean, T.N. et al. 1990. Aldicarb treatment inhibits the stimulatory activity of macrophages without affecting the T-cell responses in the syngeneic mixed lymphocyte reaction. *Int. J. Immunopharm*. 12(3):337-348.

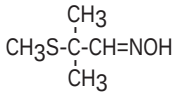
Figure 4
Aldicarb Metabolites and Contaminants



aldicarb sulfoxide

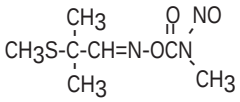


aldicarb sulfone



aldicarb oxime

dichloromethane (methylene chloride)



N-nitrosoaldicarb

offspring was also reduced, and the babies suffered from skeletal abnormalities, delayed bone formation, and ruptured blood vessels.[32]

Similar kinds of effects have been noted in birds. In ducks, application of aldicarb to eggshells during incubation caused shortening of a foot bone (the tarsus) and the middle toe.[33] Treatment of young chicks for one week with aldicarb reduced their growth for forty days after treatment had ended.[13]

Human Poisonings

In July 1985, aldicarb made headlines when almost two thousand people (mostly in Oregon[34] and California[35]) became ill after eating watermelons that were contaminated with the insecticide. Symptoms included nausea, vomiting, diarrhea, sweating, muscle twitching, slow heartbeat, seizures, loss of consciousness, and shock.[12] Six deaths and two stillbirths were reported following the poisoning episode. Illnesses were reported by individuals who had consumed watermelons with aldicarb residues too low to detect with laboratory analyses.[12] The incident was "the largest recorded North American outbreak of foodborne pesticide illness."[35]

The source of the aldicarb contamination was difficult to identify. Since aldicarb is not registered for use on melons, illegal use may have been responsible. In at least one case, contaminated watermelons were found in a field that was adjacent to a cotton field on which aldicarb had legally been used. It appeared that the melons had been contaminated when contaminated ground or surface water moved from the cotton field to the watermelon field.[36]

In addition, aldicarb contaminated cucumbers from Nebraska (two different incidents), British Columbia,[37] and California[38] have caused illnesses. Aldicarb is not registered for use on cucumbers.

In 1990, Rhone-Poulenc withdrew aldicarb's registration on potatoes after field tests found residues above tolerance levels.[3] The American Academy of Pediatrics later calculated that a child consuming a potato with aldicarb residues as high as had been measured would consume a dose equal to about one-tenth of the LD_{50} and well above the toxicity threshold.[39] Residues above the tolerance levels were also found on bananas in 1991, prompting Rhone-Poulenc to stop aldicarb use on bananas.[40]

Agricultural workers are also exposed to aldicarb. While EPA's Pesticide Incident Monitoring System was operating (1966-1982) 165 incidents involving aldicarb were reported.[41] More recently, between five and nine cases of aldicarb poisoning per year have been reported in California. Several fatalities have also been reported in California.[36] A monitoring study of German greenhouse workers found that a decrease in AChE activity could be detected up to ten days after aldicarb was applied.[42]

Contamination of Groundwater

In 1979, aldicarb residues were detected in wells in a potato-growing area on Long Island, New York where the pesticide had been used for just four years to control nematodes and Colorado potato beetles. By 1986, about 2,500 wells in the area had been found to be contaminated with concentrations exceeding New York state health guidelines. Rhone-Poulenc provided carbon filters for residences using water from these wells.[43]

Use of aldicarb was suspended on Long Island in 1979. Studies in 1983 and 1984 showed that while aldicarb contamination had declined in some wells, those in areas with a deep water table (about 30 meters) had concentrations that were still increasing.[44] About 1,400 wells were still contaminated above the state guidelines in 1986.[43]

Aldicarb's chemical characteristics make leaching to groundwater likely. It is moderately persistent (as are its metabolites),[45] highly water soluble,[46] and mobile in soils.[41] Since the contamination of the New York wells were first reported, aldicarb has been found in the groundwater in 26 other states. (See Figure 5).

Under the Safe Drinking Water Act, EPA has proposed a Maximum Contaminant Level Goal (MCLG; the contamination level at which "no known or anticipated adverse effects on the health of persons occur") of 0.001 milligrams per liter (equal to about 1 part per billion). The MCLG is based on the beagle study and the watermelon poisoning episode discussed earlier.[11] MCLGs for aldicarb sulfoxide and aldicarb sulfone were proposed at the same level.[11]

Environmental Fate

The half-life of aldicarb (the time required for half of the aldicarb applied to either be transformed to another compound or leave the sample area) was estimated to be between 1.5 and 2 months in soils from tomato fields and vineyards in central California.[47] In Florida citrus groves, the half-life of aldicarb in the soil was longer, approximately eight months.[48] In the California study, some aldicarb residues were found in the soil for as long as a year after application. In potatoes, alfalfa, mint, mustard, and radishes, residues of aldicarb and its metabolites were found up to 408 days after application.[49]

Effects on Nontarget Organisms

Birds: Acute toxicity of aldicarb to birds varies among species but is always

high. LD_{50}s for the most sensitive species (house sparrows and grackles) are 0.8 mg/kg of body weight, approximately equal to the oral LD_{50} for rats. The least sensitive species, white leghorn chickens, have an LD_{50} approximately 10 times larger (9.0 mg/kg) than that of the rat.[50] One granule of Temik is sufficient to kill over 80 percent of the house sparrows tested in one study and 40 percent of the red-winged blackbirds.[51] In general, young birds are more susceptible than adult birds.[50]

Fish: Aldicarb is also toxic to fish; LC_{50}s (the concentration of aldicarb in water required to kill 50 percent of test aquatic animals) ranged from 41 parts per billion (ppb) for sheepshead minnows to 2420 ppb for *Barbus conchonius*.[50] In at least one species, juveniles are more sensitive than older fish.[36,52] Studies on fish have also demonstrated a variety of other adverse effects caused by exposure to aldicarb. Aldicarb caused liver damage[53] and several changes in blood cells[54] in the rosy barb, a freshwater fish, at a concentration one-third of the LC_{50}, and was more injurious than an organophosphate and an organochlorine insecticide also tested.[53] At 20 percent of the LC_{50}, exposure to aldicarb caused an increase in cholesterol levels in the blood, ovary, and liver, as well as increases in liver lipids in *Barbus conchonius*.[55]

Invertebrates: Aldicarb is also highly toxic to shrimp,[56] earthworms,[50] water fleas[56] and honeybees.[50] In a water flea native to Florida ponds, *Daphnia laevis*, the EC_{50} (the concentration required to immobilize half of the animals) was less than one-fourth the concentration required to kill *Daphnia* adults.[57]

Plants and Bacteria: Aldicarb also has the potential to affect nonanimal species. Laboratory studies of the nitrogen-fixing bacterium, *Rhizobium meliloti*, showed that exposure to aldicarb caused changes in the bacterium's carbohydrate metabolism, impacting the plant-microbe interaction.[58] In potatoes, aldicarb treatments decreased the concentrations of reducing sugars, increased the amount of free amino acids, decreased the amount of phenols, and decreased the concentration of Vitamin C.[59]

Figure 5
States Reporting Aldicarb Contamination of Groundwater

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Contaminants

Temik contains dichloromethane (also called methylene chloride; see Figure 4) as a contaminant.[60] Dichloro–methane is an active ingredient in a fumigant used on strawberries and grain,[2] and is also an "inert" (secret) ingredient in over 1,750 pesticide products.[61] In humans, exposure to dichloromethane causes changes in blood cell counts, decreases in hearing and vision, lack of coordination, and death. In laboratory animals, exposure causes eye irritation, kidney and liver damage, damage to genes, and cancer. EPA classifies dichloromethane as a probable human carcinogen (Group B2).[62]

Degradation Products

In plants, microorganisms, and animals, aldicarb is transformed into several related compounds. The most common are aldicarb sulfoxide, aldicarb sulfone and aldicarb oxime.[63] (See Figure 4). The sulfoxide and the sulfone have a mechanism of toxicity similar to that of aldicarb itself. The sulfoxide is as toxic as aldicarb in both acute and long-term tests; the sulfone is less toxic.[64]

Manufacturing

One of the intermediaries used in the manufacture of aldicarb is the highly reactive compound methyl isocyanate (MIC).[5] On December 3, 1984 a toxic cloud containing MIC and other reaction products escaped from a Union Carbide plant in Bhopal, India that manufactured aldicarb and carbaryl,[65] another carbamate insecticide. Between 2500 and 5000 people died as a result of the accident, and up to 200,000 people were injured. Injuries included respiratory problems, eye damage, fetal and newborn deaths, suppression of the immune system, and changes in blood chemistry.[66] A smaller but similar accident occurred the following year at Union Carbide's aldicarb and carbaryl plant in Institute, West Virginia and 135 people were hospitalized.[65]

Summary

Aldicarb is one of the most acutely toxic pesticides registered in the U.S. Less than one thousandth of an ounce is a lethal dose for a human. In laboratory animals, it causes chronic damage to the nervous system, suppresses the immune system, and adversely affects fetuses. In human cells, aldicarb causes genetic damage. It is also toxic to birds, fish, shrimp, honey bees, and earthworms. Aldicarb's primary metabolite is almost as toxic as aldicarb itself. Aldicarb's agricultural formulation contains a toxic contaminant, dichloromethane, that causes damage to hearing, vision, kidneys, and livers and is both carcinogenic and mutagenic. Aldicarb has contaminated groundwater in 27 states and has caused the largest recorded episode of foodborne pesticide poisoning in the United States. Aldicarb manufacturing accidents have resulted in thousands of deaths and many thousands of injuries. It is critically important to implement sustainable alternatives to aldicarb's use now. ■

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