● INSECTICIDE FACTSHEET

MALATHION

Malathion, a pesticide in the organophosphate chemical family, is the most commonly used insecticide in the U.S. It is often used in federal and state insect eradication programs and in mosquito control programs.

Symptoms of exposure to malathion include headache, nausea and vomiting, burning eyes, difficulty breathing, and lethargy.

Malathion has caused genetic damage in a variety of laboratory studies, including a study of mice fed treated grain and studies of human blood cells.

According to the U.S. Environmental Protection Agency, there is "suggestive evidence" that malathion causes cancer. However, recent studies provide stronger evidence: a commercial malathion insecticide caused breast cancer in laboratory animals, and malathion use by farmers is associated with an increased incidence of a type of cancer, non-Hodgkin's lymphoma.

When fed to laboratory animals, malathion has striking effects on sperm. For example, it caused production of sperm with abnormal chromosomes and sperm that were unable to move.

Malathion concentrations of several parts per billion (ppb) harm fish: less than 1 ppb disrupted behavior, 4 ppb killed sensitive species, 10 ppb caused gill damage, and 20 ppb affected swimming ability.

In laboratory tests with birds, malathion disrupted normal thyroid hormone function and caused genetic damage. Also, bird populations have decreased after malathion spraying because their insect food is killed.

BY CAROLINE COX

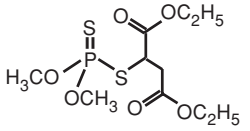
Malathion (see Figure 1) is an insecticide in the organophosphate chemical family. It is one of the oldest insecticides in that family, and has been used since 1950. Cheminova, Inc. is the major U.S. manufacturer of malathion.[1]

"Safe"[1] is a term often used to describe malathion, as are phrases such as "with proper precautions, problems should be minimal."[2] However, recent research shows that malathion poses important hazards. This article summarizes this new information.

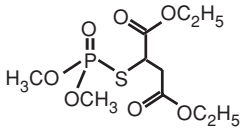
Use

Malathion is the most commonly used insecticide in the U.S.; the U.S. Environmental Protection Agency (EPA) estimates that annual use of malathion is over 30 million pounds.[3] About 60 percent of this is used in insect eradication programs (for boll weevils, grasshoppers, and fruit flies). It is also used on a variety of food crops, for mosquito control, in home yards and gardens, and to kill head lice.[4]

Figure 1
Malathion and Malaoxon



Malathion
(O,O-dimethyl phosphorodithioate of diethyl mercaptosuccinate)



Malaoxon

Mode of Action

Malathion kills insects because it is converted inside animals into malaoxon (see Figure 1), a chemical relative that inhibits an important central nervous system enzyme called acetylcholinesterase (AChE).[4] AChE is involved with the transmission of nerve impulses. When this enzyme is inhibited, the transmission system "jams," resulting in restlessness, hyperexcitability, convulsions, paralysis, and death. All insecticides in the organophosphate chemical family share a similar mode of action.[5]

In mammals, malaoxon has similar effects on AchE. However, in mammals AChE is not used in the central nervous system, but rather in nerves that connect with muscles. This means that symptoms in mammals are different than those in insects.[5]

Inert Ingredients

Like most pesticides, commercial malathion insecticides contain ingredients in addition to malathion which, according to U.S. pesticide law, are called "inert."[6] In general, they are not identified and not included in most of

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the testing required in order to register these pesticides.[7]

Hazards posed by inert ingredients in malathion-containing insecticides (based on tests with laboratory animals) include the following:

- Crystalline silica[8] is classified as a carcinogen by the International Agency for Research on Cancer and has also caused genetic damage in human and other animal cells.[9]
- Solvent naphtha[10-14] has caused irritability and depressed activity.[15]
- Naphthalene[11,12,16,17] has caused lung tumors, birth defects, and is toxic to fetuses.[18]
- 1-Butanol[19,20] has caused genetic damage, birth defects, reduced fertility, and eye irritation.[21]
- Xylenes[8,13,14,22,23] have caused birth defects, reduced fertility, miscarriages, irritability, and eye irritation.[24]
- 1,2,4-Trimethyl benzene[11,12,14] has caused genetic damage and behavioral changes.[25]

Symptoms of Exposure to Malathion

According to reports made to the California Pesticide Illness Surveillance Program between 1998 and 2001, symptoms of exposure to malathion insecticides include the following: headache, nausea and vomiting, diarrhea, dizziness, burning or watery eyes, difficulty breathing or wheezing, weakness, irritated or itchy skin, exacerbation of asthma, sore or burning throat, pallor, lightheadedness, abdominal cramps, and lethargy.[26]

Mutagenicity (Ability to Cause Genetic Damage)

The National Institute for Occupational Safety and Health (NIOSH) describes malathion as a mutagen, based on the genetic damage it caused in 29 laboratory studies published between 1978 and 1995. These studies include tests of bacteria, fruit flies, mice, hamsters, fish, and human cell cultures.[27]

Results from a variety of recent studies are consistent with those reviewed by NIOSH. A 2002 study by scientists from Assan and North-Eastern Hill Universities (India) showed that malathion given orally caused genetic damage in laboratory mice.[28] Another 2002 study, this one from Egypt's National Research Center, showed that mice fed with stored wheat that had been treated with a commercial malathion insecticide developed two kinds of genetic damage. The damage occurred at all dose levels tested in this study.[29] (See Figure 2.) Three other recent studies showed that malathion, its breakdown product malaoxon, and its contaminant isomalathion cause genetic damage in human cells. These studies, authored by scientists from the University of Vermont, the University of Lodz, and the Polish Academy of Sciences, were conducted with blood cells called lymphocytes.[30-32] (See Figure 2 for results from one of these studies.)

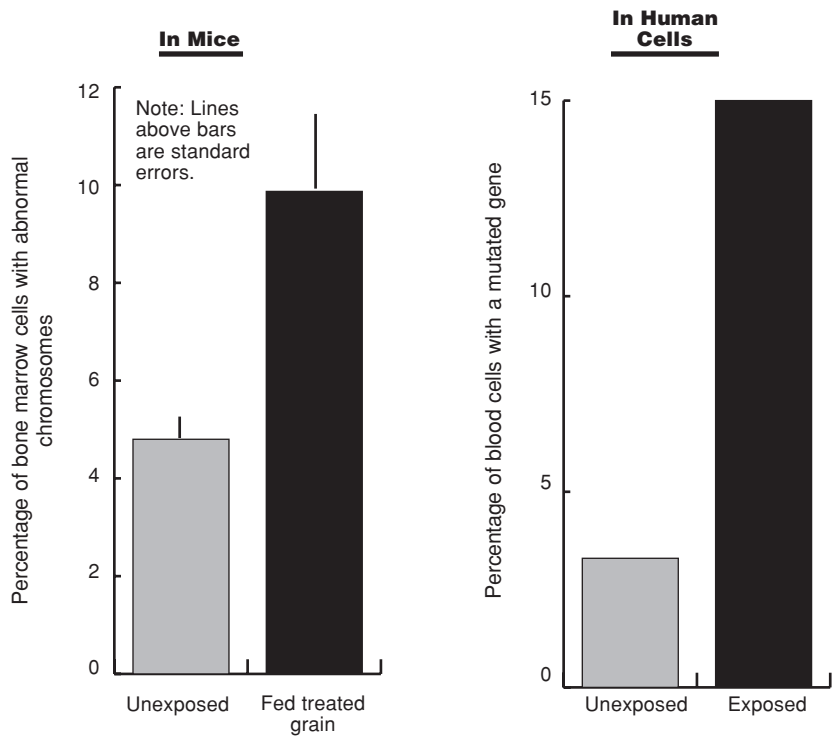
All three of the mutagenicity studies submitted to EPA by malathion's manufacturer as part of the registration process showed no "mutagenic hazard."[33]

Carcinogenicity (Ability to Cause Cancer)

In April 2000, EPA classified malathion as having "suggestive evidence of carcinogenicity but not sufficient to assess human carcinogenic potential." EPA's classification was based primarily on studies submitted by Cheminova. These studies showed that malathion caused liver tumors in both laboratory animals studied (rats and mice) at dose levels EPA considers "excessive."[34]

The results of more recent studies indicate that EPA's carcinogenicity classification should be strengthened. (See Figure 3.) A 2001 study done

Figure 2
Genetic Damage Caused by Malathion



Sources:
Amer, S.M. et al. 2002. Cytogenetic studies on the effect of feeding mice with stored wheat grains treated with malathion. *Mut. Res.* 513:1-10.
Pluth, J.M. et al. 1998. Molecular bases of *hprt* mutations in malathion-treated human T-lymphocytes. *Mut. Res.* 397:137-148.

Malathion has caused genetic damage in a wide variety of studies, including studies using laboratory animals and human cells.

Figure 3
Malathion and Cancer

Non-Hodgkin's Lymphoma in Farmers

(Percentage of farmers exposed to malathion)

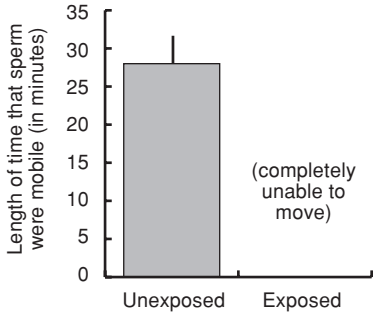
Breast Cancers in Rats

(Percentage of rats with breast cancer)

Sources:
McDuffie, H.H. et al. 2001. Non-Hodgkin's lymphoma and specific pesticide exposures in men: Cross-Canada study of pesticides and health. *Cancer Epidemiol. Biomarkers Prev.* 10:1155-1163.
Cabello, G. et al. 2001. A rat mammary tumor model induced by the organophosphorous pesticides parathion and malathion, possibly through acetylcholinesterase inhibition. *Environ. Health Persp.* 109:471-479.

Evidence for malathion's association with cancer comes from both human and laboratory studies. Farmers with the cancer non-Hodgkin's lymphoma are almost twice as likely to have been exposed to malathion as healthy farmers. In addition, a commercial malathion insecticide caused breast cancers in rats.

Figure 4
Effects on Sperm



Note: Line above bar is the standard error of the mean.

Akbarsha, M.A., P,N,L, Latha, and P. Murugaiam. 2000. Retention of cytoplasmic droplet by rat cauda epididymal spermatozoa after treatment with cytotoxic and xenobiotic agents. *J. Repro. Fert.* 120:385-390.

When rats were given malathion orally, their sperm was immobile.

by scientists at Columbia University and the Universities of Tarapacá and Concepción (Chile) found that the malathion insecticide Fyfanon increased the incidence of breast cancer in rats.[35] Another study showed that malathion caused the increase by damaging an important gene.[36]

In addition, a 2001 study by a group of scientists from an array of Canadian universities showed that men from six Canadian provinces diagnosed with the cancer non-Hodgkin's lymphoma were almost twice as likely as healthy men to have been exposed to malathion.[37] The results of the study agree with those of a study done in the 1990s in the U.S.[38]

Effects on Sperm

Recent studies have shown that malathion has a striking ability to damage sperm. A 2002 study from Egypt's National Research Center (see "Mutagenicity," above) showed that sperm from mice fed stored wheat treated with a commercial malathion insecticide had abnormal chromosomes about twice as often as did mice fed untreated wheat.[29] In 2000, scientists from Bharathidasan University (India) showed that when rats were orally given another commercial malathion insecticide, they produced sperm that were unable to move.[39] (See Figure 4.) Two additional studies, conducted at the University of Chile, found that a single dose of malathion caused mice to develop abnormal sperm.[40,41]

EPA's 2000 evaluation of malathion found that it "did not induce reproductive toxicity."[33]

Effects on Hormones

Although screening of pesticides for their potential to disrupt normal hormone function is required by law, EPA has not yet required testing of malathion for this kind of effect.[42]

Recent research, however, indicates that some hormone activities may be significantly affected by exposure to malathion. For example, a study done by a Netherlands research company found that malathion displaces sex hormones from a protein to which they normally bind in blood. This protein transports sex hormones in the blood; alterations of this activity "cause dramatic changes in the free concentrations" of these hormones.[43]

Asthma

Malathion exposure may cause wheezing, a symptom of respiratory

diseases like asthma. According to the Agricultural Health Study, a joint project of the National Institute for Environmental Health Sciences and the National Cancer Institute, malathion use is associated with the occurrence of wheezing reported by the 20,000 farm pesticide applicators in North Carolina and Iowa who are participating in this study.[44]

Based on this study, a physician from McGill University is concerned about the high insecticide exposures of people in urban areas in the U.S. and commented, "One cannot help but wonder whether exposure to insecticides in these areas may be contributing to asthma morbidity."[45]

Effects on the Immune System

In a recent comprehensive review of published research, two scientists from the University of Plymouth (UK) wrote, "Over the last 20 years experimental evidence has accumulated that OPs [organophosphate insecticides] can interfere with the immune system and cause immunotoxic effects in laboratory animals." They use malathion as an example, reviewing studies showing it causes reductions in the numbers of immune system cells, reductions in antibody responses, reductions in the activity of certain immune system cells, as well as three kinds of hypersensitivity. In general, hypersensitivity is caused by lower exposures, and the other effects by higher exposures.[46]

Special Hazards for Children

Children are more exposed to malathion than are adults. The Minnesota Children's Exposure Study found malathion breakdown products in children about five times as often as a comparable study of adults; concentrations were about 4 times higher.[47] In addition, research from Wayne State University and the Philippine Children's Medical Center showed that infants are exposed to malathion before birth.[48]

Contamination of Food

Malathion commonly contaminates food. In the U.S. Food and Drug Administration's Total Diet Study, malathion was found on 16 percent of the samples from the agency's market basket of foods purchased from grocery stores across the U.S. Only 3 of the 394 pesticides studied were detected more frequently than malathion.[49]

Researchers at the University of Georgia and Emory University found malathion in 75 percent of the meals eaten by selected individuals in the Baltimore area.[50]

Water Contamination

The U.S. Geological Survey's (USGS's) national water quality monitoring program found that malathion extensively contaminates water. Of the 36 river basins surveyed by USGS, the agency found malathion in all but two.[51] (See Figure 5.)

Urban streams are more frequently contaminated than agricultural or mixed-use streams: 21 percent of all urban stream samples were contaminated with malathion. Malathion concentrations are also higher in urban streams.[51]

In addition, USGS found malathion-contaminated groundwater in six river basins across the country.[51]

Air Contamination

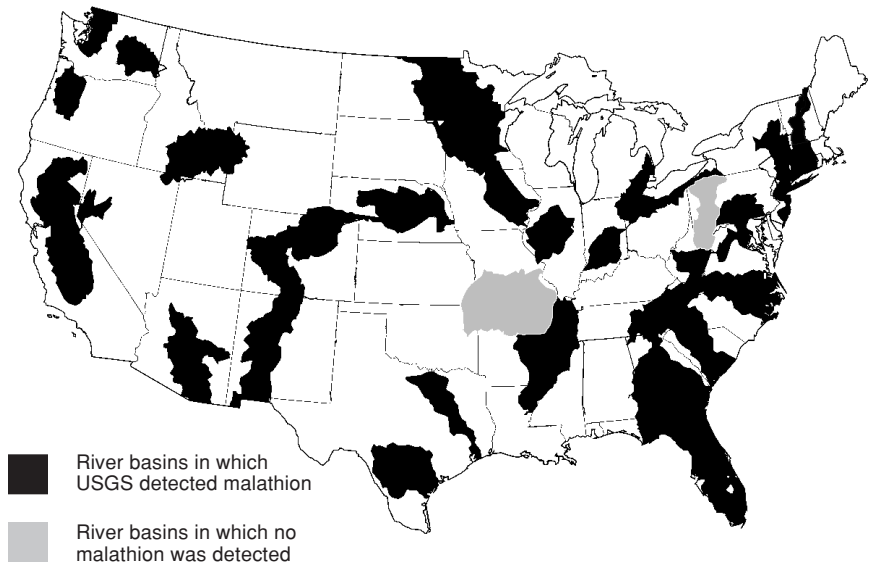
Malathion also extensively contaminates air. USGS compiled local, state, regional, and national air monitoring studies in 1995; over 80 percent of the combined samples were contaminated with malathion.[52]

Effects on Fish

Low concentrations of malathion harm fish.

Effects on fish from concentrations of a few parts per billion have been well documented since the 1970s and 1980s. For example, in 1970, EPA's Environmental Research Laboratory in Minnesota found that malathion concentrations of less than 10 parts per billion (ppb) caused deformed spines in bluegill.[53] In 1978, biologists at Northern Illinois University showed that concentrations as low as 0.25 ppb disrupted temperature selection behavior in shiners. Temperature selection is the behavior that allows fish, cold-blooded animals, to move into water

Figure 5
Water Contamination



Source: U.S. Geological Survey. National Water-Quality Assessment (NAWQA) Program. 1998-2000. Circulars 1144,1150, 1151, 1155-1171, 1201-1216. http://water.usgs.gov/pubs/nawqasum/.

Malathion is a widespread contaminant of rivers and streams.

"that is most desirable for physiological processes," including homing ability, timing of migrations, growth, and reproduction.[54] 1984 data from the U.S. Fish and Wildlife Service showed that sensitive fish species are killed by concentrations as low as 4 ppb.[55]

Recent studies with similar results include the following:

- Toxicologists from North Carolina State University showed that a malathion concentration of 1 ppb harms animals that fish use for food. In water fleas, 1 ppb significantly inhibited the transformation of the hormone testosterone, one of the hormones that regulates molting and reproduction.[56] Water fleas are an important food resource for fish, including Northwest salmon.[57]
- Biologists from Dicle University (Turkey) showed that a concentration of 10 ppb of malathion caused gill lesions in mosquitofish. This was the lowest concentration tested in this study, so it is not known whether lower concentrations have similar effects.[58]
- Scientists from the University of Missouri and the U.S. Geological Survey showed that a concentration of 20 ppb of malathion affected swimming ability of rainbow trout. This was the lowest concentration tested in this study.[59] (See Figure 6.)
- Zoologists from Panjab University (India) showed that a concentration of 50 ppb of malathion damaged red blood cells in the common fish *Channa punctatus*. Again, this was the lowest concentration tested in this study.[60]

Effects on Birds

Recent research also shows that malathion has a variety of harmful effects on birds. Malathion disrupted normal hormone activity, caused genetic damage, and reduced birds' food supply in the following studies:

- Biologists from Shizuoka University (Japan) showed that, in quail, malathion inhibits the binding of a thyroid hormone to a protein that normally transports these hormones to their target cells.[61]
- Scientists from three Indian universities showed that malathion given orally caused genetic damage in the bone marrow cells of chicks. Damage occurred following a single dose of malathion at all levels tested.[62]
- Wildlife biologists from Colorado State University studying grasshopper eradication programs in 5 western states between 1987 and 1990 found that populations of western meadowlarks decreased after malathion treatments. These "declines in bird density likely resulted from reduced food availability" when the insects the meadowlarks normally eat were killed by the malathion treatment.[63]

Effects on Frogs and Toads

Malathion suppresses the immune system in frogs and toads. For example, biologists from the Universities of Windsor and Waterloo (Canada) found that dosing northern leopard frogs in the laboratory with malathion reduced the frogs' ability to produce antibodies. The same effect was measured in frogs collected from pesticide-exposed locations.[64] Another study, from the University of Wyoming, found similar results in Woodhouse's toads; exposure to a commercial malathion insecticide disrupted immune system function and increased the incidence and severity of a bacterial disease.[65]

Effects on Earthworms

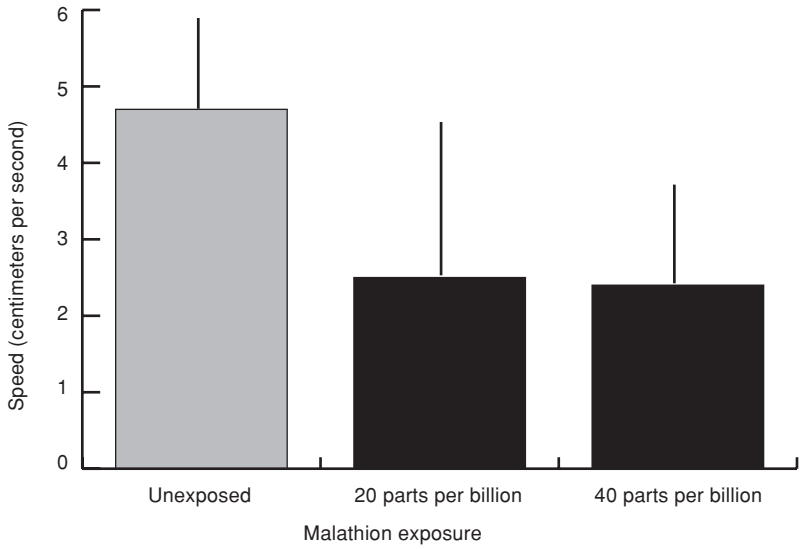
Malathion is harmful to earthworms. Scientists at Sambalpur University (India) showed that malathion treatment reduced the number of earthworms in a rice field, and decreased the rate at which they reproduced.[66]

Resistance

Insecticide resistance occurs when susceptible insects in a population are killed by an insecticide, leaving "only those that are genetically resistant to the toxicant." Resistance is then passed on to future generations of the pest population.[67]

Resistance to malathion is common. Over a hundred insect species have developed resistance to malathion, and there are more species resistant to malathion than to any other insecticides except DDT and some related chemicals.[68]

Figure 6
Effect of Malathion on Fish Swimming Speed



Source: Brewer, S.K. et al. 2001. Behavioral dysfunctions correlate to altered physiology in rainbow trout (*Oncorynchus mykiss*) exposed to cholinesterase-inhibiting chemicals. *Arch. Environ. Contam. Toxicol.* 40:70-76..

Malathion affects important fish behaviors, including how fast they swim.

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