● EDITORIAL

EMC0314

REGULATION FAILS US, AGAIN … REJUVENATION OF AN ANTIQUE HERBICIDE

Often when my phone at NCAP rings, the person on the other end asks me, "Is this pesticide better than that one?"

I have an answer to that kind of question: "NCAP promotes alternatives. All the pesticides I know about have problems. How can I decide if a pesticide that causes cancer, say, is better or worse than one that keeps salmon from spawning? Let's talk about alternatives, not which pesticide is better."

But even as I repeat the answer, I know that some pesticides have been used so widely and studied so much that we know enough to give them a special black mark.

2,4-D is one of those pesticides. It first gained notoriety as part of Agent Orange, the Vietnam War defoliant. Used for decades, both on farms and on millions of lawns, about a quarter of us carry 2,4-D in our bodies at any given moment.

Natural Resources Conservation Service; Agri-Fab

2,4-D: a common and problematic pesticide.

Studies over the years have documented a long list of problems. 2,4-D exposure is linked with genetic damage, disruption of sex hormones, immune system problems, cancer, low sperm counts, and birth defects.

2,4-D is also contaminated with dioxin, one of the most potent chemicals toxicologists have ever studied. It's frequently found in rivers and streams, in the air, and even inside our houses. It's been linked with cancer in pets, destruction of birds' food and shelter, toxicity to fish, damage to frogs' eggs, and mutations in plants. Not a pretty chemical. (For details, see the article on the next six pages.)

Last June, the U.S. Environmental Protection Agency (EPA) completed a review of 2,4-D that the agency, at least in theory, has been working on since Congress mandated these reviews in 1972. Any of you who are familiar with how EPA typically treats pesticides will not be surprised to find out that EPA essentially gave 2,4-D a clean bill of health.

There are many parts of this review that are tilted so far towards the pesticide industry that they leave me silently screaming at my desk. But probably the most frustrating is the story of EPA's waffling about whether or not 2,4-D causes cancer.

Cancer and 2,4-D first made headlines in the 1980s when the National Cancer Institute did a couple of studies to understand why non-Hodgkin's lymphoma (a cancer) was especially common among farmers. Use of 2,4-D was one of the risk factors the agency identified. Although some studies since then have not found this link, enough have been consistent with the earlier studies to raise a red flag. Scientists have also observed that 2,4-D causes cellular changes that promote cancer.

EPA's response to these studies was characteristically slow. The agency asked 2,4-D manufacturers to do more cancer tests (laboratory tests; not tests of exposed farmers). The tests took years to complete, and even longer for EPA to evaluate. EPA finally reviewed 2,4-D's ability to cause cancer in 1997 and concluded, as only a bureaucratic agency can do, that it wasn't possible to decide if 2,4-D caused cancer or not. Although this classification is usually given to pesticides that need more tests, EPA didn't require further tests of 2,4-D and is leaving 2,4-D in cancer limbo forever.

EPA has also failed to take action about 2,4-D's other health problems. The agency noted that 2,4-D disrupted hormone function, reduced the activity of the immune system, and affected development of the brain in infants and children. In all these areas, the only action EPA took was to ask for more studies.

Cancer limbo? More studies? How long will this go on? The profits to the pesticide industry from the sale of 2,4-D continue, as they have for over 50 years. To me, it clearly demonstrates that U.S. pesticide regulation has failed to protect us, our children, and the environment.

—Caroline Cox

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● HERBICIDE FACTSHEET

2,4-D

2,4-D is one of the most widely used herbicides in the world. It is commonly used on rangeland and pasture, in the production of wheat, and on home lawns.

Symptoms of 2,4-D poisoning in exposed people include irritation and inflammation of eyes and skin, hives, nausea, vomiting, throat irritation, headache, dizziness, coughing, and difficulty breathing.

In laboratory animals, human cells, and exposed people 2,4-D caused genetic damage. Scientists have also demonstrated that 2,4-D affects hormones in exposed people and laboratory animals. Three recent laboratory studies indicate that 2,4-D has the ability to reduce the effectiveness of the immune system.

2,4-D (and the entire family of phenoxy herbicides) is classified as possibly carcinogenic by the International Agency for Research on Cancer. Studies of exposed farmers support this classification.

New studies indicate that 2,4-D reduces fertility in several ways. 2,4-D exposure is associated with low sperm counts. 2,4-D also damaged sperm and male sex organs in laboratory studies. When low doses of a commercial 2,4-D herbicide were fed to pregnant laboratory animals, average litter size was reduced by about 20 percent.

According to the most recent data collected by the U.S. Environmental Protection Agency, some 2,4-D is contaminated with 2,3,7,8-TCDD, a potent dioxin.

Monitoring by the U.S. Geological Survey showed that 2,4-D is frequently found in rivers and streams. It is also often measured in air samples.

2,4-D use on lawns is linked with an increased risk of cancer in dogs.

2,4-D causes genetic damage in plants in amounts too small to cause visible damage to the plants.

BY CAROLINE COX

2,4-D (see Figure 1) is a chlorophenoxy herbicide. This herbicide family is said to have "initiated an agricultural revolution"[1] when it was first marketed in the 1940s. 2,4-D is also commonly used in weed and feed products[2] and is "one of the most widely used herbicides in the world."[1] There are over 600 2,4-D products currently on the market.[2]

Scope of this Article

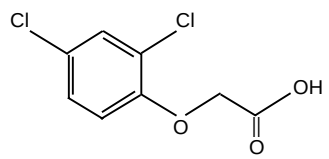
This article focuses on research published since 2000 that identifies hazards of 2,4-D use.

Use

2,4-D is used to kill broadleaf weeds.[2] Typically, grasses and their relatives are not killed by 2,4-D.[1]

The U.S. Environmental Protection Agency (EPA) recently estimated 2,4-D use based on data collected during the 1990s. A total of 46 million pounds of 2,4-D are used every year in the U.S.; about two-thirds of this is used in agriculture. Major uses include about 11 million pounds used on range and pasture, about 8 million pounds used by homeowners on their lawns, about 7 million pounds used in wheat production, and about 3 million pounds used by lawn care companies.[2]

Figure 1
2,4-D



2,4-dichlorophenoxyacetic acid

How Does 2,4-D Kill Plants?

According to EPA, 2,4-D kills plants by increasing three characteristics of the plant: the plasticity of the cell walls, the amount of proteins being made in the plant, and the amount of ethylene being produced by the plant. The effect of these changes is to cause cells to divide and the plant to grow uncontrollably. The end result is that the tissues of the plant are damaged and death occurs.[2]

Forms of 2,4-D

There are eight salts and esters of 2,4-D, in addition to 2,4-D itself (an acid), that are used as herbicides.[3] Most toxicology tests use the acid

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"INERT" HAZARDS IN 2,4-D HERBICIDES

Chemical Name	Health Hazards Identified in Laboratory Tests Compiled by the National Institute for Occupation Safety and Health
Amorphous silica	Diarrhea, tears, and obstruction of lung blood vessels
Aromatic solvent naphtha	Reduced fertility, reduced litter size, and reduced growth of newborns
Attapulgite-type clay	Cancer and tumors
1,2-Benzisothiazolin-3-one	Genetic damage in human cells, skin sensitization
n-Butyl alcohol	Severe eye irritation, genetic damage in hamsters, reduced fertility, developmental abnormalities; depressed activity
Butyl cellosolve	Severe eye irritation, genetic damage in bacterial tests, sperm damage, reduced fertility, and developmental abnormalities
Diesel Fuel No. 2	Tumors
Dimethylpolysiloxane	Diarrhea
Ethylene diaminetetra-acetic acid	Genetic damage in laboratory animals, developmental abnormalities, and reduced fertility
Ethylene glycol	Genetic damage in laboratory animals and human cells, developmental abnormalities, reduced litter size, effects on testes, reduced fertility, diarrhea, nausea, headache, reduced liver function, and damage to corneas
Hexylene glycol	Severe eye irritation, reduced kidney function
Hydrogenated aliphatic solvent	Some evidence of cancer in laboratory animals
8-Hydroxyquinoline sulfite	Genetic damage in bacterial tests and human cells
Kerosene	Severe skin irritation, genetic damage in bacterial tests, coughing, nausea, depressed activity, muscle weakness, and anemia
Kerosene/Fuel Oil No. 1	Skin inflammation
Methyl oleate	Leukemia, tumors
Methyl salicilate	Severe skin irritant, reduced newborn survival, reduced fertility, developmental abnormalities,and liver degeneration
Mineral spirits	Kidney damage, skin inflammation, and anemia
Octylphenol polyethoxylate	Genetic damage in human cells and laboratory animals, developmental abnormalities, and skin inflammation
Polyethoxylated isodecyl alcohol	Severe skin and eye irritation
Propylene glycol	Genetic damage in laboratory animals, reduced fertility, high blood sugar levels, anemia, and tumors
Quartz silica	Genetic damage in laboratory animals and human cells, cancer, lung fibrosis, diarrhea, and coughing
Sodium benzoate	Genetic damage in laboratory animals and human cells, developmental abnormalities, and reduced newborn survival
Sodium lignosulfonate	Genetic damage in laboratory animals, and reduced liver function
Titanium dioxide	Genetic damage in laboratory animals, cancer, tumors, and diarrhea

Inert ingredients in 2,4-D products identified by EPA Office of Prevention, Pesticides, and Toxic Substances's Public Information and Records Integrity Branch in response to NCAP's Freedom of Information Act request RIN-1178-99. Response dated January 28, 2004.

Hazards of inert ingredients taken from National Institute for Occupational Safety and Health's Registry of Toxic Effects of Chemical Substances. Accessed through NISC International, Inc's BiblioLine Basic Chemical Information System, www.nisc.com. Query done on November, 2005 by Chemical Abstract Services (CAS) numbers 7631-86-9 , 64742-95-6,12174-11-7, 2634-33-5, 71-36-3, 111-76-2, 68476-34-6, 63148-62-9, 60-00-4, 107-21-1, 107-41-5, 64742-47-8, 134-31-6, 8008-20-6, 64742-81-0, 112-62-9, 119-36-8, 8052-41-3, 9002-93-1, 61827-42-7, 57-55-6, 14808-60-7, 532-32-1, 8061-51-6, and 13463-67-7.

form of 2,4-D. This article will identify other forms when they are used.

Inert Ingredients

Most commercial 2,4-D herbicides contain ingredients other than 2,4-D. According to U.S. pesticide law, many of these ingredients are called "inert."[4] Typically these ingredients are neither identified on pesticide labels nor included in most of the health and safety testing required to register a pesticide.[5,6]

NCAP has identified some of the inert ingredients used in 2,4-D products through the Freedom of Information Act. For hazards of some of these chemicals, see "'Inert' Hazards in 2,4-D Herbicides," left.

Symptoms of 2,4-D Poisoning

A review of chlorophenoxy herbicide incidents reported to poison control centers in the U.S. found that about 2,000 poisoning incidents are reported every year. (2,4-D is the most common herbicide in this family.)[7]

EPA's summary of 2,4-D poisoning incidents describes the most common symptoms as irritation, inflammation, and itching of eyes and skin. Other symptoms include hives, nausea, vomiting, throat irritation, headache, dizziness, coughing, and difficulty breathing. Eye exposures are more problematic than skin exposures.[8]

Mutagenicity (Ability to Cause Genetic Damage)

In its recent review of 2,4-D, EPA concluded that "2,4-dichlorophenoxyacetic acid was not mutagenic."[9] However, other recent evidence points to a different conclusion:

- The National Institute for Occupational Safety and Health labels three forms of 2,4-D (the acid, the sodium salt, and the dimethylamine salt) as mutagens.[10]
- Research from the University of Minnesota found that the frequency of a chromosome rearrangement in pesticide applicators was correlated with the level of 2,4-D in their urine.[11]
- Scientists at the Institute for Medical Research and Occupational Health (Croatia) found that a commercial 2,4-D herbicide caused chromosome breaks in human blood cells.[12]

- Two studies (from the National Research Centre (Egypt) and the Bulgarian Academy of Sciences showed that 2,4-D caused chromosome breaks in mouse bone marrow.[13, 14]

Effects on Hormones

EPA's discussion of 2,4-D's ability to disrupt the normal functioning of hormones concludes: "Based on currently available toxicity data, which demonstrate effects on the thyroid and gonads [sex organs], there is concern regarding its endocrine disruption potential."[15] This conclusion is based on tests of laboratory animals sponsored by 2,4-D manufacturers showing that 2,4-D decreased levels of thyroid hormones and decreased the size of sex organs.[16]

Other recent research showing that 2,4-D has effects on hormones includes a study of 2,4-D applicators. The study, led by a University of Minnesota researcher, showed that 2,4-D exposure increased levels of a sex hormone in these applicators.[11]

Another University of Minnesota study shows that two commercial 2,4-D herbicides act like estrogens (sex hormones) in breast cancer cells.[17]

In addition, a recent study from the Netherlands shows that 2,4-D has the ability to displace sex hormones from the protein that normally transports these hormones in the blood.[18]

Effects on the Immune System

In EPA's recent review of 2,4-D, the agency asked 2,4-D manufacturers to conduct an additional laboratory test to address concerns about 2,4-D's toxicity to the immune system.[15]

However, research has already demonstrated that 2,4-D has significant effects on the immune system:

- Led by a toxicologist from the University of Saskatchewan, a team of Canadian researchers showed that exposure to "environmentally realistic" amounts of 2,4-D reduced the activity of at least three human genes that produce proteins with important immune system functions.[19]
- Scientists from the National Institute for Occupational Safety and Health and West Virginia University showed that 2,4-D decreased the production of cells that make antibodies in the bone marrow of mice.[20] (See Figure 2.) 2,4-D exposure also decreased the numbers of certain immune system cells made in the thymus.[21]

Carcinogenicity (Ability to Cause Cancer)

Whether exposure to 2,4-D causes cancer has been a controversial question for decades. In 1987, the International Agency for Research on Cancer classified all phenoxy herbicides, including 2,4-D, as "possibly carcinogenic to humans."[22] This classification was based primarily on studies of people who were exposed at work to phenoxy herbicides.[22] EPA evaluated 2,4-D's carcinogenicity in 1997 and concluded that 2,4-D is "not classifiable as to human carcinogenicity."[23]

Meanwhile, research continues to suggest that exposure to 2,4-D poses cancer concerns.

One type of research focuses on people who work with 2,4-D. A study led by a scientist from the University of Saskatchewan found that risk of the cancer non-Hodgkin's lymphoma was increased by exposure to 2,4-D. (See Figure 3.) This study confirms the results of four earlier studies that found a similar link.[24] A second study, conducted by an EPA researcher, found that increased cancer rates were associated with phenoxy herbicide use on farms. (This study used wheat acreage to estimate phenoxy herbicide use because 2,4-D and related herbicides are commonly used on wheat.)[25]

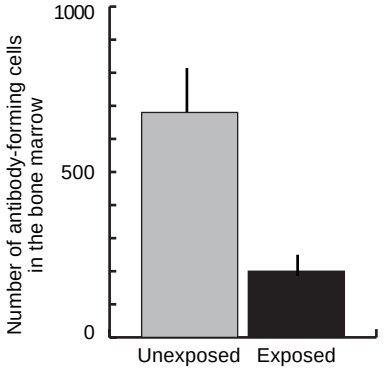
Other recent research has focused on how 2,4-D exposure affects cells in ways that promote cancer. A study led by a researcher at St. Louis University showed that rapid and repeated division of blood cells occurs in pesticide applicators who use 2,4-D.[26] These results were confirmed by laboratory tests in a study led by a researcher at the University of California, Berkeley.[27] A study led by a researcher at the Medical College of Ohio found that 2,4-D increased the activity of a tumor gene in the liver.[28]

Effects on Sperm

Effects of 2,4-D on sperm have been identified in studies of both exposed people and laboratory animals.

A study led by a physician at the University of Missouri compared 2,4-D exposure (as measured by urine 2,4-D

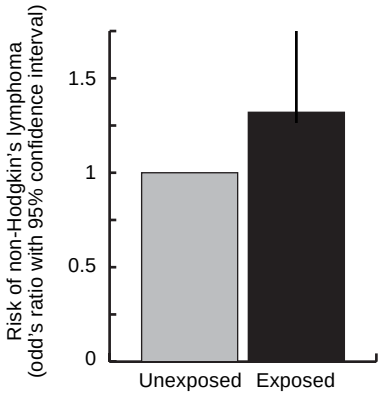
Figure 2
2,4-D and the Immune System



Salazar, K.D. et al. 2005. The polysaccharide antibody response after *Streptococcus pneumoniae* vaccination is differentially enhanced or suppressed by 3,4-dichloropropionanilide and 2,4-dichlorophenoxyacetic acid. *Toxicol. Sci.* 87:123-133.

In laboratory tests, 2,4-D reduced the production of antibodies, chemicals used to fight off infection.

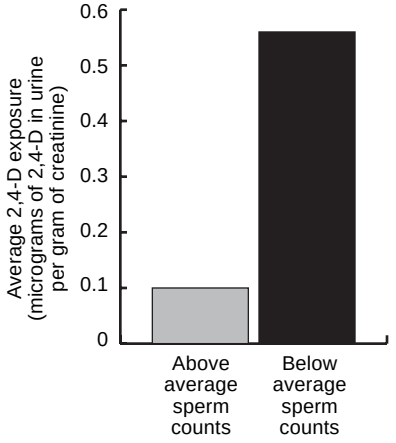
Figure 3
2,4-D and Cancer



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. Biom. Prev.* 10:1155-1163.

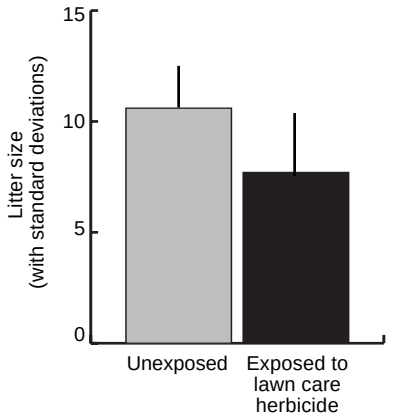
In a study of Canadian men, exposure to 2,4-D was associated with an increased risk of non-Hodgkin's lymphoma.

Figure 4
2,4-D and Low Sperm Counts



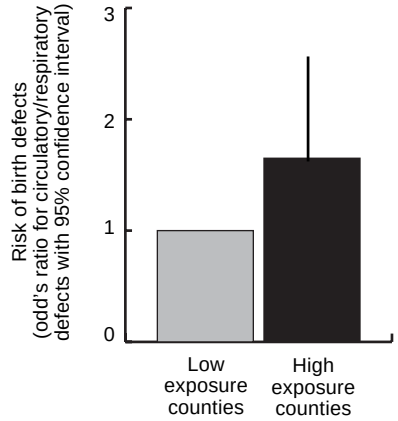
Swan, S.H. 2003. Semen quality in relation to biomarkers of pesticide exposure. *Environ. Health Persp.* 111:1478-1484.

Figure 5
2,4-D and Pregnancy Success



Cavieres, M.F., J. Jaeger, and W. Porter. 2002. Developmental toxicity of a commercial herbicide mixture in mice: 1. Effects on embryo implantation and litter size. *Environ. Health Persp.* 110:1081-1085.

Figure 6
2,4-D and Birth Defects



Schreinemachers, D.M. 2003. Birth malformations and other adverse perinatal outcomes in four U.S. wheat-producing states. *Environ. Health Persp.* 111:1259-1264.

2,4-D exposure has been linked with low sperm counts and birth defects. It also reduces fertility in laboratory tests.

levels) with sperm counts. The study found that men with low sperm counts had 2,4-D levels five times as high as those found in men with above average sperm counts.[29] (See Figure 4.)

In addition, EPA lists a variety of effects on male sex organs that were identified in laboratory tests sponsored by 2,4-D manufacturers. These include atrophy of the testes, degeneration of sperm-producing tissues, and decreased numbers of sperm in the testes.[30] 2,4-D also caused an increase in the numbers of abnormal sperm in a study conducted at the National Research Centre (Egypt).[13]

Effects on Children

Some of the most troubling concerns about 2,4-D are its potential to harm children:

- **Pregnancy problems**. EPA's recent review of 2,4-D did not identify significant pregnancy problems caused by 2,4-D exposure except to note that spontaneous abortions increased in rabbits following high-dose exposure.[30]

  However, research from the University of Wisconsin-Madison shows that environmentally relevant exposures to a commercial 2,4-D herbicide reduced litter size in laboratory animals. The study used a lawn care product containing three herbicide chemicals (2,4-D, mecoprop, and dicamba) and an unknown number of inert ingredients. When pregnant animals drank water during their pregnancies containing small amounts of this herbicide, their litters were about 20 percent smaller than litters from animals drinking uncontaminated water.[31] (See Figure 5.)
- **Birth defects**: An EPA researcher studying birth defects in rural parts of Minnesota, Montana, North Dakota, and South Dakota showed that defects related to the respiratory and circulatory system were more common in counties with high 2,4-D use than in low-use counties. Wheat acreage was used as an estimate of 2,4-D use.[32] (See Figure 6.)
- **Contaminated breast milk**: Two recent studies (one of rats, done at the University of Rosario [Argentina][33] and the other of goats, sponsored by a 2,4-D manufacturer[34]) show that mothers exposed to 2,4-D produce 2,4-D-contaminated milk. The Argentine study also showed that 2,4-D moved from the milk to the blood and brain of the offspring.[33]
- **Brain development**: EPA states that "there is a concern for developmental neurotoxicity resulting from exposure to 2,4-D."[35] (Developmental neurotoxicity is the ability of chemical exposures in the womb or during childhood to affect the developing brain and nervous system.) EPA's only response to this concern was to require another study from 2,4-D manufacturers.[35]

  However, a series of studies by researchers at the University of Rosario have already demonstrated that 2,4-D exposure impacts brain development. Recent studies show that exposure of laboratory animals during pregnancy and nursing affected neurotransmitters[36,37] (the chemicals that allow nerve impulses to move between cells in the brain), reduced brain size,[38] and disrupted developing connections between nerve cells in the brain.[39]

Dioxin Contamination

According to EPA, 2,4-D is contaminated with dioxin (2,3,7,8-TCDD),[40] a stunningly toxic molecule. 2,3,7,8-TCDD, according to the National Institute of Occupational Safety and Health, is carcinogenic, mutagenic, and causes reproductive problems at minute doses.[41]

EPA's data dates from the 1990s and

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shows that 2 out of 8 samples of 2,4-D analyzed were contaminated with 2,3,7,8-TCDD. Other related dioxins were also found. 2,4-D is the seventh largest source of dioxin in the U.S.[40]

Dioxins have also been found in a Japanese 2,4-D herbicide.[42]

Contamination of People

According to a survey conducted by the Centers for Disease Control and Prevention, about 25 percent of Americans carry 2,4-D in their bodies. (See Figure 7.) Levels of 2,4-D are higher in children than they are in adults.[43]

Contamination of Rivers, Streams, and Wells

2,4-D is found in rivers and streams in both agricultural and urban areas. The U.S. Geological Survey's (USGS's) national water quality monitoring program found 2,4-D in about 15 percent of the samples the agency collected in agricultural areas. Urban streams were contaminated equally often.[44]

Wells are also contaminated by 2,4-D, according to USGS, but not as often as rivers and streams.[45]

Contamination of Air

USGS compiled air monitoring data from across the country in 1995. The agency found that 2,4-D contamination of air is widespread; almost 60 percent of the samples in the USGS compilation were contaminated with 2,4-D.[46] (See Figure 8.)

Indoor Contamination

Although 2,4-D is used outdoors, it can be tracked inside after lawn care applications and contaminate homes. Researchers from EPA and Battelle Memorial Institute found 2,4-D on dust particles in the air inside homes after lawn treatments, as well as on tables, window sills, and floors.[47]

Drift Problems

Drift of 2,4-D is common. When the Association of American Pesticide Control Officials surveyed state pesticide agencies in 1999, 2,4-D was one of the top five pesticides involved in drift incidents in over 26 states.[48]

Effects on Pets

2,4-D is linked with both cancer and testicular problems in dogs.

Veterinarians from Purdue University studying bladder cancer in Scottish terriers showed that exposure of terriers to lawns treated with phenoxy herbicides is associated with an increased risk of bladder cancer. The risk of this cancer was four times greater in exposed dogs than in unexposed dogs. The results of this study are consistent with an earlier study showing that use of 2,4-D herbicides on lawns was associated with another cancer, lymphoma, in dogs.[49]

According to laboratory studies sponsored by 2,4-D manufacturers, exposure to 2,4-D also decreases the size of testicles in dogs.[50]

Effects on Birds

Although EPA recently concluded that "risks to birds from 2,4-D exposure are not of concern,"[51] 2,4-D impacts birds when its use alters the plant community that provides birds with food and shelter.

For example, reviews done by USGS regarding the sage-grouse state that "spraying of herbicides [often 2,4-D] not only eliminates large blocks of sagebrush, leading to increased habitat fragmentation, but also may poison insects and other invertebrates eaten by sage-grouse."[52]

In another review, USGS noted that 2,4-D spraying caused changes in what Brewer's sparrows eat, reducing their consumption of insects.[53]

Effects on Fish

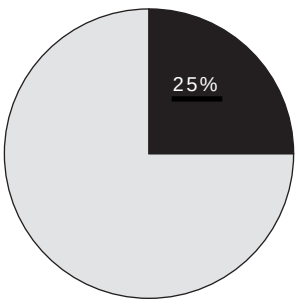
EPA requires 2,4-D products to be labeled with a warning about toxicity to fish.[54] Recent research shows that some of these toxic effects occur at minute concentrations.[55]

Researchers at the University of Maryland looked at an effect called "peroxisomal proliferation" in fish. This term refers to an increase in certain specialized cell structures and has been associated with disruptions of sex hormones and development. In this study effects occurred at a concentration of only 10 parts per billion.[55]

Effects on Frogs

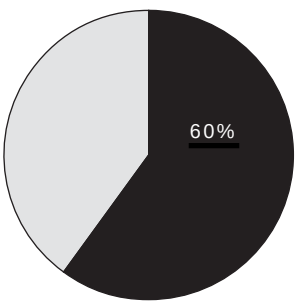
EPA's review of 2,4-D states the 2,4-D is "practically non-toxic"[56] to frogs. However, recent research shows that 2,4-D has troubling effects on frogs. Researchers at Willamette University showed that 2,4-D interferes with a sex hormone and stops frog eggs from

Figure 7
2,4-D in Our Bodies



Department of Health and Human Services. Centers for Disease Control and Prevention. 2005. Third national report on human exposure to environmental chemicals. http://www.cdc.gov/exposurereport/.

Figure 8
2,4-D in Air



Majewski, M.S. and P.D. Capel. 1995. *Pesticides in the atmosphere: Distribution, trends, and governing factors.* Chelsea, MI: Ann Arbor Press. Pp. 78-79.

A surprising number of Americans carry 2,4-D in their bodies. It is also frequently found in studies of air contamination.

maturing.[57]

Effects on Plants

As an herbicide, it is not surprising that 2,4-D damages plants. What is surprising is that 2,4-D can cause genetic damage to plants at concentrations "that did not have any visible physiological effects."[58] Biologists at the University of Lethbridge (Canada) showed that 2,4-D caused mutations in a mustard at concentrations as low as 3 parts per billion, below drinking water guidelines in Canada.[58]

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