



Breast Cancer and Environmental Risk Factors

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FACT SHEET #14

Q & A's from the Cornell University Program on Breast Cancer
and Environmental Risk Factors in New York State

Pesticides and Breast Cancer Risk, An Evaluation of 2,4-D

What is 2,4-D?

2,4-D (2,4-dichlorophenoxyacetic acid) is one of the most widely used herbicides in the United States (U.S.). Herbicides are chemicals used to control weed growth. 2,4-D belongs to the group of related synthetic herbicides called *chlorophenoxy herbicides*. The chemical structure of 2,4-D resembles indoleacetic acid, a naturally occurring hormone produced by plants to regulate their own growth. This resemblance allows 2,4-D to artificially regulate plant growth. Some of the common trade names of 2,4-D containing products sold in the U.S. are Chloroxone, Salvo, Weed-no-More and Aqua-Kleen. While 2,4-D itself is rapidly broken down in the soil, 2,4-D preparations made before the mid-1970s were often contaminated with more persistent chemicals called dioxins.

What is the history of 2,4-D's use?

2,4-D was originally developed in 1941 to increase plant growth. Soon, it was discovered to have an even more useful role in agriculture as an herbicide to control weed growth. A mixture of 2,4-D and a related chemical called 2,4,5-T was found to be a more effective herbicide than 2,4-D alone. This mixture was called Agent Orange and was used by the U.S. during the Vietnam War to increase the visibility for war planes by destroying plant undergrowth and crops. The usage of 2,4-D and 2,4,5-T increased through the next 15 years. In response to its potential to cause cancer, and other health concerns, use of 2,4,5-T was banned by the U.S. Environmental Protection Agency (EPA) in 1983. Although 2,4-D use has been allowed to continue by the EPA, its health effects are under review.

How is 2,4-D used currently?

During the early 1990s, 42 million pounds of 2,4-D were used per year on U.S. croplands making it the fourth most used herbicide in U.S. agriculture. At the same time, the annual use of 2,4-D in New York State was estimated to be 141,665

pounds, making it the seventh most used herbicide in this state. 2,4-D's primary use in agriculture is to control weeds in wheat and corn fields. It is used, but much less so, in orchards to prevent fruits from dropping prematurely. 2,4-D has many non-agricultural uses; it is used to control weeds in forests, rangelands/pastures, parks, athletic fields, golf courses, ponds and lakes, and to clear land for roadways and railway tracks. In addition, it is used in home lawns and gardens, to control broad-leaf weeds like dandelions. The EPA has estimated that 12 to 28 million pounds of 2,4-D is used each year in non-agricultural settings.

How do federal agencies regulate 2,4-D to protect the consumer?

The EPA has required that before 2,4-D is approved for re-registration, health effects from its exposure must be re-examined in experimental animals. Meanwhile, the Industry Task Force II on 2,4-D Research Data (ITF) has agreed to a recommendation by the EPA to put new labels on all 2,4-D containing products. The guidelines on these new labels are designed to help the consumer use the product correctly and with minimal exposure. The U.S. Occupational Safety and Health Administration (OSHA) regulates 2,4-D levels in the workplace. The EPA sets the maximum level of 2,4-D that is allowed in public drinking water supplies. This *maximum contaminant level* for 2,4-D is set at no more than 70 micrograms of 2,4-D per liter of drinking water (one microgram is one-millionth of a gram, one liter of water is approximately one quart). The U.S. Food and Drug Administration (FDA) and the U.S. Department of Agriculture (USDA) monitor the levels of 2,4-D in domestic and imported foods.

Who might be exposed to 2,4-D?

People who were most likely to have been exposed to this chemical in the past are:

- Workers involved in the manufacture of 2,4-D



- Pesticide applicators who treated lawns, turf, recreational areas, highways and railways with 2,4-D
- Agricultural and forestry workers who treated fields or forests with 2,4-D, or worked in fields or forests that were being sprayed
- Homeowners who treated their lawns and gardens with 2,4-D containing products
- People who handled or laundered 2,4-D-contaminated clothing
- Vietnam War veterans who sprayed Agent Orange, and military personnel and civilians who were on the ground in areas that were being sprayed with Agent Orange
- Individuals who used lawns or recreational areas too soon after 2,4-D application

How can we be exposed to 2,4-D today?

Since 2,4-D is still in use, the way people are exposed to 2,4-D today is not very different from the past. Those who work in manufacturing plants, or as herbicide applicators, forestry, agricultural, and lawn care workers, could be exposed to 2,4-D if not properly protected. People who apply 2,4-D to their own lawns and do not wear appropriate protective clothing can be exposed to 2,4-D. Homeowners should read and follow the package instructions on the proper use, storage, and disposal of weed killers that contain 2,4-D. These instructions guide the user on ways to minimize exposure through the use of protective clothing, proper laundering of soiled clothes, and limiting access to treated areas after application. Since 2,4-D does not persist in the environment and does not accumulate in animal fat, food is unlikely to be a major source of exposure for humans.

Does 2,4-D cause cancer in animals?

2,4-D fed to laboratory mice over long periods of time did not cause tumors. One study observed an increased incidence of a type of brain tumor called “brain astrocytoma” in male rats fed 2,4-D for two years. However, these results could not be repeated in a second study on rats that were fed higher doses of 2,4-D.

In a highly debated study, a small increase in the incidence of a type of blood cancer called canine lymphoma was observed in pet dogs of owners whose lawns were frequently treated with 2,4-D. This increase was seen only in the dogs that were allowed access to areas that had been treated with 2,4-D. However, this study relied on homeowners to remember the pesticides that they had used years ago, and

was criticized for the lack of information on the actual exposure of the dogs to 2,4-D and other lawn chemicals.

2,4-D may act with other carcinogens to “promote” lung tumors in mice. Urethan is a known cancer-causing substance (carcinogen). Mice that were exposed to a commercial formulation of 2,4-D in drinking water, followed by an injection of urethan, developed more lung tumors than the mice that were injected with the same carcinogen, but not given 2,4-D.

Does 2,4-D cause cancer in humans?

There are no reports that indicate a direct link between 2,4-D exposure and cancer in humans. However, there is some concern about the higher rates of a type of cancer called non-Hodgkin’s lymphoma among farmers, agricultural workers, manufacturing workers and pesticide applicators who were previously exposed to 2,4-D. But results from different studies are not consistent. While one half of the studies indicated higher rates of non-Hodgkin’s lymphoma among populations exposed to 2,4-D, the other half did not. Often in these studies, 2,4-D exposure was accompanied with exposure to many other chemicals, including other pesticides and dioxin contaminants of 2,4-D. This makes it difficult to assess whether exposure to 2,4-D, some other chemical, or another factor caused the increase in cancer rates reported in some of the studies. The incidence of non-Hodgkin’s lymphoma needs to be followed further in studies of workers who were exposed to 2,4-D during its manufacture or application.

Most studies have not found a relationship between exposure to the group of chlorophenoxy herbicides and the development of a type of cancer called soft-tissue sarcoma in humans. These studies did not look at exposure to 2,4-D alone, but included populations exposed to 2,4-D and other related herbicides.

Does 2,4-D cause breast cancer?

No differences have been reported in breast cancer rates of women who were previously exposed to 2,4-D through their occupation in either agriculture, manufacture of chlorophenoxy herbicides or service in Vietnam during the war. The few studies that have been done so far are not adequate to assess the risk of breast cancer, since they studied very small groups of women who had been exposed to many other chemicals besides 2,4-D.

One study initially reported an increase in the combined number of benign and cancerous breast tumors in female rats



fed high levels of 2,4-D over a long period of time compared to rats not fed 2,4-D. On re-analysis, the incidence of cancerous breast tumors alone was not found to be significantly higher in the animals fed 2,4-D. The EPA has concluded that this study was not valid because it was not conducted according to animal testing guidelines. Later studies did not observe an increase in the number of breast tumors in animals treated with 2,4-D. Therefore, there is no clear evidence that 2,4-D causes breast tumors in experimental animals.

How can 2,4-D affect breast cancer risk?

Lifetime exposure to the female hormone estrogen has been linked to an increase in breast cancer risk. Estrogen is a female hormone that helps control the reproductive cycle and breast growth. There is a concern that synthetic chemicals that can act like estrogen or affect the body's level of estrogen may also increase a woman's risk of developing breast cancer. In one laboratory test, 2,4-D did not act like estrogen. A study that has been published only as a short summary has reported that 2,4-D could disrupt the length of hormone-dependent reproductive cycles in female rats. There are many possible causes for such disruptions and these results do not indicate that 2,4-D was estrogenic. Further studies are needed in rats to determine the reason for the disruption of the length of reproductive cycles by 2,4-D, and the relevance of the disruption to breast cancer risk.

The immune system of the body plays an important role in the body's defense system against cancer. There is a concern that chemicals that damage the immune system may affect cancer risk. One study observed that farmers exposed to 2,4-D and MCPA (another chlorophenoxy herbicide) had weaker immune systems for short periods of time following exposure. Further studies are needed to evaluate if the changes in the immune system caused by 2,4-D persist, and if they affect the risk of breast cancer or other cancers.

Is 2,4-D present in breast milk?

2,4-D does not persist or accumulate in the breast tissue or breast fat. No studies, to our knowledge, have reported its presence in human milk.

Conclusions

Current evidence does not indicate that exposures to 2,4-D are linked with an increase in incidence of breast cancer in humans or in experimental animals. The few studies of women who were exposed through their occupation to 2,4-D and other chemicals have not shown an increase in incidence of breast

cancer. 2,4-D fed to experimental animals over long periods of time did not cause an increase in the incidence of breast tumors. There is very limited evidence that 2,4-D can act as a tumor promoter and affect the immune system. Further studies are needed to understand these mechanisms and to determine if they affect breast cancer risk.

Where is more research needed?

- Large-scale studies are needed on breast cancer incidences among women who were exposed primarily to 2,4-D, and in women with a well-documented history of 2,4-D-exposures.
- There is some evidence that 2,4-D can act with carcinogens as a lung tumor "promoter" in mice. Further animal studies are needed to determine if 2,4-D can act as a mammary gland tumor promoter in combination with breast carcinogens (chemicals known to cause breast cancer).
- Animal studies are needed to determine if 2,4-D can cause long-term damage to the body's immune system and, if the damage affects the animal's ability to fight cancer.

Is more research being done?

- The National Institutes of Health (NIH) have recently funded a study on the incidences of cancers that involve the immune system among agricultural workers exposed to 2,4-D.
- A large scale, long-term study in Iowa and North Carolina will investigate the health effects, including cancer incidences, of 2,4-D use among farmers, wives of farmers, and male and female pesticide applicators.
- 2,4-D is often applied along with other herbicides. An animal study will evaluate the health effects of 2,4-D in combination with another herbicide, MCPA.

How can I minimize exposure to 2,4-D?

- If you treat your lawn with 2,4-D, follow the manufacturer's guidelines on the product label to minimize exposure to yourself, family members and pets.
- Wait for a calm, wind-free day to apply any products that contain 2,4-D.
- Remove clothes that are soiled during application of the herbicide immediately, and launder them separately.
- Avoid using recreational areas and lawns that are marked with flags or signs as having been freshly treated with herbicides.



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Please note: An extensive bibliography on 2,4-D and Breast Cancer Risk is available on the BCERF web site (<http://www.cfe.cornell.edu/bcerf/>).

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