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Pesticides and Breast Cancer: Prevention is Crucial

PESTICIDES AND BREAST CANCER: PREVENTION IS CRUCIAL

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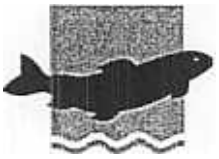

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This report is published by the Northwest Coalition for Alternatives to Pesticides. NCAP is a nonprofit, five-state regional organization that promotes sustainable resource management, prevention of pest problems, use of alternatives to pesticides, and the right to be free from pesticide exposure. NCAP strives to substantially reduce or eliminate the use of pesticides as a preferred method of pest control in the Northwest and elsewhere.

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The photograph on the front cover of this report was taken by Lise Beane from the Women's Community Cancer Project (Boston, Massachusetts). The photograph shows participants at the Massachusetts Breast Cancer Coalition's Stop the Epidemic March and Rally in 1994.

The illustration on page 4 is by Kate Pryka.

PESTICIDES AND BREAST CANCER: PREVENTION IS CRUCIAL

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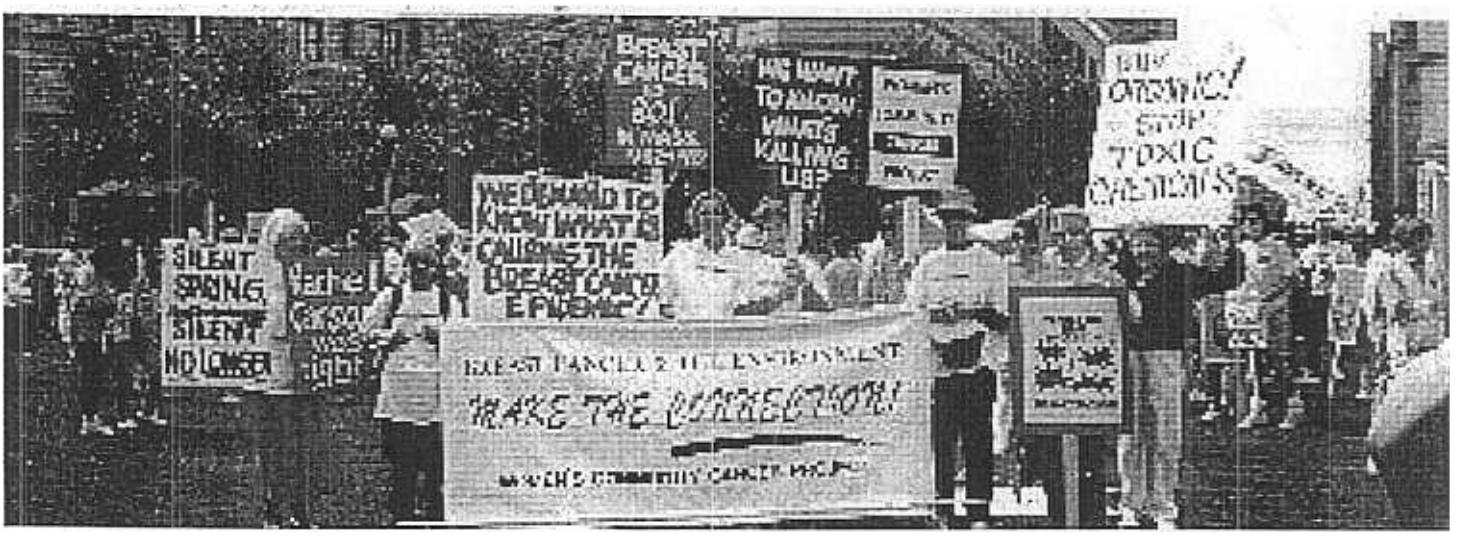

NCAP

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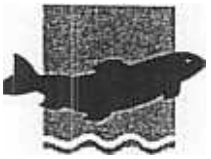
EXECUTIVE SUMMARY



Breast cancer is a disease whose frequency has been increasing in the U.S. for the last forty years. Recent research indicates that we have an opportunity to prevent some of this disease.

A series of studies has shown that women who have been exposed to higher levels of the organochlorine insecticide DDT have a risk of breast cancer that is between two and four times the risk of cancer in women with lower exposures.

Laboratory studies indicate that DDT and its breakdown products promote the formation of a hormone, nicknamed "bad" estrogen, that is linked with breast cancer.

This research gives us the opportunity to set policies that will reduce our risk of breast cancer:

We need to reduce our exposure to DDT and related chemicals, and stop using other pesticides that cause breast cancer in laboratory tests. The herbicide atrazine is particularly important: it is nearly as potent as the most potent breakdown product of DDT in promoting formation of the "bad" estrogen, is one of the most widely used pesticides in the U.S., and has extensively contaminated U.S. wells and rivers.

We need to support farmers as they develop and implement successful and cost-effective alternative pest management techniques.

Our emphasis must be on preventing breast cancer.

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EVIDENCE OF A LINK

Cancer is a word that strikes fear in the hearts of most Americans. Most of us have either struggled with the disease or know and love someone who has. It's a mysterious disease, and often invisible. It requires treatments that seem worse than the disease itself. It strikes people who are healthy in other ways and often robs them of years of life.

Breast cancer is no different. Over 180,000 U.S. women are diagnosed with breast cancer every year;[1] it is the most prevalent cancer in U.S. women.[2] Over the last two decades, the incidence of breast cancer has increased at a rate of nearly 2 percent per year.[3] (See Figure 1.) In 1940, a women's lifetime risk of breast cancer was 1 in 16; that figure has now risen to 1 in 8.[4]

No one should live in fear. What is needed instead is a good hard look at the causes of breast cancer so that as individuals, as a country, and as a planet we can make changes in our personal habits and in our country's pesticide policies that will prevent this terrible disease. This report looks at the evidence scientists have recently collected that indicates pesticides may cause breast cancer, and the implications this research has for pesticide policy.

A series of studies completed in the last five years has showed an association between breast cancer risk and a woman's exposure to organochlorine insecticides. These studies are what's known as epidemiology. They are not controlled laboratory studies; instead they attempt to correlate real-life exposures and cancer risks.

The first well-publicized study was done in Israel by two scientists, Jerome Westin and Elihu Richter, at the Hebrew University School of Medicine.[5] They were interested in what they call the "Israeli breast-cancer anomaly." During the late 1970s and early 1980s, Israel's breast cancer rate, particularly in young women, was much higher than that of other countries. While data from most countries showed there was a strong association between the amount of fat in a typical diet and the incidence of breast cancer among young women, data from Israel indicated there was about twice as much breast cancer as might be expected from a typical Israeli diet. Remarkably, this high rate of breast cancer dropped significantly between 1976 and 1986, a time when breast cancer rates were rising in most other countries.

Westin and Richter looked at a number of the factors that are usually associated with breast cancer risk and found that they had changed during this period of time, but in such a way that the changes should have resulted in more breast cancer, not less.

Then they looked at levels of three organochlorine insecticides in milk: DDE (a major metabolite of DDT), lindane, and α-HCH (α–hexachlorocyclohexane, a chemical relative of lindane also known as α–benzene hexachloride). In the mid-1970s, Israeli milk had some of the highest levels of these insecticides in the world; mean levels were 5 to 100 times greater than those found in U.S. milk at the time. Israeli women also had higher levels of these insecticides in their breast milk. In 1978, "public outcry followed by the threat of Supreme Court action resulted in the banning first of alpha-BHC, then of lindane, from the cowshed." Contamination levels in cow and breast milk dropped precipitously (up to 98 percent) by 1980. Westin and Richter believed that the drop in breast cancer resulted from this decline.

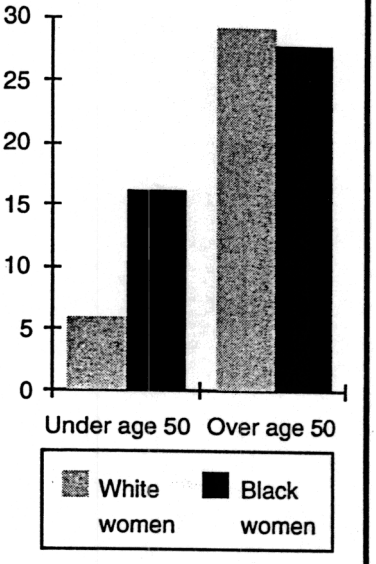
A 1990 study from Finland also showed a relationship between organochlorine insecticides and breast cancer. Dr. Mussalo-Rauhamaa and his co-workers found that tissue from 40 breast cancer patients had higher levels of the organochlorine insecticide β-HCH than tissue from women without breast cancer. DDD and DDT levels did not differ.[6]

In 1992, Frank Falck, a doctor at the University of Michigan, and his co-workers completed a pilot study of the relationship between pesticides and breast cancer in the U.S.[2] The study looked at the levels of six organochlorine compounds in breast fat tissue taken from women who were undergoing surgical biopsies of suspected breast cancer or mastectomies. Levels in 20 women who were diagnosed with breast cancer were compared with levels in 20 women who were diagnosed with benign breast disease.

The study found that average concentrations of DDE and DDT were from 50 to 60 percent higher (almost 1900 parts per billion (ppb) compared to about 1200 ppb) in women who had breast cancer. They calculated that a 10 ppb increase in the DDE concentration of breast fat corresponded to a 1 percent increase in breast cancer risk.

Figure 1
Increase in Breast Cancer Incidence

(percent increase between 1973 and 1990)



Source: Adamson, R.H. 1993. Statement before the Subcommittee on Health and the Environment, Committee on Energy and Commerce. U.S. House of Representatives. Washington, D.C. (Oct. 21.)

One of Falck's co-workers, Mary Wolff from New York's Mount Sinai School of Medicine, went on to lead a more in-depth study of the relationship suggested by the Falck study.[7] From over 14,000 participants in a women's health study conducted by New York University, they selected 53 who had been diagnosed with breast cancer within six months of joining the study. (The study enrolled women between 1985 and 1991.) They used blood samples that had been frozen and stored since the beginning of the study and compared organochlorine levels in the blood of these 53 women to those of 173 study participants who did not develop breast cancer.

The results of the study supported the results of the Falck study: DDE levels were about 35 percent higher in women who were later diagnosed with breast cancer. Wolff calculated that each 0.1 ppb increase in DDE levels in blood resulted in a 0.9 percent increase in breast cancer risk. Blood levels of DDT-related compounds are about 200 times less than levels in fat tissues because they are stored most readily in fat tissue.[8] This means these results are similar to those of the Falck study.[7]

Wolff also collaborated on a larger study that was completed in 1994.[9] Led by Nancy Kreiger from the Kaiser Foundation Research Institute in California, the study made use of a collection of over 50,000 frozen blood samples that had been collected by the Kaiser Permanente Medical Care Program as part of in-depth health examinations between 1964 and 1969. Kreiger's study looked at organochlorine levels in the blood samples of 150 women who were diagnosed with breast cancer following their exam, but before 1991. Each breast cancer patient was matched with a control patient, a patient not diagnosed with breast cancer, and the organochlorine levels compared. The study was designed to look for potential differences between racial groups, so equal numbers of white women, black women, and Asian women were studied.

Blood levels of DDE were much higher than those measured in the earlier U.S. studies. These high levels occurred because body burdens were much higher when these samples were collected (in the late 1960s), since DDT was still being used in the U.S.[9] Overall, the study found no differences in DDE levels between women who were diagnosed with breast cancer and women who were not. In white women and black women, however, the risk of breast cancer was between 2 and 4 times as great for women who had the highest DDE levels as compared to women with the lowest DDE levels.[10] (It should be noted that the difference was not statistically significant.) Asian women typically have very different breast cancer risks than other ethnic and racial groups; researchers believe that their diets may lower their risk.[1] The increase in risk in white and black women was about the same size as that measured in the earlier Falck and Wolff studies.[9]

A recent study from Quebec, Canada, also found a relationship between breast cancer and DDT. Dr. Eric Dewailly and coworkers found that levels of the DDT breakdown product DDE were three times higher in 9 women with hormone responsive breast cancer than in 17 women with benign breast disease.[11]

Overall, how much does DDT exposure increase a women's risk of breast cancer? The relative risks calculated in these studies for women with the highest DDT exposure are between 2 and 10. This means that their risk of breast cancer is between 2 and 10 times the risk faced by a women with low DDT exposure. These risks, when compared to other known risk factors for breast cancer, are "among the higher risks for breast cancer observed in the epidemiologic literature."[12]

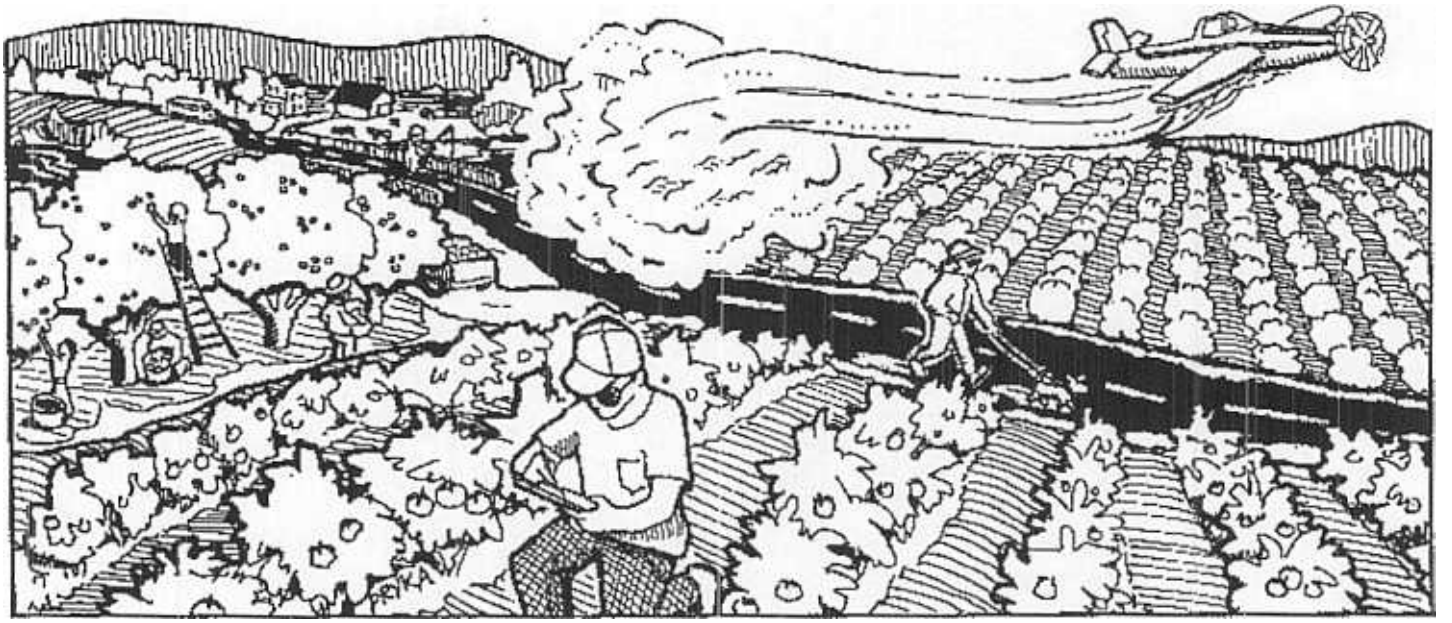
UNDERSTANDING HOW DDT INCREASES BREAST CANCER RISK

Taken as a whole, these epidemiological studies provide evidence that there is a strong association between a woman's exposure to certain organochlorine insecticides, particularly DDT, and her risk of breast cancer. Epidemiology, however, is not able to provide answers to questions about cause and effect; there is always the possibility that DDT exposure did not *cause* the increased breast cancer risk. Instead, both high DDT levels and cancer risk might be caused by an unknown or unstudied third factor. Only a controlled experiment is able to establish a cause. Obviously, a controlled experiment exposing women to organochlorines intentionally to determine breast cancer risk is out of the question.

So scientists next look to see if there is a realistic mechanism that can explain how DDT might cause breast cancer. If a sound mechanism is documented, the mechanism (together with the association provided by the epidemiology) provides strong support for the hypothesis that increased DDT exposure causes an increased risk of breast cancer.

When scientists began looking for a mechanism by which exposure to DDT could increase breast cancer risk, the group of hormones known as estrogens seemed a likely place to start.[1] Estrogens are produced mainly by women's ovaries and are responsible for the development and maintenance of secondary sexual characteristics and behavior. For example, women's menstrual cycles are regulated by rising and falling levels of several hormones. Estrogens refer to a whole family of compounds; one potent estrogen produced by women is called estradiol.[13]

Most of the known risk factors for breast cancer involve in one way or another an increase in the amount of estrogen, primarily estradiol, to which a woman is exposed during her lifetime. These include such factors as age (older women, who have had a higher total exposure to estrogen, have a higher risk of breast cancer than younger women), an early onset of menstruation (estrogen production begins early), late menopause (estrogen production ends late),[1] and long-term use of synthetic estrogens (estrogen replacement therapy).[14] Diets high in animal fat or alcohol have also been associated with higher risks of breast cancer.[1] Since fat cells make estrogen,[1] and alcohol can increase estrogen production,[15] these risk factors may also be associated with estrogen exposure. Known risk factors that do not appear to be related to estrogen are inheritance of the "breast cancer gene," a gene that greatly increases the risk of breast cancer in young women, and exposure to X-rays or other radiation.[16] Known risk factors only account for about 30 percent of breast cancer cases,[17] so



looking at other sources of estrogen exposure seems reasonable.

This is not to say that estrogen is unhealthy - obviously it is necessary for the normal functioning of women's bodies. But it does indicate that it may be easy to get too much of a good thing. DDT and related compounds have long been known to have estrogenic effects; the first of these studies was done in the late 1960s.[8] Compounds like DDT that have estrogenic effects but are not made by biological processes are called xenoestrogens. The estrogenic activity of DDT seemed like a reasonable starting point when looking for a mechanism by which DDT exposure might increase breast cancer risk.

Recent research by Leon Bradlow of New York's Strang-Cornell Cancer Research Laboratory (together with four co-workers) has documented such a mechanism.[18] Bradlow began his research after Wolff completed the 1993 epidemiological study mentioned above. Bradlow was convinced that DDT could not really increase a woman's breast cancer risk, and he studied mechanisms as a way of showing that the epidemiological association must be caused by something else. "I was wrong," Bradlow said after finishing the study.[19]

The study looked at two products that can be formed during the breakdown of the common estrogen estradiol. One of these breakdown products (2-hydroxyestrone) has minimal estrogenic activity[17] and is not toxic to genetic material (genes). The other (16α-hydroxyestrone) is a fully potent estrogen, produces tumors, and is toxic to genes. The two estrogens have been nicknamed "good" and "bad" estrogen in analogy with the "good" and "bad" cholesterols that have received much recent publicity. Women with breast cancer have nearly five times as much of the "bad" estrogen in their breast tissues as do women without cancer.[18]

Bradlow's study showed that o,p'-DDT (a chemical making up about 15 percent of commercially-produced DDT[8]), p,p'-DDE, and o,p'-DDE (both are long-lasting breakdown products of DDT) change the way that estrogen is broken down in human cells. In normal cells, there is only a little more "bad" estrogen than there is "good" estrogen. When the DDT-like chemicals were added, the ratio between the two types of estrogen increased, and there was between 8 and 15 times as much of the "bad" estrogen as there was of the "good" estrogen.[18]

Additional research has shown that o,p'-DDT also causes certain cells in the mammary glands of adolescent rats to increase in number (proliferate).[20] This proliferation "may be a critical factor in chemical carcinogenesis."[20] Four DDT-related compounds, p,p'-DDT (which makes up about 85 percent of commercially-produced DDT[8]), o,p'-DDT, p,p'-DDE, and o,p'-DDE, cause human breast cancer tissue culture cells to proliferate.[21]

Although there is not yet a scientific consensus,[22] these mechanism studies together with the epidemiology studies provide solid evidence that DDT exposure may increase breast cancer risk. This increased risk is an unnecessary risk. It's time to develop and implement pesticide policies that will prevent our exposure and reduce our risk of breast cancer.

POLICY RECOMMENDATIONS

We can significantly reduce our exposure to pesticides linked with breast cancer in three important areas:

• **Stop using DDT.** DDT's uses in the United States were canceled in 1972.[23] Since the amount of DDT used and the amount in American women's bodies has declined since then, the risk of breast cancer should also be declining. However, DDT is still used outside the U.S. and residues come to the U.S. on produce, in the blood and tissues of migratory animals, and on contaminated dust particles blown globally by the wind. A recent study of the global distribution of organochlorine insecticides in tree bark found that residues were ubiquitous and not limited to areas where DDT is still being used.[24] High concentrations of the DDT breakdown product DDE were found in parts of the midwestern and southwestern U.S.[24]

•Stop using DDT.

There are several steps the U.S. can take to reduce American's exposure to DDT. The U.S. needs to strengthen residue standards for DDT and its breakdown products on commodities entering the U.S. Because the U.S purchases a large amount of imported food, this will discourage its use in other countries. U.S. agricultural aid packages also need to be built around nonchemical methods of managing pests.

• **Stop using insecticides related to DDT.** Certain insecticides that are chemically related to DDT are still in widespread use in the U.S. Methoxychlor is used for insect control on fruit and vegetable crops, on shade trees, and in dairy barns.[25] Endosulfan is used on vegetable crops.[21] Endosulfan and methoxychlor have both shown estrogenic activity in laboratory tests using breast cancer cell cultures;[20] methoxychlor has also shown a variety of estrogenic effects in laboratory animals.[26-28] We need immediate action to end the use of these pesticides in the U.S. and abroad. Government policies should cancel uses of these insecticides in the U.S. and reduce legal contamination levels on imported food. These policies need to be coupled with worldwide educational programs that give farmers the tools they need to successfully use more sustainable pest management practices.

•Stop using insecticides related to DDT.

• **Stop using other pesticides linked with breast cancer.** Sixteen currently-used pesticides have been linked with breast cancer in laboratory tests. (See pp. 10-11 for a complete list.) Most compelling are the triazine herbicides, some of the most commonly used herbicides in the U.S. Atrazine is used on corn, sugar cane, and sorghum. Simazine is used on corn, citrus orchards, and nut orchards. Cyanazine is used on corn and cotton.[29] While triazine herbicides do not appear to be estrogenic,[21] all three of these herbicides have been shown to cause mammary tumors in female rats;[29] atrazine has also caused mammary tumors in male rats.[30] Atrazine was nearly as potent as DDE in promoting the formation of the "bad" estrogen that is linked to breast cancer. Atrazine in particular, and the other triazines, often contaminate water. Many studies of stream and river water in the Midwest's corn belt have found atrazine in over 90 percent of the samples analyzed. Atrazine was the second most commonly detected pesticide in the U.S. Environmental Protection Agency's (EPA's) national survey of drinking water wells.[29]

•Stop using other pesticides linked with breast cancer.

When EPA proposed to initiate the process of examining the triazines' cancer risks to see if more regulatory actions were required (this process is called a Special Review), they received 80,000 comments mostly opposing the Special Review.[31] Many of these comments were from farmers stating that they would suffer economic damages if the use of triazine herbicides were further restricted.

EPA now needs to hear from, and take notice of, the millions of women at risk of breast cancer. Alternatives to the use of these herbicides exist and are profitable. The U.S. should not engage in the almost science fiction-like task of weighing a woman's breast cancer risks against pesticide manufacturers' profits. We need to stop using these herbicides and support farmers who are using the many successful and cost-effective alternatives that are available.

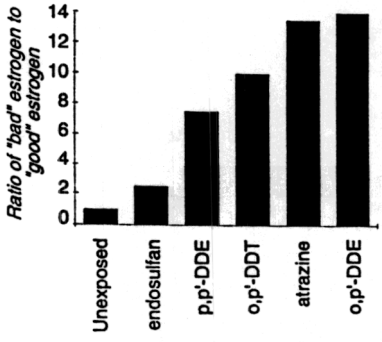
•Use alternatives to pesticides.

"If reducing avoidable exposures to xenoestrogens made it possible to avert only 20 percent of breast cancers every year," wrote cancer researchers Devra Lee Davis and H. Leon Bradlow, "at least 36,000 women — and those who care about them — would be spared this difficult disease, and the public would be spared the burgeoning expenses of treatment and care. Such prospects are too tantalizing to ignore."[1] It is rare that we, as a nation, have the ability to prevent a disease. We must seize this opportunity and take the steps necessary to prevent pesticide-related breast cancers.

•Emphasize prevention of breast cancer.

CURRENTLY-USED PESTICIDES LINKED WITH BREAST CANCER

Figure 2
Effect of Pesticides on "Good" and "Bad" Estrogen in Breast Cancer Cells



Source: Bradlow, H.L. et al. 1995. Effects of pesticides on the ratio of 16α/2-hydroxyesterone: A biologic marker of breast cancer risk. *Environ. Health Persp.* 103(Suppl. 7):147-150.

Endosulfan, atrazine, and DDT all promote the formation of "bad" estrogen. In this experiment, concentrations between 2 and 4 parts per million were used.

Atrazine is a triazine herbicide used in the production of corn and sorghum.[32] Atrazine is the most heavily-used (total annual use, by weight) pesticide in U.S. agriculture.[33] Feeding atrazine to rats caused increases in benign and malignant mammary gland tumors in females.[32] One study found that it increased the incidence of typically rare benign mammary tumors in males.[30] Atrazine is nearly as potent as the DDT breakdown product DDE in promoting the formation of the "bad" estrogen, 16α-hydroxyestrone, that has been linked with breast cancer.[18] (See Figure 2.)

Cyanazine is a triazine herbicide used primarily on corn.[34] It "ranks in the top five most commonly used pesticides in U.S. agricultural production."[34] Feeding of cyanazine to rats caused a significant increase in malignant mammary gland tumors in females.[32] Cyanazine production in the U.S. will end by December 31, 1999; use will continue for three additional years.[34]

1,3-Dichloropropene (Telone) is a soil fumigant[35] and is one of the top ten pesticides used in U.S. agriculture.[33] It causes mammary tumors in mice and rats.[36]

Dichlorvos is an organophosphate insecticide used in greenhouses, on fruit and vegetable crops, on livestock, and as a fumigant. It has been used to make pet flea collars and pest strips.[37] Feeding of dichlorvos to rats caused an increase in mammary gland tumors in females.[38]

Endosulfan is an insecticide used on a strikingly wide variety of fiber, fruit, and vegetable crops.[39] It is the fifth most commonly detected pesticide on U.S. produce.[40] It is estrogenic in laboratory tests (causes breast cancer cells to increase in number)[21] and promotes formation of the "bad" estrogen linked to increased risk of breast cancer.[18]

Ethalfluralin is an herbicide used prior to planting in the production of soybeans, dry beans, and sunflower seeds. Feeding of ethalfluralin to rats caused mammary gland tumors.[41]

Ethylene oxide is a fumigant and sterilant used to fumigate spices and sterilize cosmetics and hospital equipment. A study in which female mice inhaled ethylene oxide showed that the frequency of mammary gland tumors, as well as several other cancers, was increased.[42]

Etridiazole (Terrazole) is a fungicide. It is applied to soil and is also used to treat seeds.[35] Feeding of etriadiazole to rats caused an increase in mammary tumors.[36]

Methoxychlor is an insecticide closely related to DDT. Production and use in the U.S. totals about a half million pounds per year; about 60 percent of this is used in agriculture.[43] Methoxychlor causes breast cancer tissue culture cells to increase in number.[21]

Oryzalin is a dinitroaniline herbicide. Major uses include turf, almond orchards, and grape vineyards. Feeding of oryzalin to rats increased the incidence of mammary gland tumors in females.[44]

Prometon is a triazine herbicide.[35] In feeding studies with rats, it causes mammary tumors in females.[36]

Propazine is a triazine herbicide used prior to planting in the production of sorghum, as well as after planting in carrots, celery, and fennel. Feeding of propazine to female rats increased the incidence of benign and malignant mammary gland tumors.[45]

Simazine is a triazine herbicide used to kill unwanted plants in corn production; in fruit, nut, and citrus orchards; and in non-crop areas.[32] It is one of the 25 most heavily-used (total annual use, by weight) agricultural pesticides in the U.S.[33] Feeding rats simazine caused an increase in the incidence of malignant mammary gland tumors in females.[32]

Terbuthylazine is a triazine herbicide used to kill algae in commercial cooling towers, ponds, fountains, and aquariums. In female rats, feeding of high doses increased the incidence of malignant mammary gland tumors.[46]

Terbutryn is a triazine herbicide used to kill unwanted plants prior to planting of sorghum and on uncultivated land.[35] In a feeding study using rats, terbutryn increased the number of malignant mammary gland tumors.[47]

Tribenuron methyl (Express) is a sulfonylurea herbicide used primarily in wheat and barley production. Feeding of tribenuron methyl to rats caused an increase in the frequency of malignant mammary gland tumors in females.[48]

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