

ENVIRONMENTAL ESTROGENS AND BREAST CANCER

Presented by Daryl Sumner, Ph.D., DABT

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INTRODUCTION

Anti-chemical activists have initiated an extensive campaign to associate pesticide exposure with estrogenicity and breast cancer. An activist group is holding public meetings in several U.S. cities (Pope, 1995). Bills declaring the association are proposed in California and New York. In contrast, published scientific reports show that women with the highest exposures to pesticides do not have increased incidences of breast cancer mortality (Rubin, 1993; Cantor, 1995).

BIOLOGICAL EFFECTS OF ESTROGEN

Estrogens are the class of hormones responsible for the development of female sexual characteristics and are involved in reproductive cycling. The physiological responses to estrogen include preparation of the uterus for implantation of a fertilized egg.

THERAPEUTIC USE OF ESTROGENS

In human females, secretion of estrogen essentially stops after menopause. Replacement estrogen therapy often is used to ease the discomfort of menopause and reduce the risks of heart disease, osteoporosis and some gastro-intestinal cancers. Therapeutic use of estrogen increases the risks of endometrial cancer and possibly breast cancer; however, most medical authorities believe that these risks are outweighed by the benefits of estrogen therapy. Estrogens also are a component of birth control pills.

PRESENCE OF ESTROGENIC COMPOUNDS

Many estrogenic compounds are found in foods. Endogenous animal estrogens usually are steroid hormones, and plants also produce estrogenic compounds (Jones, 1992). Most plant phenols are estrogenic and several are found in vegetables, grains, tree crops and tubers. Some synthetic chemicals also show estrogenic properties (Davis, 1993). (Some compounds, natural and synthetic, block the action of estrogens and are considered anti-estrogens. Examples include tamoxifen -- used to treat breast cancer -- and dioxin).

THRESHOLD EFFECTS OF ESTROGENS

Hormones exert their effects by binding to biological "receptor sites" and triggering a response. For

the response to occur, concentrations of hormones must reach sufficient levels, and a sufficient number of "sites" must be activated. Endocrine effects are threshold mediated; that is, below a critical concentration, there is no biological effect and a sufficient concentration must be achieved before any response occurs. Animals possess both male and female hormones; only those hormones which exceed the threshold concentrations produce biological effects (Goodman and Gilman, 1990).

ESTROGENIC POTENCY

Estrogenic compounds vary considerably in regard to potency. For instance, if estradiol (a standard estrogen) potency is equal to 1, ethinyl-estradiol (used in birth control pills and estrogen replacement therapy) is ten times more potent and would be 10. Correspondingly, DDT is much weaker than estradiol and has a potency factor ranging from 0.0001 (Kupfer and Bulger, 1982) to 0.000001 (Safe, 1995), depending upon the laboratory model used. This means that in order to "trigger" the estrogen receptor, the body would need concentrations of DDT up to 1,000,000 times higher than estradiol. Corresponding calculations can be made for plant estrogens (potency range from 0.01 to 0.0001), showing how foods can be consumed without adverse effects (Jones, 1992). Potency calculations show a daily birth control pill to have about 10 billion times more estrogenic activity than the dietary intake of organochlorine pesticides (Safe, 1995). While foods containing endogenous estrogens can be eaten without apparent risk, this cannot be said for some estrogenic mycotoxins. Zearalenone-contaminated (estrogenic NOEL 0.05 mg/kg/day) feedstocks have produced adverse effects in swine (Dacasto, 1995). Interestingly, pesticides have been shown to reduce the amount of zearalenone in tomatoes (El-Morshedy and Aziz, 1995). This effect sets up some intriguing questions about dietary estrogenic intake and pesticide use.

PESTICIDE USE IS NOT ASSOCIATED WITH BREAST CANCER

A few reports are frequently cited to link pesticides to breast cancer. A study by Wolff (1993) makes a correlation between DDT blood levels and the diagnosis of breast cancer. A larger study by Kreiger (1994) showed no such correlation. No increases in breast cancer are seen in areas where pesticides, including DDT, have been used most heavily. In Asia, DDT was used to control mosquitoes for many years after it was banned in the U.S. Yet Asia has very low mortality from breast cancer. In Europe, at the end of World War II, much of the military and civilian population was treated directly with DDT to prevent disease, and no subsequent epidemic of breast cancer was observed. The use of DDT to control insects that carry typhus was credited with saving more than 12,000,000 lives in the 1940s (Mellanby, 1992). The U.S. stopped using DDT in 1972. If the DDT/breast cancer correlation were correct; a decrease in breast cancer should have been seen in the U.S. The demographics of breast cancer in the U.S. (Tanne, 1993) also indicate that pesticide use is not correlated with breast cancer. Urban areas have a higher risk of breast cancer than rural. Rural women have the same exposure routes as urban women, plus the associated occupational exposures: proximity of use, washing exposed clothes and working on farms. Northern states have higher breast cancer rates than southern states. Growing seasons are longer and pests are present longer in southern regions; this leads to greater pesticide use in the south today, just as in the days of DDT. Breast cancer is more prevalent in wealthy Americans than poor Americans. Intuitively, one would expect that less affluent Americans are more exposed to pesticides.

Epidemiological studies examining breast cancer mortality and chemical exposure have not generally found an association. A study by NIOSH examined the relationship between occupation and breast cancer; it found that the odds ratio for women involved in forestry, farming and fishing was 0.84 (Rubin, 1993). This means that women working in these jobs had a probability of cancer mortality which was 16 percent less than the nation as a whole. Forestry and farming have opportunities for much higher pesticide exposure than the general population. Cantor et al., of the National Cancer Institute, examined the data base for specific compound associations and did not detect any increased risk associated with pesticide exposure (herbicides and insecticides were considered). Of

course, one cannot draw final conclusions from these studies, since they do not prove the null hypothesis. However, it is difficult to rationalize how the higher-exposed groups consistently show lower mortality from breast cancer if pesticides were causative.

IDENTIFICATION OF ESTROGENIC ACTIVITY

Several tests among the standard toxicology studies required for pesticide registration are capable of detecting estrogenic activity. Although reproduction studies should show the effect of hormone imbalance, multigeneration studies would be the most sensitive. Avian reproduction studies would also detect estrogenic activity. In addition, weights of organs with hormone-sensitive tissue are measured in the range finding, subchronic and chronic studies. Considering that maximum tolerated doses are used in the toxicology studies, estrogenic activity relevant to human, animal or ecological effects would be detected in these standard tests.

CONCLUSIONS

The data show that a cause/effect relationship between pesticide and breast cancer is very unlikely. Yet, many individuals feel that resources should be directed toward this unlikely relationship because breast cancer is so significant and without many established causes. In fact, it is because breast cancer is so important that the best science available should be utilized to help learn its causes and cures. If resources were devoted to "chasing the pesticide shadow," such efforts would divert valuable public and private funds from approaches or programs which could help combat this tragic disease.

AFTERTHOUGHT: ECOLOGICAL EFFECTS OF ESTROGENS

Estrogenic effects on ecological systems have been presented by some individuals and groups. However, conclusions concerning environmental effects require that all of the following steps be developed:

- a) Determine the type of effect.
- b) Identify agents which could be responsible.
- c) Establish a dose response relationship.
- d) Show that environmental concentrations match the effect.

In general, the claims of environmental effects address items a) and b), but items c) and d) frequently are not considered. Without c) and d), one cannot eliminate unmeasured factors as causative. Point sources of sufficient magnitude could cause localized effects, so these types of claims need to be fully evaluated.

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American Association of Pesticide Safety Educators (AAPSE)

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