A review of research and literature linking breast cancer to pesticides

Patricia L. Pellegrino-Peard

Follow this and additional works at: https://scholarworks.lib.csusb.edu/etd-project

Part of the Environmental Education Commons

Recommended Citation
https://scholarworks.lib.csusb.edu/etd-project/1216

This Thesis is brought to you for free and open access by the John M. Pfau Library at CSUSB ScholarWorks. It has been accepted for inclusion in Theses Digitization Project by an authorized administrator of CSUSB ScholarWorks. For more information, please contact scholarworks@csusb.edu.
A REVIEW OF RESEARCH AND LITERATURE LINKING BREAST CANCER TO PESTICIDES

A Project
Presented to the
Faculty of
California State University,
San Bernardino

In Partial Fulfillment
of the Requirements for the Degree
Master of Arts
in
Education: Environmental Option

by
Patricia L. Pellegrino-Peard

June 1995
A REVIEW OF RESEARCH AND LITERATURE LINKING BREAST CANCER TO PESTICIDES

A Project
Presented to the
Faculty of
California State University,
San Bernardino

by
Patricia L. Pellegrino-Peard
June 1995

Approved by:
Dr. Darleen K. Stoner, First Reader
Dr. Thom G. Gehring, Second Reader

June 15, 1995
ABSTRACT

The purpose of this project was to examine research attempting to ascertain a link between breast cancer and a type of pesticide, organochlorines. Six known epidemiological studies were conducted in this regard. Analysis of the studies revealed two of them, at best, calculated into their results all recognized breast cancer risk factors. These factors account for only 20-30% of the total factors in breast cancer development. Seventy to 80% of the risk factors are not officially recognized but several are highly suspected, and many studies did not address those potential risks. The studies as a group should be compared with caution since no two calculated the exact same risk factors into their findings. Also, prudence is necessary when interpreting results of individual studies failing to calculate known risks into their results. Consequently, further studies on breast cancer and organochlorines are warranted and such research should include calculation of all known and those most highly suspected breast cancer risk factors. Review of articles commenting on the six studies was conducted. Some articles contained information taken out of context or misrepresented from original research reports. An attempt was made to address biases in some of the aforementioned articles. Alternatives to traditional pesticide use and an overview of pesticide legislation was provided with proposed changes in hope of reducing the existing relation, if any, between pesticides and breast cancer.
ACKNOWLEDGMENTS

For:
My darling husband, David, who endlessly supports and encourages me to pursue my dreams.

My loving parents and sisters who enrich my life in so many ways.

In Acknowledgment of:
Rachel Carson, Sharon, and all women afflicted with breast cancer.

Dr. Darleen Stoner who instilled a love of education in me and who was a constant reminder that education can only come after attempting to objectively present and consider all angles of an issue.

Dr. Thom Ghering who reminded me of the necessity of being an idealist and having passion for one's beliefs and acting upon that passion in an attempt to improve the world.
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABSTRACT</td>
<td>iii</td>
</tr>
<tr>
<td>ACKNOWLEDGMENTS</td>
<td>iv</td>
</tr>
<tr>
<td>LIST OF TABLES</td>
<td>ix</td>
</tr>
<tr>
<td>CHAPTER ONE</td>
<td></td>
</tr>
<tr>
<td>Preview</td>
<td>1</td>
</tr>
<tr>
<td>Research Limitations</td>
<td>5</td>
</tr>
<tr>
<td>Definition of Terms</td>
<td>6</td>
</tr>
<tr>
<td>CHAPTER TWO</td>
<td></td>
</tr>
<tr>
<td>Review of Related, and Background Literature</td>
<td>13</td>
</tr>
<tr>
<td>Insecticides - A Type of Pesticide</td>
<td>13</td>
</tr>
<tr>
<td>Chlorinated Hydrocarbons (Organochlorines)</td>
<td>17</td>
</tr>
<tr>
<td>PCBs</td>
<td>18</td>
</tr>
<tr>
<td>DDT</td>
<td>19</td>
</tr>
<tr>
<td>Concentration of DDT in Adipose Tissue</td>
<td>20</td>
</tr>
<tr>
<td>DDT and its Effect on Birds</td>
<td>22</td>
</tr>
<tr>
<td>Organochlorines' Continued Presence</td>
<td>23</td>
</tr>
<tr>
<td>Organophosphates and Carbamates</td>
<td>25</td>
</tr>
<tr>
<td>Synergistic Effects of Pesticides</td>
<td>25</td>
</tr>
</tbody>
</table>
Breast Cancer .......................................................... 29
Rising Incidence and Mortality Rates in Women .......... 29
Risk Factors ............................................................ 31
Age, Family or Personal History, Reproductive Factors, Obesity, Education, and Socioeconomic Status ........ 31
Estrogens ............................................................... 32
Fat .................................................................. 38
Race ................................................................. 39
Environmental Factors ............................................ 41
Improved Detection ............................................... 43
Organochlorines Linked to Mammary Cancer in Laboratory Animals ....................................................... 44
Contaminated Breast Milk ....................................... 47

CHAPTER THREE

Review of Epidemiological Studies Suggesting a Link Between Breast Cancer, and Pesticides ..................... 53

1984 - Unger et al. .................................................. 54
1990 - Mussalo-Rauhamaa, et al. ................................ 55
1992 - Falck et al. .................................................. 59
1993 - Wolff et al. .................................................. 60
1994 - Dewailly et al. ............................................. 63
1994 - Kreiger et al. ............................................. 65
LIST OF TABLES

Table 1. Major Types of Pesticides .............................. 14
Table 2. Some Pesticides Taken Off the Market .................. 27
Table 3. Experimental Evidence on Estrogenicity of Some Organochlorines ............................................. 37
Table 4. Experimental Evidence on Mammary Carcinogenesis of Some Organochlorines ............................................. 46
Table 5. DDE and PCBs in Breast Milk in Selected Countries .......... 49
Table 6. Studies on Breast Cancer and Organochlorines ................. 68
Table 7. Analysis of Studies Linking Breast Cancer to Pesticides with Respect to Taking into Account Known Breast Cancer Risk Factors and Those Considered to Likely Attribute to Breast Cancer Development ............................................. 71
Table 8. Major Pesticide Legislation .................................. 91
Table 9. Environmental Laws Regulating Toxic Substances ............ 94
CHAPTER ONE

PREVIEW

Breast cancer is the leading cause of death among American women between the ages of 40 and 55 years (Harris, Lippman, Veronesi, & Willett, 1992, p. 319). It is the second most prevalent cancer in women in the United States where estimates suggest 2 million will be diagnosed with the disease in the 1990s and 460,000 will die of it (Cancer Facts and Figures - 1994, 1994, p. 6; Moses, 1993, p. 3). The disease kills almost 50,000 American women each year. Fifty years ago, 1 in 20 women got breast cancer. Today, a woman has a 1 in 8 chance of getting breast cancer during her lifetime (D'Argo & Thorton, 1993, p. 1; Greene & Ratner, 1994, p. 866).

Since 1984, at least six epidemiological studies were conducted by the medical community (Key & Reeves, 1994, p. 1520). The goal of these studies was to determine whether or not a link exists between breast cancer and organochlorines, also known as chlorinated hydrocarbons, such as Dichlorodiphenyltrichloroethane (DDT), and its metabolite, Dichlorodiphenyldichloroethane (DDE), and Polychlorinated biphenyls (PCBs).

The purpose of this research was to analyze the six studies conducted to ascertain whether such a link exists. Analysis revealed the studies could not
be compared as they now exist since no two studies factored into their results all of the same risk factors for breast cancer.

A number of articles have been written about the studies' combined results. Since the majority of the studies did not calculate all known risk factors for breast cancer into their findings, comparison of their results should be done with caution. Also, some articles written about the studies have conflicting interpretations of their findings. Debate continues over the tests and their results.

The ability to recognize authors' biases is essential when evaluating these articles. It is also necessary to recognize potential biases in those conducting the research and to be aware of such biases when interpreting studies. Unfortunately, different players have diverging interests in evaluating the research conducted to determine if a connection exists between breast cancer and pesticides. It is safe to assume that all people would like to find the cause and cure for breast cancer. However, it must not be forgotten that certain entities have a vested interest in the production of pesticides, and the suggestion that some of their products may be an associated risk factor in breast cancer development can potentially create bias on their behalf in interpreting the results of certain studies.

Continuing research aimed at impartiality is necessary despite the fact that DDT and a number of other pesticides have been banned in the United
States since the early 1970s. Such research needs to factor into the results all known risk factors, as well as those highly suspected.

It is also necessary to investigate the laws that enable banned chemicals to still have a presence in the United States. Though their use is illegal in this nation, some synthetic chemicals are still produced here and exported to nations where their use is legal. Residues from the banned chemicals often return to the United States on produce. Therefore, even though DDT is now illegal in America, employees of DDT manufacturers may come into contact with the chemical, residues are consequently released in the environment, and the chemical is ingested when Americans consume imported produce containing DDT residues. Of further concern is the fact that these persistent, fat-soluble pesticides accumulate in adipose tissue and their rate of excretion is not known (Mercier, 1981, p. 3).

It is further necessary to question why our government allows its people to manufacture a chemical deemed too dangerous for the populous, yet allows for its exportation for use in other nations. We need to be aware of these disparities and use our democratic process to invoke change. If such activity may potentially increase the risk of breast cancer, it is our duty and civil right to call for the cessation of the manufacturing and exportation of illegal pesticides.

Undeniably, humankind has benefited from the use of pesticides. Pesticides have made substantial contributions to the agriculture of both
developed and developing countries (Gunn & Stevens, 1976, p. v). Synthetic pesticides act as a primary weapon against pest losses during crop growth, transport, and storage after harvest. Their use in chemical weed control is a major factor in increased labor efficiency and reduced drudgery. Proponents of pesticides argue that their use has led to improved public health resulting from control of flies, mosquitoes, and other vector-born diseases; better health through adequate nutrition; and supplies of reasonably priced, wholesome food (Gunn & Stevens, 1976, p. 10).

While proponents of pesticides argue pesticides are necessary to allow us to grow enough food to feed our ever-growing population, evidence suggests they have adverse effects on the environment and human health. Despite one's viewpoint on the risks associated with pesticides, we cannot afford to ignore evidence suggesting a risk to human health as a result of their use. Since breast cancer takes the lives of so many women on the planet today, our duty is to examine this evidence with an open mind, even if we are an owner of a chemical company or have vested interest in the use of pesticides, as chances are such a person has a mother, wife, sister, or daughter who may be at risk.
RESEARCH LIMITATIONS

One noteworthy limitation of this particular analysis of articles commenting on the aforementioned studies is the inability to analyze all articles written on the subject. This limitation is due to time constraints and available resources. Another noteworthy limitation is my personal inability to examine the articles with complete objectivity and understanding. Part of this constraint is due to being human and the latter part is due to a limited medical and science background. This latter limitation would be true of nearly all people attempting to understand this issue.

A further limitation has been the inability to adhere to a particular tense throughout the text. There was a need to implement both the present and past voice. While some events relating to the topic have previously occurred, many are ongoing. Whenever possible, however, the past tense was used.
In consideration of the reader, the following is a list of defined terms that have been used throughout the text. The first time each of these words appears in the text, it is in bold print:

**DEFINITION OF TERMS**

**Arochlor** - Trade name for PCBs manufactured by the company, Monsanto (Nadakavukaren, 1995, p. 239).

**Atrazine** - Persistent herbicide found to cause mammary cancer in rats (Moses, 1993, p. 3).

**Benzene hexachloride (BHC)** - Isonomer of lindane and persistent insecticide that remains in sandy soil at least 11 years after application. Found to leave high levels of residue in certain plant tissues (Carson, 1962, pp. 58-59, 196).

**Beta-hexachlorocyclohexane (beta-HCH)** - Neutral organochlorine that is an isonomer of hexachlorocyclohexane, which is the insecticidally active ingredient in the insecticide, lindane (Harte, Holdren, Schneider, & Shirley, 1991, p. 336; Mussalo-Rahamaa, Häsänen, Pyysalo, Antervo, Kauppila, & Pantzar, 1990, p. 2124).

**Biologically amplification** - Increase in concentration of DDT, PCBs, and other slowly degradable, fat-soluble chemicals in organisms at successively higher tropic levels of a food chain or web (Miller, 1994, p. 338).
**Carbamate** - Class of contact insecticides that supplement organophosphates. Also used as fungicide, herbicide, molluscicide, nematicide, and plant regulator (Hallenbeck & Cunningham-Burns, 1985, p. 30; Stevens & Klarner, 1990, p. 185).

**Chlorinated Hydrocarbon** - Part of a broader class of hydrogenated hydrocarbons. Type of insecticide that is an organic compound made up of atoms of carbon, hydrogen, and chlorine. A hydrocarbon in which one or more hydrogen atom was replaced with chlorine. Examples include DDT, lindane, chlordane, and PCBs. Concern about potential hazards of certain chlorinated hydrocarbons is based on their ubiquity; persistence in the environment; and capacity to accumulate in living organisms, including humans and the human fetus; and experimental evidence of potential carcinogenic effects (Harte et al., 1991, p. 116; Miller, 1994, p. 339; Stevens & Klarner, 1990, p. 185; Winter, 1992, p. 91).

**Chlorinated Organic** - Another name for a chlorinated hydrocarbon and an organochlorine.

**Cocarcinogen** - Factor that, in combination with other factors, produces cancer (Dorland's Illustrated Medical Dictionary, 1988, p. 350).

**Colostrum** - Secretion of mammary glands produced a few days before or after child birth. Differs from typical milk in its higher concentration of protein and antibodies, vitamins, and minerals, and its lower content of sugars and fats (Dorland's Illustrated Medical Dictionary, 1988, p. 360; Gove, 1986, P. 450).
DDE (Dichlorodiphenyldichloroethane) - DDT metabolite (Moses, 1993, p. 3).

DDT (Dichlorodiphenyltrichloroethane) - Chlorinated hydrocarbon that was widely used as a pesticide. Banned in the United States in the 1970s but still manufactured in the country and exported to countries where it is legal (Miller, 1994, pp. 165, 340).


Haloginated biphenyl - White crystalline hydrocarbon combined with halogen and used chiefly in a mixture with phenyl ether as an industrial medium (Gove, 1986, pp. 219, 1023).

Hazard - Something that can cause injury, disease, economic loss, or environmental damage (Miller, 1994, p. 342).

Hexachlorobenzene (HCB) - Also known as perchlorobenzene. An organochlorine pesticide that is a colorless crystalline solid. Used as a fungicide. As HCB is a by-product of chlorine gas preparation and chlorinated hydrocarbon production, it probably also enters the environment from industrial sources (Mercier, 1981, pp. 137-138).
Lindane (gamma-HCH) - Also known as hexachlorocyclohexane (HCH). Often incorrectly called benzene hexachloride (BHC), which is actually an isomer of BHC. Trade names include Agronexit, Lindafor, Gamma BHC, and Kwell (shampoo). Once a popular household fumigant. Commercially produced in the United States between 1945 and 1976, and is now imported in undisclosed amounts. Slightly more toxic than DDT. Comprises the insecticidally active component of the commercially available product, hexachlorocyclohexane (HCH) (Carson, 1962, p. 196; Harte et al., 1991, pp. 336-337).

Metabolite - Substance produced by metabolism that is usually more or less toxic to the organism producing it (Gove, 1986, p. 1419).

Methoxychlor - White crystalline insecticide derived from ether and chloral hydrate. Dissolves in alcohol, but not in water. Effective against flying insects. Considered faster acting and less toxic to warm-blooded animals than DDT. Also used in deodorant sprays. Moderately toxic by ingestion, and skin absorption, it is an irritant, allergen, and a suspected cancer-causing agent and mutagen. Emits highly toxic fumes when heated (Gove, 1986, p. 1423; Winter, 1992, p. 189).

Oncogenic - Giving rise to tumors or causing tumor formation (Dorland's Illustrated Medical Dictionary, 1988, p. 1176).

Organochlorine - Same as chlorinated hydrocarbon and chlorinated organic (Harte et al., 1991, p. 116).
**Organophosphates** - Includes malathion and diazinon, and have replaced chlorinated hydrocarbons because they control insects and are biodegradable (Stevens & Klarner, 1990, p. 185).

**Parity** - Condition of a woman with respect to her having borne viable offspring (Dorland's Illustrated Medical Dictionary, 1988, p. 1232).

**PCBs (polychlorinated biphenyls)** - Group of 209 different toxic, oily, synthetic, chlorinated hydrocarbon compounds that can be biologically amplified in food chains and webs (Miller, 1994, p. 346).

**Pesticide** - Any chemical designed to kill or inhibit the growth of an organism that people consider to be undesirable. Examples of pesticides include: a) fungicide (aimed at killing fungus), b) herbicide (kills or inhibits plant growth), c) insecticide (kills insects), and d) rodenticide (rodents) (Miller, 1994, pp. 342, 343, 345, 347).

**Polycyclic aromatic hydrocarbons (PAHs)** - Highly reactive compounds consisting of hydrogen and carbon atoms arranged in multiple rings (Harte et al., 1991, p. 445).

**Risk** - The probability something undesirable will happen from deliberate or accidental exposure to a hazard (Miller, 1994, p. 347).

**Risk Assessment** - Process of gathering data and making assumptions to estimate short- and long-term harmful effects on human health or the environment from exposure to hazards associated with the use of a particular product or technology (Miller, 1994, p. 347).
Risk Management - Uses risk assessment and other information to determine options and make decisions about reducing or eliminating risks (Miller, 1994, p. 347).

Statute - Also referred to as "legislation," a positive statement of legal rules enacted by a legislature versus case law. Used to create new areas of law, to fill gaps in the law, and to change court-made rules. A collection of statutes arranged by subject are known as codes (Jacobstein & Mersky, 1990, p. 7).

Synergism - Phenomenon where the interaction of two or more substances produces an impact greater than the sum of their independent effects (Nadakavukaren, 1995, p. 225).

Synthetic pesticide - Widely used after World War II, and replaced inorganic and botanical, or naturally occurring compounds. Often more toxic and less expensive than pesticides used previously (Harte et al., 1991, p. 113).

Teratogenic - Causing developmental malformations (Gove, 1986, p. 2358).

Tolerance - Maximum amount of a pesticide residue permitted in or on a food (Food and Drug Administration [FDA], 1993, p. 1).

Total Diet Study - Study wherein Food and Drug Administration personnel purchase foods from supermarkets or grocery stores four times per year from four geographic regions of the country. The foods are analyzed for pesticides and other toxins (FDA, 1993, p. 5).

Triazines - Algaecide, fungicide, and herbicide (Hallenbeck & Cunningham-Burns, 1985, p. 137).
Xenoestrogen- Chemicals that function as estrogens but not produced in the body (McCarthy, 1993, p. 25).
CHAPTER TWO

REVIEW OF RELATED, AND BACKGROUND LITERATURE

The following is a review of literature, commencing with background information on insecticides, especially organochlorines. The section is a reminder that these synthetic chemicals remain in our environment and possibly, in our bodies.

The next aspect of the literature review addresses breast cancer and its established and hypothesized risk factors. This background, along with the literature on pesticides, is provided in an attempt to facilitate review of the six studies conducted regarding organochlorines and breast cancer.

Insecticides - One Type of Pesticide

Pests compete with people for food, and some spread disease. Pesticides are defined as any chemical designed to kill or inhibit the growth of an organism that people consider to be undesirable. These synthetic chemicals are classified into subcategories based upon their target pest (see Table 1). For example, insecticides are a type of pesticide that is targeted at insects. Most of the thousands of insecticides used today fall into one of four classes of compounds: a) chlorinated hydrocarbons, b) organophosphates, c) carbamates, or d) pyrethroids (Miller, 1993, pp. 307-308).
### Table 1. Major Types of Pesticides

<table>
<thead>
<tr>
<th>Type</th>
<th>Examples</th>
<th>Persistence</th>
<th>Biologically Amplified?</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Insecticides:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chlorinated hydrocarbons</td>
<td>DDT, aldrin, dieldrin, toxaphene, lindane, mirex, chlordane, methoxychlor</td>
<td>High (2-15 years)</td>
<td>Yes</td>
</tr>
<tr>
<td>Organophosphates</td>
<td>Malathion, parathion, diazinon mevinphos, TEPP, DDVP</td>
<td>Low to moderate (1-12 weeks), but some can last several years</td>
<td>No</td>
</tr>
<tr>
<td>Carbamates</td>
<td>Aldicarb, carbaryl (Sevin), propoxur, maneb, zineb</td>
<td>Low (days to weeks)</td>
<td>No</td>
</tr>
<tr>
<td>Botanicals</td>
<td>Rotenone, pyrethrum, camphor from plants, synthetic pyrethroids (variations of pyrethrum), and rotenoids (variations of rotenone)</td>
<td>Low (days to weeks)</td>
<td>No</td>
</tr>
<tr>
<td>Microbotanicals</td>
<td>Various bacteria, fungi, protozoans</td>
<td>Low (days to weeks)</td>
<td>No</td>
</tr>
<tr>
<td><strong>Herbicides:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Contact chemicals</td>
<td>Atrazine, simazine, paraquat</td>
<td>Low (days to weeks)</td>
<td>No</td>
</tr>
<tr>
<td>Systemic chemicals</td>
<td>Two, 4-D, 2,4,5-T, Silvex diruron, daminozide (Alar), alachlor (Lasso), glyphosate (Roundup)</td>
<td>Mostly low (days to weeks)</td>
<td>No</td>
</tr>
<tr>
<td><strong>Fungicides:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Various chemicals</td>
<td>Captan, pentachlorphenol, zeneb, methyl bromide, carbon bisulfide</td>
<td>Mostly low (days)</td>
<td>No</td>
</tr>
<tr>
<td><strong>Fumigants:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Various chemicals</td>
<td>Carbon tetrachloride, ethylene dirbome, methyl bromide</td>
<td>Mostly high</td>
<td>Yes (for most)</td>
</tr>
</tbody>
</table>

(Miller, 1994, p. 200)
In diverse ecosystems, pest populations are kept in control by a variety of natural enemies. Since 1945, vast fields planted with only one crop or only a few crops, as well as home gardens and lawns, have been treated with a variety of pesticides (Miller, 1993, p. 307). Worldwide, about 2.3 million metric tons (2.5 million tons) of synthetic pesticides are used each year, an average of 0.45 kilograms (1 pound) for each person on earth. About 85% of all pesticides are used in more-developed countries, but use in lesser-developed countries is growing rapidly (Miller, 1993, p. 308).

In the United States about 600 biologically active ingredients and 1,477 inert ingredients are mixed to make some 55,000 pesticide products. Between 1964 and 1981, pesticide use in the United States leveled off at around 500 million kilograms (1.1 billion pounds). At that rate, an average of 2.0 kilograms (4.4 pounds) of these products is used for each American per year (Miller, 1993, p. 308). Insects, weeds, and plant pathogens are responsible for the loss of an estimated 30-35% of the global harvest each year, despite 50 years of escalating pesticide application against agricultural pests (Nadakavukaren, 1995, p. 281).

About 20% of the pesticides used each year in the United States is applied to lawns, gardens, parks, golf courses and cemeteries. The majority of pesticides are used in agriculture; however, about 260 million pounds are used annually to control fungi and other pests in a great variety of products, including paints, dentures, shampoos, disposable diapers, mattresses, flea
powders, and contact lenses (Harte et al., 1991, p. 112). The average homeowner in the United States applies about 5 times more pesticide per unit of land than do farmers (Miller, 1993, p. 308). Because of their extensive use and the manner in which they are applied, pesticides are found everywhere, in drinking water, food, air, and soil (Harte et al., 1991, p. 112).

Drawbacks to using DDT, as well as other synthetic chemicals, include their ability to contaminate soil and groundwater, and to adversely effect organisms in the process. Another detriment to using pesticides is they often do not discriminate as to which pests they kill (Miller, 1993, p. 308). Only a small percentage of insect species are considered pests. Unfortunately, the most widely used synthetic insecticides are broad-spectrum poisons, killing not only target pests, but also nontarget pests (Nadakavukaren, 1995, pp. 304-5).

Another serious shortcoming to pesticide use is most pest species, especially insects, can develop genetic resistance to a chemical poison through natural selection (Miller, 1993, p. 308). The widespread, frequent, and intensive application of chemicals, such as DDT, in the years following the Second World War created a new environmental challenge initially successful in drastically reducing pest populations, but that eventually was responsible for providing the selective forces which would produce new strains of insects able to render original poisons worthless (Nadakavukaren, 1995, p. 302). Most pest species, especially insects and disease organisms, can produce a large number of similarly resistant offspring in a short time. For example, the boll
weevil, a major cotton pest, can produce a new generation of offspring every 21
days (Miller, 1993, p. 308). At present more than 500 species of insects and
mites are resistant to common pesticides. This number represents more than
double the amount of pests resistant 20 years ago (Nadakavukaren, 1995, p.
504). Resistant species of rodents, fungi, and weeds are also on the rise

**Chlorinated Hydrocarbons (Organochlorines)**

Chlorinated hydrocarbons, also known as organochlorines, act primarily
on the central nervous system, causing the insect to go through a series of
convulsions prior to death. Members of this group are broad spectrum
insecticides, meaning they kill a wide variety of insects and other arthropods,
and are also persistent in the environment, breaking down very slowly. Thus,
chlorinated hydrocarbons retain their effectiveness for a relatively long period
after application (Nadakavukaren, 1995, p. 296).

Organochlorines are a class of industrial chemicals made from chlorine
and carbon-based organic matter. They include such highly persistent and
toxic substances as DDT and PCBs. Almost 80% of all chlorine is used in the
chemical industry to produce PVC (vinyl) and other plastics, pesticides,
industrial solvents, and other chemicals (D'Argo, Weinberg, Finaldi, Thorpe,
Bogart, & Stairs, 1993, p. 9).
PCBs

PCBs are a class of industrial chemicals (Castleman, 1992, p. 24). First synthesized in 1929, they were put on the market under the trade name, Aroclor. Although designed for industrial use, PCBs can escape into the environment via water contamination, vaporization from paints or landfills, and burning of PCB-containing material. Accidental spills or illegal dumping are also a concern due to the high cost of legally disposing of PCBs. Though ingestion of PCBs with food is the primary route of human exposure, PCBs can also be inhaled or absorbed through the skin (Nadakavukaren, 1995, pp. 239-240).

In 1964 Soren Jensen, a Swedish chemist, began a project to determine DDT levels in human fat and wildlife samples; instead he discovered the tissues examined contained large amounts of PCBs. His findings were met with widespread surprise and disbelief, since, unlike DDT and other organochlorines, PCBs were not being deliberately released into the environment (Nadakavukaren, 1995, p. 238).

Subsequent research in various countries confirmed Dr. Jensen's findings. Virtually every tissue sampled tested, including birds, fish, and polar bears, contained detectable amounts of PCBs. The Environmental Protection Agency (EPA) calculated that 91% of all Americans have detectable levels of PCBs in their fatty tissue. Also PCBs, and DDT as well, have been detected in

In 1973, the Food and Drug Administration (FDA) established tolerance levels for PCBs in food. Passage of the Toxic Substances Control Act in 1976 specifically banned the production, sale, distribution, and use of PCBs in open systems. In 1977, Monsanto, the sole United States manufacturer of the chemicals, terminated PCB production (Nadakavukaren, 1995, p. 241).

Although PCB production in the United States halted in 1977, the chemicals are still present in the country. During the years 1929-1977, 1.4 billion pounds of PCBs were produced in the United States. Hundreds of millions of pounds are still in use in closed systems, especially by the utility industry as coolants and in electrical transformers (Nadakavukaren, 1995, p. 243).

**DDT**

DDT is an insecticide that falls into the category of chlorinated hydrocarbons. It was first synthesized by a German chemist in 1874, but its properties as an insecticide were not discovered until 1939 (Carson, 1962, p. 20). First exposures to DDT date from about 1942 for military personnel and from about 1945 for civilians (Carson, 1962, p. 226). In 1948, Swiss chemist Paul Müller received the Nobel Prize in medicine for discovering the insecticidal properties of DDT. Through its use to control mosquito
populations, DDT saved untold lives from malaria. But within 10 years, the insecticide had produced so many adverse effects that it had been banned or its use severely restricted in several parts of the world (Kubasek & Silverman, 1994, p. 166).

**Concentration of DDT in adipose tissue.**

DDT in powder form is not readily absorbed through the skin. It is toxic when dissolved in oil. If swallowed, it is absorbed through the digestive tract and may be absorbed through the lungs (Carson, 1962, p. 21). DDT is a slowly degradable pesticide and, like many other chlorinated hydrocarbons, becomes concentrated in the fatty tissue of organisms (Miller, 1994, p. 165). Once it enters the body it is stored largely in organs rich in fatty substances. This storage of DDT begins with minute intakes of the chemical and continues to amass. The fatty storage depots act as **biological magnifiers**, so an intake of as little as 1/10 of one part per million results in the storage of about 10 to 15 parts per million. This represents an increase of 100 fold or more. In animal experiments, three parts per million of DDT was found to inhibit an essential enzyme in heart muscle. Only five parts per million brought about necrosis or disintegration of the liver; only two and one-half parts per million of the closely related chemicals, diedrin and chlordane, did the same (Carson, 1962, p. 21). Small amounts of this synthetic chemical are released by respiration and excretion. The resulting large concentration of DDT, or other slowly
biodegraded, fat-soluble organic chemicals, can kill organisms, reduce their
ability to reproduce, or make them more vulnerable to diseases, parasites and
predators (Miller, 1994, p. 165).

The principal biochemical mechanisms and pathways for DDT
elimination from the body are not known. It is suggested by time course data
that DDT is converted into DDA. DDT is also converted by dehydrochlorination
into DDE, which is retained in body fat (Mercier, 1981, p. 3).

The changes in storage and excretion of DDT in rats as a result of
starvation have been studied. Mobilization of body fat increases the
concentration of DDT and its metabolites in the fat, and the other tissues
examined. In spite of decreased intake of DDT, increased excretion of DDT
metabolites occurred during starvation. However, this increased excretion did
not prevent an increase in concentration of DDT-derived compounds in tissues
examined. Also, female rats have been found to be more susceptible than
males to repeated doses of DDT. When fed the same dosage level, female
rats store more DDT in their fat than males (Mercier, 1981, pp. 3-4).

A wide species variation in rates of detoxication of DDT to TDE or DDE
gives rise to differing storage levels of DDT in adipose tissue. There are also
interspecies differences in the capacity for eliminating fat-stored DDT. Humans
show extremely slow elimination compared with monkeys, rats, or dogs
DDT and its effect on birds.

During the 1950s and 1960s, populations of ospreys, cormorants, brown pelicans, and bald eagles plummeted since these birds at the top of aquatic food chain mostly feed on fish. Thus, they ingested large quantities of biologically amplified DDT in their prey. Prairie falcons, sparrow hawks, Bermuda petrels, and peregrine falcons also died off when they ate animal prey containing DDT, such as rabbits, ground squirrels, and other crop-damaging small animals (Miller, 1994, p. 165).

Although DDT did not appear to have direct lethal effects on the adult birds, studies determined that the organochlorine interfered with their ability to metabolize calcium (Nadakavukaren, 1995, p. 302). Research has shown that DDE, a breakdown product of DDT, accumulated in the bodies of the affected birds. This chemical reduced the amount of calcium in the shells of their eggs. The fragile shells broke, and the unborn chicks died (Miller, 1994, p.165).

Since the United States ban on DDT in 1972, most of these species have made a comeback. In 1980, however, DDT levels were again rising in species such as peregrine falcons and ospreys. These species may be picking up biologically amplified DDT and other banned pesticides in Latin America, where they winter. In those countries the use of such chemicals is still legal. Illegal use of DDT and other banned pesticides in the United States may also play a role (Miller, 1994, p. 165).
Organochlorines' Continued Presence

In the mid-1970s, DDT and most other slowly degradable, chlorinated hydrocarbon insecticides (except benzene hexachloride) were banned or severely restricted in the United States and most more-developed countries (MDCs) (see Table 2). However, many of these compounds are present in the United States, despite the fact they are illegal.

DDT, as well as some other organochlorines, are still produced in the United States and exported to other countries, mostly lesser-developed countries (LDCs), where they have not been banned (Miller, 1993, p. 308). According to one estimate, DDT and benzene hexachloride account for about three-quarters of the total pesticide use in India (Postel, 1988, p. 23). Though no longer legal in the United States, organochlorines continue to be present in the country. The Food and Drug Administration found residues of DDT, endosulfan, and lindane, among others, in its 1993 regulatory monitoring (p. 8). Researchers reported finding organochlorines in human tissue due to their being inefficiently metabolized and their solubility in lipids, which lead to lifelong sequestration in adipose tissue. Their persistence in the body and continuing presence in the environment have made it possible to detect them now even in American women, despite their use being banned in 1972 (Pesticide and Toxic Chemical News, 1993, p. 17).
The production of certain organochlorines in the United States may be an explanation for their presence in the country. Since hexachlorobenzene is a by-product of chlorine gas preparation and chlorinated hydrocarbon production, it is probable that HCB also enters the environment from industrial sources (Mercier, 1981, p. 138).

A further means for organochlorine presence in the United States is through importation. Residues of pesticides banned in the United States often return to the country in the form of residues of produce from imported goods. This is another means by which Americans may be continuing to ingest DDT and to accumulate the chemical in adipose tissue.

Migrating foul may also be a way DDT returns to countries where it is deemed illegal. Part of the year animals may migrate to countries where the synthetic chemical is legal and ingest it via fish or other means. Since DDT is biologically amplified in food chains, human beings are at risk as most of them feed at the top of the food chain (Greene & Ratner, 1994, p. 866; Miller, 1994, p. 165). Thus, particular caution should be paid to ingesting any migrating species.

Some environmentalists would like to see organochlorines be treated as a class of chemicals versus being treated individually, as is currently the case. There are 80,000 chemicals in commerce today, and 11,000 of them are organochlorines, and thousands more are said to form as accidental by-products. Some argue these chemicals are considered innocent until proven
guilty. Due to a number of studies having demonstrated adverse effects of organochlorines, such as DDT and PCBs, which later led to their being banned, some environmentalists are calling for a precautionary approach that reverses the burden of proof (Goldfarb, 1995, p. 127).

**Organophosphates and Carbamates**

In the United States and most MDCs, chlorinated hydrocarbon insecticides have been replaced by a number of more rapidly degradable pesticides, especially organophosphates and carbamates. Some of these compounds, primarily parathion, are more toxic to birds, people, and other mammals than are the chlorinated hydrocarbon insecticides they replaced. They are also more likely to contaminate surface water and groundwater because they are water-soluble, whereas chlorinated hydrocarbon insecticides are insoluble in water but soluble in fats. Furthermore, to compensate for the rapid breakdown, farmers usually apply nonpersistent insecticides at regular intervals to ensure more effective insecticide control. That means they are often present in the environment almost continuously, like the slowly degradable pesticides they substituted (Miller, 1993, p. 308).

**Synergistic Effects of Pesticides**

Human exposure to cancer-causing chemicals, including pesticides, are often uncontrolled and they come from multiple sources. Culmination of safe-level exposures to certain chemicals may render toxic results. One chemical
may act on another to alter its effect, or there may be interaction between a physical and chemical agent, such as water and pesticides (Carson, 1962, pp. 237-238).

Virtually all laboratory tests to determine carcinogenicity of suspected substances are based on responses to single-source exposures. Results of such testing methods may significantly underestimate risks in the real world because it is accepted that certain substances in combination are far more hazardous than either one would be if acting independently. This phenomenon, where the interaction of two or more substances produces an impact greater than the sum of their independent effects, is known as synergism (Nadakavukaren, 1995, p. 225).
### Table 2.

**Some Pesticides Taken Off the Market**

<table>
<thead>
<tr>
<th>Pesticides</th>
<th>Use</th>
<th>Concerns</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALDRIN</td>
<td>Insecticide</td>
<td>Oncogenicity</td>
</tr>
<tr>
<td>CHLORDANE (agricultural uses; termite uses suspended or canceled)</td>
<td>Insecticide (termites, ants)</td>
<td>Oncogenicity; reductions in nontarget &amp; endangered species</td>
</tr>
<tr>
<td>COMPOUND 1080 (livestock collar retained; rodenticide use under review)</td>
<td>Coyote control, rodenticide</td>
<td>Reductions in nontarget &amp; endangered species; no known antidote</td>
</tr>
<tr>
<td>DIBROMOCHLOROPROPANE (DBCP)</td>
<td>Soil fumigant, fruits &amp; vegetables</td>
<td>Oncogenicity, mutagenicity, reproductive effects</td>
</tr>
<tr>
<td>DDT &amp; related compounds</td>
<td>Insecticide</td>
<td>Ecological (eggshell thinning); carcinogenicity</td>
</tr>
<tr>
<td>DIELDRIN</td>
<td>Insecticide</td>
<td>Oncogenicity</td>
</tr>
<tr>
<td>DINOSEB (in hearings)</td>
<td>Herbicide/crop desiccant</td>
<td>Fetotoxicity; reproductive effects; acute toxicity</td>
</tr>
<tr>
<td>ENDRIN (avicide use retained)</td>
<td>Insecticide/avicide</td>
<td>Oncogenicity, teratogenicity, reductions in nontarget &amp; endangered species</td>
</tr>
<tr>
<td>ETHYLENE DIBROMIDE (EDB) (very minor uses &amp; use on citrus for export retained)</td>
<td>Insecticide/fumigant</td>
<td>Oncogenicity, mutagenicity, reproductive effects</td>
</tr>
</tbody>
</table>
Table 2., Cont.

**Some Pesticides Taken Off the Market**

<table>
<thead>
<tr>
<th>Pesticides</th>
<th>Use</th>
<th>Concerns</th>
</tr>
</thead>
<tbody>
<tr>
<td>HEPTACHLOR (agricultural uses; termiticide uses</td>
<td>Insecticide</td>
<td>Oncogenicity, reductions in nontarget &amp; endangered species</td>
</tr>
<tr>
<td>suspended or canceled)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>KEPONE</td>
<td>Insecticide</td>
<td>Oncogenicity</td>
</tr>
<tr>
<td>LINDANE (indoor smoke bomb canceled; some some uses</td>
<td>Insecticide/</td>
<td>Oncogenicity, teratogenicity, reproductive effects, acute toxicity;</td>
</tr>
<tr>
<td>restricted)</td>
<td>vaporizer</td>
<td>other chronic effects</td>
</tr>
<tr>
<td>MERCURY</td>
<td>Microbial uses</td>
<td>Cumulative toxicant causing brain damage</td>
</tr>
<tr>
<td>MIREX</td>
<td>Insecticide/fire</td>
<td>Nontarget species; potential oncogenicity</td>
</tr>
<tr>
<td>ant control</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SILVEX</td>
<td>Herbicide/forestry,</td>
<td>Oncogenicity, fetotoxicity</td>
</tr>
<tr>
<td>teratogenicity,</td>
<td>rights-of-way,</td>
<td></td>
</tr>
<tr>
<td>weed control</td>
<td></td>
<td></td>
</tr>
<tr>
<td>STRYCHNINE (rodenticide use &amp; livestock colar retained)</td>
<td>Mammalian predictor</td>
<td>Reductions in nontarget &amp; endangered species</td>
</tr>
<tr>
<td></td>
<td>control, rodenticide</td>
<td></td>
</tr>
<tr>
<td>2,4,5,-T</td>
<td>Herbicide/forestry,</td>
<td>Oncogenicity, teratogenicity, fetotoxicity</td>
</tr>
<tr>
<td></td>
<td>rights-of-way, weed</td>
<td></td>
</tr>
<tr>
<td></td>
<td>control</td>
<td></td>
</tr>
<tr>
<td>TOXAPHENE (livestock dip retained)</td>
<td>Insecticide, cotton</td>
<td>Oncogenicity, reductions in nontarget species, acute toxicity to aquatic</td>
</tr>
<tr>
<td></td>
<td></td>
<td>organisms, chronic effects on wildlife</td>
</tr>
</tbody>
</table>

(Kubasek & Silverman, 1994, p. 177)
Breast Cancer

Rising Incidence and mortality rates in women

Rates of breast cancer have been steadily increasing in the United States since the formal tracking of cases through registries began in the 1930s (Harris et al., 1992, p. 319). According to some estimates, the rate of increase is about 1% every year since the mid-1930s, and since 1980 rates have increased 2% annually (Cancer Facts and Figures - 1994, 1994, p. 10; Watson, 1994, p. 59). During 1982, and 1986, the rate rose to 4% (Harris et al., 1992, p. 319).

Improvements in the thoroughness of the registry, whose coverage became virtually complete in the early 1970s, are unlikely to account for more than 25% of the increase that occurred before 1982. On the basis of incidence rates for 1983 through 1987 in the United States, 12% of all women will be diagnosed with breast cancer (Harris et al., 1992, p.319). The American Cancer Society estimated 182,000 new cases among women in the United States during 1994 (Cancer Facts and Figures - 1994, 1994, p.10).

Breast cancer incidence rates increase rapidly during the 4th decade of a woman’s life and further increase before the age of 50. After menopause, the incidence rates continue to increase with age, but less dramatically than before. Breast cancer is the leading cause of death among American women who are 40 to 55 years of age (Harris et al., 1992, p. 319).

The breast cancer epidemic is not unique to the United States. Breast cancer incidence and mortality are growing in virtually all of the world's industrialized countries (D'Argo & Thorton, 1993, p.1; Davis, Bradlow, Wolff, Woodruff, Hoel, & Anton-Culver, 1992, p.372). Interestingly, cancer rates around chemical production facilities, including rural areas, have been found to be greater than in the rest of the nation (Cohen & O'Connor, 1990, p.16).

In less affluent parts of the world and in the Far East, the same pattern of increase in breast cancer with age is seen, but the absolute rates are much lower at each age. In Japan, for example, the overall incidence of breast cancer is about one-fifth of that in the United States (Harris et al., 1992, p. 319). International variability in cancer incidence rates, especially fat intake, may increase risk (Cancer Facts and Figures - 1994, 1994, p. 10).

World-wide in 1980, 560,000 women were documented to have died of breast cancer (D'Argo & Thorton, 1993, p.1). In general, all women are at greatest risk from their middle to later years (Harris et al., 1992, p. 319).
Unfortunately, changes in documented risk factors for breast cancer and rates of screening cannot completely explain recent increases in incidence or mortality (Davis et al., 1993, p. 372).

Risk Factors

Many breast cancer risk factors are under debate. Only 20-30% of breast cancer risk factors are accounted for by the American Cancer Society and the National Cancer Institute. The remaining 70-80% majority have yet to be formally recognized by such institutions (D'Argo & Thorton, 1993, p. 2). The scientific community offers potential risk factors for the remaining 70-80%, but there is not unilateral agreement as to what they are, and to what percentage of risk each poses in breast cancer development.

Age, Personal or Family History, Hormonal and Reproductive Factors, Obesity, Education, and Socioeconomic Status

The American Cancer Society officially recognizes the following risk factors for the disease: a) increase of risk with age, significantly increasing after the age of 40; b) personal or family history of breast cancer; c) reproduction factors such as early age at menarche, late age at menopause, never having children or first live childbirth after age 30; d) obesity; e) higher education and socioeconomic status (Cancer Facts and Figures - 1994, 1994, p. 10; California Cancer Facts and Figures - 1995, 1994, p. 18). In short, these
cancer establishments suggest that the cause is primarily personal. The
aforementioned personal risk factors reportedly account for only 20 to 30% of
all incidents of breast cancer. However, the vast majority of breast cancer
cases, 70 to 80%, do not fall into any of the three risk categories. The majority
of breast cancer risk factors are either unknown or highly debated. In fact, the
American Cancer Society recognized that other reasons for long-term
incidence increases are not yet understood (Cancer Facts and Figures - 1994,

Estrogens

All of the 20-30% risk factors accepted by the American Cancer Society,
with the exception of family history, are linked to high estrogen levels (Green &
Ratner, 1994, p. 866). According to Dr. Davis, epidemiologist and senior
science advisor at the Heath and Human Services Department, “There’s only
one common thread tying together all of the known risk factors: The more
estrogen in a woman’s life, the greater her risk of breast cancer” (Greene &
Ratner, 1994, p. 866). Estrogens are hormones that are important in the
sexual development of females (McCarthy, 1993, p. 25). Disruption of hormone
regulation is considered to play a critical role in the development of breast
cancer (D' Argo & Thorton, 1993, p. 1; Moses, 1993, p. 3). Some scientists
consider the disease to be determined primarily by total cumulative exposure to
bioavailable estrogens (Davis et al., 1992, p. 372). It has been suggested that
a high fat diet gives rise to critical concentrations of carcinogenic estrogens or their formation in the digestive tract (Unger, Klær, Blichert-Toft, Olsen, & Clausen, 1984, p. 27). The American Cancer Society, however, does not officially recognize estrogens to play a role in breast cancer development and reports further research on the subject is necessary (Cancer Facts and Figures - 1994, 1994, p. 19).

Chemicals which function as estrogens but are not produced in the body are often referred to as "xenoestrogens." In other words, xenoestrogens are estrogenic substances that are foreign to the body and, like estrogen, affect reproduction. Experimental evidence reveals that certain compounds affect estrogen production and metabolism and thus, function as xenoestrogens. These substances mimic the action of estrogen, or increase the production of the hormones in the body, which is believed by some scientists to increase cancer risk (Epstein, 1992, p. 16). These compounds include some organochlorines, such as the insecticide DDT and its metabolite, DDE; polycyclic aromatic hydrocarbons (PAHs); and certain pharmaceuticals. There is in vivo and in vitro evidence that organochlorines can produce estrogenicity (see Table 3). Many of these xenoestrogenic compounds also experimentally induce mammary carcinogenesis (Davis et al., 1993, p. 372).

When researchers combined pollutants and breast cells in the laboratory, some of the chemicals appeared to attach to the receptor molecule, just as estrogen does. DDT, PCBs, and even some natural substances, have
been considered to be "environmental estrogens" for their ability to imitate the natural hormone, and researchers fear these xenoestrogens have the power to promote tumor formation (Watson, 1994, p. 59).

Laboratory experiments have shown some pollutants act very similar to estrogen. Estrogen encourages breast cells to divide by attaching itself to a molecule, called the estrogen receptor, inside the cell. Normally this happens during puberty, when the breasts are developing. But for unknown reasons, estrogen occasionally triggers cell division after puberty, encouraging tumors to form (Watson, 1994, p. 59).

Xenoestrogenic pesticides currently in wide use in agriculture are the chlorinated hydrocarbons, endosulfan, a pesticide widely used on fruits and vegetables, and methoxychlor (Moses, 1993, p. 3; Pesticide and Toxic Chemical News, 1993, p. 18). They are much less persistent than DDT and are not stored in body fat. Other pesticides besides the chlorinated hydrocarbons, however, may increase the risk of breast and other cancers in women by acting as xenoestrogens (Moses, 1993, p. 3).

Some scientists state that the evidence for environmental estrogens is too preliminary. They point out that just because two chemicals bind in a petri dish does not give cause to believe they will stick for long, or at all, in the living cells of a woman. Even if a pollutant does stick to the estrogen receptor in a woman's breast, they contend, it might not simulate as much cell division. Critics also note that women produce far more of their own, decidedly more
potent, estrogen than they could absorb from the environment. According to Brian Henderson, epidemiologist and president of the Salk Institute, “Even giving women extra doses of their own estrogen, either as post-menopausal hormone therapy, or as birth control pills, increases cancer risk only a small amount, if at all” (Watson, 1993, p. 60).

On October 21, 1993, the Health and Environment Subcommittee of the United States House of Representatives' Energy and Commerce Committee heard from physicians and scientists suggesting that estrogenic agents, including some pesticides, may be contributing to the rise in the frequency of breast cancer (McCarthy, 1993, p. 25).

In testimony, Ana Soto, M.D., Associate Professor, Department of Anatomy and Cellular Biology, Tufts University School of Medicine, described her finding that the most popular food pesticides in use today, including in the United States, endosulfan, produced estrogenic effects in her laboratory as potent as those of DDT or PCBs (Feldman & Schubert, 1993, p. 1). She also noted recent reports showed a correlation between plasma levels of DDE and breast cancer. Soto conducted tests with human breast cancer cells and found that estrogenic pesticides accelerated reproduction of breast cells. She said the cumulative effect of exposure to several related organochlorine insecticides could be significant (Pesticide and Toxic Chemical News, 1993, p. 18).

As a result of the findings, Soto suggested that “estrogenicity is a frequent finding to justify that chemicals should be tested for this activity before
they are released into the environment." Assistant Administrator, Lynn Goldman, said the EPA was working to upgrade its test guidelines for pesticides to include estrogenic effects, according to Penny Fenner-Crisp, Director of Health Effects Division of the EPA (Pesticide and Toxic Chemical News, 1993, p. 18). Currently, the EPA's pesticide registration only considers the action of pesticides individually and does not examine synergistic or additive effects (McCarthy, 1993, p. 25).

Reportedly, effects from estrogenic pesticides are cumulative. According to Soto, "These chemicals are active in the body because they mimic native hormones. When you put several estrogens in the system, they act additively. I took 10 pesticides that act like estrogen, applied them at one-tenth the usual dosage, put them together and they acted like one dose. You have to assume that if you add more estrogen, you can increase risk." M. Wolff of Mt. Sinai School of Medicine noted that certain "persistent organochlorines" in the environment, including DDT and PCBs, "are biologically persistent." She added that their persistence in the body and continuing presence in the environment have made it possible to detect them now in American women, despite their being banned in 1970. She further noted assessing cumulative exposures is difficult because exposures that exert effects can occur 20-30 years before final effects are seen (Pesticide and Toxic Chemical News, 1993, p. 20).
<table>
<thead>
<tr>
<th>Chemical</th>
<th>In vivo evidence</th>
<th>Reference</th>
<th>In vitro evidence</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>DDT</td>
<td>Uterotropic (causes increased uterine weight) in rats</td>
<td>Welch et al., 1969, pp. 358-367</td>
<td>Inhibits the binding of [3H] estradiol to rat uterine cytosolic estrogen receptor</td>
<td>Nelson, 1974, pp. 447-451</td>
</tr>
<tr>
<td>Methoxychlor</td>
<td>Initiated implantation &amp; maintained pregnancy in rats</td>
<td>Johnson et al., 1992, pp. 42-48</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chlordecone (Kepone)</td>
<td>Initiated implantation &amp; maintained pregnancy in rats</td>
<td>Johnson et al., 1992, pp. 42-48</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCBs</td>
<td>Initiated implantation &amp; maintained pregnancy in rats</td>
<td>Johnson et al., 1992, pp. 42-48</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(Davis et al, 1993, p. 373).
Fat

Diet, in particular dietary fat, has long been suspected of playing a role in the etiology of breast cancer (Mussalo-Rauhamaa, Hasanen, Pyysalo, Kauppila, & Pantzar, 1990, p. 2126). As Director of the Pesticide Education Center in San Francisco, Dr. Marion Moses noted "Fat is a sink for toxic chemicals, and the more fat you have, the more chemicals you can absorb." She further noted, "Since women have a higher percentage of body fat than men, particularly in the breast, they are at greater risk" (Greene & Ratner, 1994, p. 866). Since organochlorines or their metabolites break down slowly and are stored in fatty tissue, residues can remain in the body years after exposure (Moses, 1993, p. 3). Although the EPA banned the use of DDT in the United States in 1972, it and its chemical relatives may continue to be present in the adipose tissue (McCarthy, 1993, p. 25).

According to the American Cancer Society, however, a causal role for dietary factors between breast cancer and risk, has not firmly been established (Cancer Facts and Figures - 1994, 1994, p. 10). However, epidemiological studies involving a large number of participants have shown breast cancer to be linked to dietary fat, with increasing amounts of fat creating an increased risk of breast cancer. The most compelling studies traces the risk of Japanese women, who adhere to the nation's traditional low-fat diet, have a low breast cancer rate compared to American women. The rate in Japanese women is 7.9 per 100,000, while the rate for American women is 22.4 per 100,000. But when
Japanese-born women move to the United States and begin to consume higher fat foods, their breast cancer rates rise. Also, American-born ethnic Japanese women, raised on a high-fat diet, have been reported to have higher breast cancer rates than Japanese-born immigrant women (Castleman, 1992, p.24).

The connection between a fatty diet and breast cancer is by no means a simple one. Some countries with diets relatively high in fatty meats, fish, and oils, such as Sweden, France, and Spain, have breast cancer rates considerably lower than those in the United States (Castleman, 1992, p. 24). These findings may help exclude race as a risk factor for breast cancer; however, they increase the likelihood that diet and environment are risk factors in the development of the disease.

Race

Among women age 50 years and older, Caucasian women were most likely to report having had a mammogram within the past two years (75%), and Hispanic women were the least likely to report having had one (61%) in the past two years (California Cancer Facts and Figures - 1995, 1994, p. 16). The fact that Hispanic women may be less likely to receive early detection has not resulted in higher rates of breast cancer among Hispanic versus White women. In fact, projections state that approximately 1 in 9 Caucasian, 1 in 11 African American, and 1 in 20 Hispanic women and women of other race/ethnicities,
will develop breast cancer sometime during their lifetimes (California Cancer Facts and Figures - 1995, 1994, p. 16).

African Americans, however, were found to have lower five-year relative survival rates for breast cancer than Caucasians. Factors that may contribute to this finding may have more to do with socioeconomic class than race. African Americans are reported to have more limited access to medical resources than do Caucasians (Wyngaarden, 1989, p. 200).

As with the majority of breast cancer risk factors, there is division among scientists as to whether or not race plays a role in breast cancer development. For example, some scientists believe Jewish women of East European origin run a 50% higher risk of developing breast cancer than do other women (Schemo, 1992, p. B1). This fact poses several question including whether or not child-bearing, breastfeeding, dietary, or other potential risk factors would be a factor versus heritage.

The fact that the United States is a nation of immigrants has fostered comparative studies of cancers among migrants and those still in the homeland. All studies have yielded the same general finding, that migrants soon evidence a breast cancer risk approaching that of natives of the new land. Thus, it is accepted among many members of the medical community that different rates of breast cancer among different ethnic groups are largely, if not totally, due to environmental differences (Austin, 1989, p. 587).
Environmental factors - synthetic carcinogens

Variations in rates of breast cancer internationally are not readily explained by known risk factors. Therefore, other environmental factors, such as exposure to carcinogenic chemicals, may partly explain increasing breast cancer incidence rates. Differences in exposures might account for disparate rates of the cancer between racial groups, and between countries with similar diets (Falck, Ricci, Wolff, Godbold, & Deckers, 1992, p. 145).

Scientific evidence suggests that cancer is, in large part, an environmental disease (D'Argo & Thorton, 1992, p.2). The fact that an environmental agent can cause cancer was reported in 1775 when an English physician, Sir Percival Pott, recognized an associated between cancer of the scrotum and exposure to soot. Every patient he examined with this relatively rare disease had, as a child, worked as a chimney sweep, wherein their scrotums were covered with soot when they were lowered naked into chimneys to remove the substance. Due to the low standards of hygiene, the soot remained on the scrotum for long periods and resulted in later development of scrotal cancer (Nadakavukaren, 1995, p. 221).

Further research supports the contention that environmental agents can be carcinogens. In the early 1900s studies revealed the cancer-causing properties of a number of coal tar products and of x-rays (Nadakavukaren, 1995, p. 221). Also, arsenic has been associated with cancer. It is one of the earliest pesticides associated with cancer, occurring in sodium arsenite as a
weed killer, and in calcium arsenate and various other compounds as insecticides (Carson, 1962, p. 222).

In St. Louis Park, Minnesota, where contamination of water supply with creosote (rich in PAH compounds) has occurred, elevated rates for breast cancer have been found (Mussalo-Rauhamaa et al., 1990, p. 2124). Another example of communities with persistently high incidence of breast cancer among women is found in Nassau and Suffolk Counties, Long Island, New York. Residents of these higher-cancer areas and many experts are divided over whether the environment or the profile of Long Island’s women are more responsible for the frequency of the illness. To many scientists, the cause of the high incidence is attributed to the following common denominators among most Long Island women: a) high socioeconomic status and high education, b) lateness bearing their first children, c) the tendency to have smaller families, and d) a tendency not to breast feed. In general, suburbs are recognized to have higher rates of breast cancer than cities (Schema, 1992, pp. B1 & B4).

Results from an epidemiological study conducted by the New York State Health Department confirmed Long Island was a hot spot for breast cancer incidence. The study reveals that women living within 1 kilometer (0.6 miles) of chemical factories on Long Island had a 60% higher risk of developing post-menopausal breast cancer than did women living farther away. The study did not prove chemical emissions from the factories were a direct environmental
cause of the observed cancers, but did raise concern and demand for additional research (Nadakavukaren, 1995, p. 224).

**Improved Detection**

Although some of the recorded increase in breast cancer reflects improved detection, changes in known risk factors for the disease cannot completely explain recent patterns. Mammography utilization is considered to attribute to a rise in incidence rates, but other reasons for a longer-term increase in the disease are not yet understood (Cancer Facts and Figures - 1994, 1994, p. 10). In 1992 a study by E.J. Feuer and L.M. Wun entitled, "How much of the recent rise in breast cancer can be explained by increases in mammography utilization?" was conducted. The study estimated age-specific rates of mammography from a Gallup Poll and concluded that much of the recorded increase in incidence during the 1980s may be due to screening mammography, but a sustained 1% annual increase in breast cancer mortality has occurred since the 1940s (Davis et al., 1992, p. 372). Screening mammography has been shown to lead to early diagnosis and reduced mortality from breast cancer (California Cancer Facts and Figures - 1995, 1994, p. 16). However, screening is mainly found to be successful in women over age 50, since below this age the tissue in the breast tends to be denser and tumors are often more difficult to detect (Brown, 1993, p. 36).
Organochlorines Linked to Mammary Cancer in Laboratory Animals

Since the 1970s, many organochlorines have been banned for most uses in the United States because animal testing has shown them to be carcinogenic (Nadakavukaren, 1995, p. 297) (see Table 4). A 1993 report in the Journal of the National Cancer Institute by M.S. Wolff and M. Rivera from Mt. Sinai School of Medicine, and P.G. Toniolo, N. Dublin, and E.W. Lee of New York University Medical Center, noted that certain "persistent organochlorines" (chlorinated hydrocarbons) in the environment, including DDT, lindane, and halogenated biphenyls such as polychlorinated hydrocarbons, including PCBs, are carcinogenic in animals (Pesticide and Toxic Chemical News, 1993, p. 17). Also, PAH compounds have been found to act as mammary carcinogens (Mussalo-Rauhamaa et al., 1990, p. 2124).

It is generally believed laboratory test results on rats can be qualitatively applied to humans, but to what degree quantitative interspecies extrapolation is valid is unknown. In human and rat epithelial cells many aspects of carcinogen metabolism of benzo(a)pyrene and 7, 12-dimethylbenz(a)anthracene have been found to be similar, although not identical. Some scientists hypothesize that neutral chlorinated hydrocarbon compounds such as DDT compounds, hexachlorobenzene (HCBs), isomers of hexachlorohexane (HCH), and PCBs may also be cancer inducers in humans (Mussalo-Rauhamaa et al., 1990, p. 2124).
The prevailing assumption among researchers is that the basic biological processes in all mammals are fundamentally the same. Every substance known to induce human cancer can act as a carcinogen in animals as well, with the exception of arsenic, a human carcinogen which has not been proven to be carcinogenic in animals. Thus, it seems logical that the opposite may be true, and animal testing is a potentially valid method to determining which chemicals are carcinogenic. Use of animals provides one of several methods for studying the mechanics of cancer. Other approaches include mutagenesis studies using bacteria, tissue culture research, and epidemiological studies (Nadakavukaren, 1995, p. 223).
Table 4.

Experimental Evidence on Mammary Carcinogenesis of Some Organochlorines

<table>
<thead>
<tr>
<th>Chemical</th>
<th>Animal evidence</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Organochlorines:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DDT</td>
<td>Accelerator of mammary tumors in male mice treated with 2-acetamidophenanthrene</td>
<td>Scribner &amp; Mottet, 1981, p. 73</td>
</tr>
<tr>
<td>Triazines</td>
<td>Increased incidence of mammary tumors in male rats (750 ppm for 126 weeks)</td>
<td>Pinter et al., 1990, p. 32</td>
</tr>
<tr>
<td>Benzene</td>
<td>Breast cancer, oral and respiratory routes</td>
<td>Maltoni et al., 1989, p. 74</td>
</tr>
<tr>
<td><strong>Polycyclic aromatic hydrocarbons:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benzo[a]pyrene</td>
<td>Mammary tumors, gastrointestinal route</td>
<td>Huggins &amp; Yang, 1962, p. 74</td>
</tr>
<tr>
<td>Dibenz[ah]anthracene</td>
<td>Mammary tumors, gastrointestinal route</td>
<td>Snell &amp; Steard, 1962, p. 76</td>
</tr>
</tbody>
</table>

(Davis et al., 1993, p. 373)
Contaminated Breast Milk

During breast feeding, chlorinated hydrocarbons are mobilized from their storage house in adipose tissue to human milk (Mussalo-Rauhamaa et al., 1990, p. 2127). Dr. Wolff noted that scientists at the National Institute for Environmental Health Sciences in the 1980s found that women with higher levels of DDE reported shorter duration of lactation, suggesting a hormonal effect (Pesticide and Toxic Chemical News, 1993, p. 17). Research has suggested that mothers nursing their second or later child have lower levels of pesticides in their milk than mothers nursing their first child. Thus, lactation may be a way to decrease the mother's body burden of pesticides by passing the burden to her infant (Moses, 1993, p. 3).

Many pesticides banned in the United States are still widely used in developing countries in agriculture and for vector control for malaria and other tropical diseases. Women in developing countries thus suffer the greatest exposure to pesticide residues; their children are much more likely to be breast fed and for a much longer period of time (Moses, 1993, p. 3). Breast milk contaminated with xenoestrogenic and carcinogenic pesticide residues has been found even in remote villages in Papua New Guinea and India. Studies in India's Pujals region have shown that, through their mother's milk, some babies ingest 21 times the amount of DDT and benzene hexachloride considered acceptable (Postel, 1988, 23).
Table 5 demonstrates the need for further research of breast contamination. It also brings into question whether or not colostrum may hold greater concentrations of DDE, and other pesticides than regular breast milk. A further issue raised is whether or not during colostrum excretion, the majority of organochlorines are released from the body. This raises concern as to where the potential concentrations are transferred. Table 5 does not provide enough data to make such a determination; however, a review of Norway's DDE breast milk contamination, wherein levels of DDE are often higher in colostrum than regular breast milk, espouses the need for further research in that regard.
### Table 5.

**DDE and PCBs in Breast Milk in Selected Countries**

[Mean in parts per million (fat basis)]

<table>
<thead>
<tr>
<th>Country</th>
<th>Year</th>
<th>Cases</th>
<th>DDE</th>
<th>PCBs</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia</td>
<td>1979</td>
<td>95</td>
<td>---</td>
<td>---</td>
<td>Stacey, Perriman, &amp; Whitney, 1985, pp. 102-108</td>
</tr>
<tr>
<td></td>
<td>1979</td>
<td>31</td>
<td>0.810</td>
<td>---</td>
<td>Stacey, Perriman, &amp; Whitney, 1985, pp. 102-108</td>
</tr>
<tr>
<td></td>
<td>1991</td>
<td>128</td>
<td>---</td>
<td>---</td>
<td>Stevens, Ebell, &amp; Psaila-Savona, 1993, pp. 238-241</td>
</tr>
<tr>
<td></td>
<td>1983</td>
<td>7c</td>
<td>0.900</td>
<td>---</td>
<td>Matuo, Lopes, Casanova, et al., 1992, pp. 167-175</td>
</tr>
<tr>
<td>Canada</td>
<td>1984</td>
<td>16</td>
<td>1.137</td>
<td>0.891</td>
<td>Davies &amp; Mes, 1988, pp. 647-654</td>
</tr>
<tr>
<td></td>
<td>1987</td>
<td>18</td>
<td>0.759</td>
<td>0.012</td>
<td>Mes, Doyle, Adams, et al., 1984, pp. 217-223</td>
</tr>
<tr>
<td>Finland</td>
<td>1981</td>
<td>50</td>
<td>0.850</td>
<td>0.450</td>
<td>Wickstrom, Pyysalo, &amp; Sümes, 1983, pp. 251-256</td>
</tr>
<tr>
<td></td>
<td>1981</td>
<td>10</td>
<td>0.850</td>
<td>---</td>
<td>Wickstrom, Pyysalo, &amp; Sümes, 1983, pp. 251-256</td>
</tr>
<tr>
<td>France</td>
<td>1990</td>
<td>20</td>
<td>2.183</td>
<td>0.052</td>
<td>Bordet, Mallet, &amp; Maurice, 1993, pp. 425-432</td>
</tr>
<tr>
<td>India</td>
<td>1981</td>
<td>50</td>
<td>4.780</td>
<td>---</td>
<td>Jani, Patel, &amp; Shah, 1988, pp. 201-204</td>
</tr>
</tbody>
</table>
Table 5., Cont.

DDE and PCBs in Breast Milk in Selected Countries
[Mean in parts per million (fat basis)]

<table>
<thead>
<tr>
<th>Country</th>
<th>Year</th>
<th>Cases</th>
<th>DDE</th>
<th>PCBs</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iraq (Baghdad)</td>
<td>1983</td>
<td>50</td>
<td>2.040</td>
<td>---</td>
<td>Al-Omar, Tawfiq, &amp; Al-Ogaily, 1985, pp. 65-67</td>
</tr>
<tr>
<td>Japan (Osaka)</td>
<td>1984</td>
<td>16</td>
<td>---</td>
<td>0.374</td>
<td>Taguchi &amp; Yakushiji, 1988, pp. 65-71</td>
</tr>
<tr>
<td></td>
<td>1984</td>
<td>7</td>
<td>---</td>
<td>0.261</td>
<td>Taguchi &amp; Yakushiji, 1988, pp. 65-71</td>
</tr>
<tr>
<td>Norway (Oslo)</td>
<td>1981</td>
<td>16</td>
<td>1.054c</td>
<td>1.165c</td>
<td>Skaare, Tuveg, &amp; Sande, 1988, pp. 55-63</td>
</tr>
<tr>
<td></td>
<td></td>
<td>20</td>
<td>0.640c</td>
<td>0.866c</td>
<td>Skaare, Tuveg, &amp; Sande, 1988, pp. 55-63</td>
</tr>
<tr>
<td></td>
<td></td>
<td>7</td>
<td>8.570c</td>
<td>---</td>
<td>Skaare, Tuveg, &amp; Sande, 1988, pp. 55-63</td>
</tr>
<tr>
<td></td>
<td></td>
<td>16</td>
<td>0.820</td>
<td>0.810</td>
<td>Skaare, Tuveg, &amp; Sande, 1988, pp. 55-63</td>
</tr>
<tr>
<td></td>
<td></td>
<td>20</td>
<td>0.970</td>
<td>1.000</td>
<td>Skaare, Tuveg, &amp; Sande, 1988, pp. 55-63</td>
</tr>
<tr>
<td></td>
<td></td>
<td>7</td>
<td>4.421</td>
<td>---</td>
<td>Skaare, Tuveg, &amp; Sande, 1988, pp. 55-63</td>
</tr>
</tbody>
</table>
Table 5., Cont.

<table>
<thead>
<tr>
<th>Country</th>
<th>Year</th>
<th>Cases</th>
<th>DDE</th>
<th>PCBs</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Papua New Guinea</td>
<td>1990</td>
<td>13</td>
<td>0.716</td>
<td>---</td>
<td>Spicer &amp; Kereu, 1993, pp. 540-546</td>
</tr>
<tr>
<td></td>
<td>1990</td>
<td>28</td>
<td>0.331</td>
<td>---</td>
<td>Spicer &amp; Kereu, 1993, pp. 540-546</td>
</tr>
<tr>
<td>South Africa</td>
<td>1986</td>
<td>132</td>
<td>7.060</td>
<td>---</td>
<td>Bouwman, Cooppan, Reinecke, et al., 1990, pp. 761-768</td>
</tr>
<tr>
<td>(Natal)</td>
<td>1986</td>
<td>88</td>
<td>0.922</td>
<td>---</td>
<td>Bouwman, Cooppan, Reinecke, et al., 1990, pp. 761-768</td>
</tr>
<tr>
<td>Turkey</td>
<td>1984</td>
<td>61</td>
<td>2.710</td>
<td>---</td>
<td>Karakaya, Burgaz, &amp; Kanzik, 1987, pp. 506-510</td>
</tr>
<tr>
<td></td>
<td>1984</td>
<td>50</td>
<td>2.560</td>
<td>---</td>
<td>Karakaya, Burgaz, &amp; Kanzik, 1987, pp. 506-510</td>
</tr>
<tr>
<td>USA</td>
<td>1978</td>
<td>868g</td>
<td>2.270</td>
<td>1.680</td>
<td>Rogan, Glade, McKinney, et al., 1986, pp. 172-177</td>
</tr>
<tr>
<td>(N. Carolina)</td>
<td>1979</td>
<td>54</td>
<td>0.200</td>
<td>0.800</td>
<td>Takei, Kauahikaua, &amp; Leong, 1983, pp. 606-613</td>
</tr>
<tr>
<td></td>
<td>1986</td>
<td>15m</td>
<td>1.050</td>
<td>0.460</td>
<td>Krauthacker, 1991, pp. 797-802</td>
</tr>
<tr>
<td></td>
<td>1986</td>
<td>18m</td>
<td>1.080</td>
<td>0.570</td>
<td>Krauthacker, 1991, pp. 797-802</td>
</tr>
</tbody>
</table>

**DDE and PCBs in Breast Milk in Selected Countries [Mean in parts per million (fat basis)]**
### Table 5., Cont.

**DDE and PCBs in Breast Milk in Selected Countries.**

*Mean in parts per million (fat basis)*

<table>
<thead>
<tr>
<th>Key</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>c</td>
<td>A specialized secretion of mammary glands produced during the first few days after birth. Differs from typical milk in its higher concentration of protein and antibodies, vitamins, and minerals, and its lower content of sugars and fats (Gove, 1986, p. 450).</td>
</tr>
<tr>
<td>g</td>
<td>Geometric mean</td>
</tr>
<tr>
<td>m</td>
<td>Median</td>
</tr>
</tbody>
</table>

Moses, 1993, pp. 4-5
CHAPTER THREE

REVIEW OF EPIDEMIOLOGICAL STUDIES SUGGESTING A LINK BETWEEN BREAST CANCER AND PESTICIDES

To date, an estimated six epidemiological studies have been conducted with the focus of ascertaining the existence of a link between breast cancer and an environmental factor, specifically, pesticides. The particular group of pesticides in question is the chlorinated hydrocarbons, particularly DDE and PCBs. It is important to recognize that common traits exist in all studies conducted. However, when comparing the studies, those traits that differ among the studies must be duly noted. Differences include known risk factors for breast cancer and those highly suspected, such as race, place of residence, diet, breast feeding practices, and smoking history. Even within an individual study such differences should not go unrecognized.

With such a small percentage of breast cancer risk factors (20-30%) officially recognized, epidemiological studies failing to factor into their results those risks, are encouraged to be read with caution. There are a number of potential risk factors that may comprise the remaining 70-80% breast cancer risk factors. Some of these have greater proof to exist than others, and those with substantial evidence behind them should also be considered in epidemiological studies linking breast cancer to organochlorines.
In 1984 Mogens Unger and colleagues examined the burden of PCBs and DDE in breast fat tissue from mammary cancer patients in as early a diagnosis state of disease as possible. This study used samples from both living and deceased subjects. Samples were analyzed from the fat tissue taken at autopsy of 18 deceased cancer patients and 35 deceased controls. Tissue samples taken during surgery from 14 living cancer patients were also compared with samples from 21 living controls.

Of note, “the patients were unmatched with regard to whether or not they have been nursing” (Unger et al., 1984, p. 25). This is important information as it may significantly influence the results. Some scientists hypothesize that lactation may considerably reduce concentrations of persistent organochlorines stored in adipose tissue. Knowing which patients did breastfeed, the number of times and the length of each, should be factored into the data to ensure optimum results. Information regarding whether or a subject's was breast fed by her mother, and what number child the subject was to be breast fed, may also be significant to the findings.

In this study, the youngest of the noncancer, deceased subjects was 15 years versus 43 years for the youngest cancer subject. This raises issues that may directly impact the results. A 43-year-old woman is more likely to have breast fed than a 15 year old. According to some scientists, the concentration of organochlorines in the 43-year-old's mammary adipose tissue would have
decreased via lactation and at the time of the study, may have been similar to
that of a 15 year old, leaving no significant difference between both tissue
samples. Further, it is unknown whether or not high levels of organochlorines
could have induced carcinogenic activity prior to breast feeding since their
concentration may have been reduced via lactation. This potential discrepancy
also applies to adipose samples taken from the living subjects, wherein the
youngest member of the noncancer patients was 19 versus the 25-year-old
cancer patient. Again, it is critical to know whether or not the subjects in
question breast fed, and the number and length of times to determine if the
results would be effected.

The results of Unger's study indicate "human mammary tissue is not a
target organ for PCB or DDE concerning carcinogenesis. However, malignant
development in other organs seems to be more strongly associated with PCB
and DDE burden" (Unger et al., 1984, pp. 25-6). Again, when considering
these results, it must be borne in mind that controls and subjects should be
paired on more than just age, which is only one of the recognized breast
cancer risk factors.

1990 - Mussalo-Rauhamaa, Häsänen, Pyysalo, Antervo, Kauppila, and Pantzar

A second study was performed in 1990 by Mussalo-Rauhamaa,
Häsänen, Pyysalo, Antervo, Kauppila, and Pantzar. The residue levels of PAH
and neutral organochlorine compounds, including DDT compounds, **hexachlorobenzene (HCB)**, isomers of **beta-hexachlorocyclohexane (Beta-HCH)**, and PCBs, in breast fat of 44 breast cancer patients and 33 women free of cancer were determined.

Breast adipose tissue was obtained from the 44 breast cancer patients from October 1985 to February 1986. The 10 to 20 gram adipose sample was taken as near the malignant tissue as possible. Patients completed a questionnaire prior to the procedure. Questions posed included the patient's age, height, weight, smoking, and fish-eating habits, **parity**, and previous breast-feeding periods (Mussalo-Rauhamaa et al., 1990, p. 2124).

As controls, breast tissue samples were taken during routine postmortem examinations at the Department of Forensic Medicine, University of Helsinki, Finland, from 33 fatalities. These researchers obtained data concerning each control's weight, height, occupation, place of residence, fish consumption and smoking habits and number of children were obtained by interviewing the deceased controls' relatives. The scientists noted, "Data on diet for the accidental fatalities (controls) cannot be obtained very reliably from their relatives" (Mussalo-Rauhamaa et al., 1990, p. 2127). Data on smoking or dietary habits of controls were obtained from only 18 cases. It is imperative to note information regarding breast feeding was not mentioned as being obtained on the controls. This is important since breast feeding may potentially be the
most significant way to reduce the concentration of organochlorines in the adipose tissue.

Both cases and controls had their permanent residence in the Helsinki area. Since suburbs are generally found to have higher incidences of breast cancer, it may be helpful to know whether or not each woman lived in the suburbs or directly in Helsinki (Scheme, 1992, pp. B1 & B4).

The researchers obtained data on occupation and divided this category into upper white-collar personnel, lower white-collar personnel, workers, retired, housewife, and unknown. However, it may be statistically significant to know the general type of work performed. For instance, whether or not the upper white collar worker was a chemist or a hotel manager may alter the results. Also of note, occupational information was obtained only on current employment status, and nothing is known of previous employment history.

Mussalo-Rauhamaa et al. found that neither, age, weight, and height statistically differed significantly between cases and controls. Parity, however, was potentially found to differ among the two groups. Data revealed that 14 of the breast cancer patients had no children while only 4 of the controls were nulliparous. However, parity was unknown for two cases and nine controls.

No difference of statistical significance between cases and controls was found for PAH residues. In fact, concentrations found were near the minimum detectable level. Detectable amounts of alpha-chlordane were found in four cancer patients and eight controls; trans-nonachlor in one control; gamma-HCH.
(lindane) in four cancer patients and four controls; and delta-HCH in one cancer patient and three controls. The findings also revealed no statistically significant differences in residue levels of chlorinated hydrocarbons between different types of breast cancer patients.

Residues of beta-HCH in cancer patients compared to controls were significantly more frequent statistically. Neutral organochlorine compounds are thought to be absorbed mainly from foodstuffs, especially fish. Of the HCH compounds, beta-HCH, is the most permanent; gamma-HCH (lindane) may be metabolized principally to beta-HCH in the human body. This study indicates an association between beta-HCH and breast cancer.

Increased mean tissue levels of HCH were reported in two of three studies of autopsy patients; in one of these, involving four liver cancer patients, the level of beta-isomer was abnormally high. In cancer patients with childhood colorectal carcinoma, mean serum levels of beta-HCH were no higher than in controls. This may indicate HCH levels were not a risk factor for the children. The difference found in the study may partly be due to differences in parity between cases and controls. This study may also have different results due to differences in diet between breast cancer patients and controls.

In dietary studies in Finland, approximately 25% of HCH compounds are estimated to be obtained from fats and oils, which is said to be where organochlorines are stored. Approximately 27% of HCH compounds come from dairy products, which are often high in fat, and 19% from meat products,
wherein organochlorines are biologically magnified with increased tropic levels, and which are also high in fat. An estimated 25% of HCH compounds come from fish and 18% from eggs. The proportion of fats and oils as a source of HCH compounds in Finland is high. Thus, increased beta-HCH concentration among breast cancer patients may reflect increased use of dietary fat, a well known possible risk factor for breast cancer.

1992 - Falck, Ricci, Wolff, Godbold, and Deckers

A research team led by a University of Michigan physician and toxicologist, Frank Falck, Jr., linked human breast-cancer risk to several environmental contaminants, including the pesticides DDT and DDE, and a class of industrial chemicals, PCBs. The 1992 study by Dr. Falck and colleagues involved 40 Caucasian women who had breast lumps removed at Connecticut's Hartford Hospital from May through September 1987.

Age was similar for cases and controls. Patient height, weight, and smoking history were obtained from medical records or from brief telephone interviews. Other data, such as specific dietary histories, were unavailable. No mention is made in the study as to whether family history of breast cancer, breast feeding, child bearing, residence, occupational, or socioeconomic history was obtained.

Falck's group analyzed fatty tissue from the breasts of 20 women with cancerous lumps and 20 women whose lumps were benign. In the breast-fat
tissue of the women with cancer, Falck found significantly higher levels of DDT, DDE, and PCBs. Results indicate mean concentrations of PCBs and DDE were 50-60% higher in tissues of women with breast cancer than controls. The differences were statistically significant. The coefficients for DDE and PCBs are approximately 0.001, which suggest a 10 parts per billion increase is tissue levels, equaling a 1% increase in risk of breast cancer. As a result, Falck and his team "suggest a role for environmentally derived, suspect carcinogens in the genesis of mammary carcinoma" (Castleman, 1992, p. 24).

1993 - Wolff, Toniolo, Lee, Rivera, and Dubin

According to a 1993 study conducted by M.S. Wolff, P.G. Toniolo, E.W. Lee, M. Rivera and N. Dubin, reported in the Journal of the National Cancer Institute, the possibility that organochlorine (including DDT and PCBs) residues may be related to breast cancer arises from several observations. Wolff et al. further reported that DDT and its metabolite DDE, similar pesticides, and related chemicals such as PCBs, are known animal carcinogens and suspected human carcinogens, and they may compromise immune function. Both DDT and PCBs have been shown to be tumor promoters and to have estrogenic activity. Moreover, their inefficient metabolism and their high solubility in lipids, leads to lifelong sequestration in adipose tissue.

These scientists examined the association of breast cancer with individual exposure to DDE and PCBs by measuring the levels of the
organochlorines in blood serum (p. 648). The subjects studied by Wolff et al. were a subset of participants in the New York University Women's Health Study, a cohort study of hormonal and environmental factors and cancer in women. Between 1985 and 1991, 14,290 New York women consented to having 30 mL of venous blood drawn. Study subjects were aged 35-65 years and 80% were Caucasian. Control subjects were selected at random from risk sets consisting of all cohort members who were alive and free of cancer at the time of the cancer diagnosis in a case patient and who matched the case patient on menopausal status, age at entry into the study (= 0.5 year), number and dates (=0.25 year) of blood donations, and if premenopausal, day of menstrual cycle at the time of first blood drawing. Two control subjects were selected for each postmenopausal case patient (n=34), and four were selected for each premenopausal case patient (n=24) (p. 649).

According to the study, case and control subjects did not differ with regard to socioeconomic status (as defined by years of school) (p. 649). Occupation would have been important to factor into the equation. Whether or not a subject worked in a chemical factory could alter the findings significantly. Review of previous occupations, as well as current and past residences, would be also important to factor into the findings.

DDE and PCBs analyses were performed on specimens from the 58 breast cancer case patients and their 171 matched control subjects. According to the researchers, the mean levels of both DDE and PCBs were higher among
the breast cancer patients than among their matched control subjects. The paired differences were statistically significant only for DDE, which was approximately 35% higher in cancer patients than in control subjects. PCBs were 15% higher in the cancer patients versus control subjects. After adjustment for first-degree family history of breast cancer, lifetime lactation, and age at first full-term pregnancy, the odds ratio for breast cancer increased markedly with increasing quintile of DDE concentration. When serum DDE was examined as a continuous risk factor, there was a 1.09 increase (9%) in the adjusted odds ratio for breast cancer per unit increase in DDE. This increase corresponded to a four-fold risk for an elevation of serum DDE from the 10th percentile to the 90th percentile (p. 649).

Interestingly, the effect of lactation was found to be protective. When Wolff and colleagues examined months of lactation as a continuous variable, the decrease in odd ratios for breast cancer per additional month of lactation was 0.88 (p. 649). The implications of these findings suggest further research is indicated on this matter and strengthens the necessity to factor lactation history into any study conducted regarding organochlorines and breast cancer.

Wolff et al. reported organochlorine residues may be found throughout the body, especially in adipose tissue. Overall, the epidemiological data suggest estrogens exert a cancer-promoting effect and a diet rich in animal products and fat may increase a woman's risk of breast cancer. The study further suggested that DDT and its metabolites exert estrogenic effects because
of their ability to interact with estrogen-binding protein and to promote estrogenic tumors.

Wolff et al. noted previous studies raised the question of organochlorine residues and their possible association with breast cancer. The researchers performing the study stated this study differed from previous ones in that it adjusted for known breast cancer risk factors, and individually matched case patients for some risk factors and statistically adjusted for others. It is the first known study to factor into its results all recognized breast cancer risk factors. Further, this study had significantly more case patients than its predecessors. An even higher number of subjects as well as an analysis of adipose tissue along with blood serum may have even further strengthened Wolff and her colleagues' findings since fat soluble organochlorines persist in human adipose tissue, reaching levels 200-300 times higher than those in serum (Kreiger, Wolff, Hiatt, Rivera, Vogelman, & Orentreich, 1994, p. 590).

1994 - Dewailly, Dodin, Verreault, Ayotte, Sauvé, Morin, and Brisson

A 1994 study conducted by Dewailly, Dodin, Verreault, Ayotte, Sauvé, Morin, and Brisson evaluated the role of environmental organochlorine exposure to breast cancer risk. This study took into account estrogen receptor (ER) status of primary tumors. Between November of 1991 and May of 1992, 41 women aged 40 to 69 years who had a biopsy for a breast mass participated.
With the exception of two women, all participants resided in the Quebec City region. Again, differentiating between suburb or city residence may have been important. The patients completed a questionnaire about age, weight loss, parity, and breast feeding. The mean age of the 20 case patients and 17 control subjects was 54.1 and 51.2 years, respectively. Case patients and controls reported an average body-weight reduction of 1.5 kg over the previous year. Parity was also similar for case patients and controls. Among case patients, 88.9% never breast fed, compared with 76.5% among control subjects. All this information is vital to obtain optimum results, although current weight, height, family history of breast cancer, occupation/socioeconomic status, age at menarche, and age at menopause may have also been useful.

Participants included 20 women with breast cancer and 17 controls. Originally there were 21 controls; however, 4 were excluded due to atypical mammary conditions.

Breast adipose tissue (0.2-1.0 grams) was collected for organochlorine analysis. In addition, organochlorine content was determined in plasma from participants after having fasted. Although adipose tissue and plasma concentrations of most organochlorines were higher in case patients than in control subjects, a statistically significant difference was observed only for hexachlorobenzene in plasma.

Control subjects were compared with ER-negative and ER-positive case patients. These two subgroups were comparable for age, body weight
changes, and parity. Data should be obtained on all known and potential risk factors for optimum results. It is also vital to the study's integrity to compare similar subjects with respect to individual risk factors, as this study has done.

The study's results suggest women with hormone-responsive breast cancer, but not those with hormone-nonresponsive breast cancer, have a higher DDE body burden than women with benign breast diseases. It also supports the theory that exposure to estrogenic organochlorines may affect the incidence of hormone-responsive breast cancer. This study differs from others as it differentiates between hormone-responsive and nonresponsive patients.

1994 - Kreiger, Wolff, Hiatt, Rivera, Vogelman, and Orentreich

A 1994 study was conducted by N. Kreiger, M. S. Wolff, R. A. Hiatt, M. Rivera, J. Vogelman and N. Orentreich. The study entitled, "Breast cancer and serum organochlorines: a prospective study among White, Black and Asian women" was conducted to test the hypothesis that organochlorines are a risk factor for breast cancer. Whether or not race is a breast cancer risk factor is still highly debated. Occupational and residential tendencies, diet, family size, and breast feeding may have more to do with incidence of breast cancer for a particular race than the issue of race itself.

The researchers gathered data on serum levels of DDE and PCBs from blood taken from subjects in the late 1960s of women who took a multiphasic
health examination, independent about concern about risk of breast cancer. The blood was frozen and stored until 1990, when follow-up occurred.

A nested case-control study was performed of 150 case patients and 150 matched control subjects. A random sample of 50 women per racial/ethnic group who had been diagnosed with breast cancer more than six months after the multiphasic examination was selected, and each case patient was matched with a cancer-free control subject.

Matched analyses found no differences in case patients' and control subjects' serum levels of DDE or PCBs. DDE levels, however, tended to be higher among African American case patients compared to their matched controls, and PCBs were lower among White case patients compared with White controls. Also, organochlorine levels were found to be significantly higher among Black and Asian women compared with White women.

Results were not altered by adjusting for relevant confounders, and the lack of association between exposure to organochlorines and breast cancer was present regardless of length of follow-up, year of diagnosis, or the case patient's menopausal and estrogen receptor status. This study concluded that the data do not support the hypothesis that exposure to DDE and PCBs increases risk of breast cancer. The study does call for further research into biologic mechanisms involved and variations of exposure to chemical pollutants and of breast cancer incidence rates among diverse groups of women.
Comparison of Research Studies

A comparison of the studies is summarized in Table 6.

This is only a superficial overview of the research and does not take any other information into account other than the name of the researchers, the year of publication, the number of subjects, the sample type, and the findings.
Table 6.

**Studies on Breast Cancer and Organochlorines (DDE and PCBs)**

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th># Case/Controls</th>
<th>Sample</th>
<th>Statistically Significant Difference:</th>
<th>DDE</th>
<th>PCBs</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unger et al.</td>
<td>1984</td>
<td>14/21 &amp; 18/35</td>
<td>Adipose Tissue</td>
<td></td>
<td>No</td>
<td>No</td>
<td>---</td>
</tr>
<tr>
<td>Mussalo-Rauhamaa et al.</td>
<td>1990</td>
<td>44/33</td>
<td>Adipose Tissue</td>
<td></td>
<td>No</td>
<td>No</td>
<td>Beta-HCH</td>
</tr>
<tr>
<td>Falck et al.</td>
<td>1992</td>
<td>20/20</td>
<td>Adipose Tissue</td>
<td>Yes(1)</td>
<td>Yes</td>
<td>No</td>
<td>DDT(2)</td>
</tr>
<tr>
<td>Wolff et al.</td>
<td>1993</td>
<td>58/171</td>
<td>Blood Serum</td>
<td>Yes(3)</td>
<td>No</td>
<td></td>
<td>---</td>
</tr>
<tr>
<td>Dewailly et al.</td>
<td>1994</td>
<td>20/17</td>
<td>Adipose Tissue &amp; Blood Serum</td>
<td>Yes(4)</td>
<td>Yes(5)</td>
<td>HCB(6)</td>
<td></td>
</tr>
<tr>
<td>Kreiger et al.</td>
<td>1994</td>
<td>150/150</td>
<td>Blood Serum</td>
<td>No</td>
<td>No</td>
<td></td>
<td>---</td>
</tr>
</tbody>
</table>

**Key:**

1: Remained significant only when smoking (not an officially recognized risk for breast cancer) was not factored into the results.

2: Was not statistically significant when age and smoking were not factored into the results.

3: Increased with adjustment for lactation.

4: In estrogen receptor-positive case patients versus controls in both adipose tissue and blood serum.

5: In estrogen receptor-positive case patients versus controls in adipose tissue only.

6: In blood serum only.
It is impossible to perform the "perfect" epidemiological study. Unfortunately, one does not have the resources to obtain an adequate number of subjects with identical breast cancer risk profiles. Adjustments can be made to factor unparalleled risk profiles into a study's results. Unfortunately, not all of the six studies conducted to determine the existence of a link between breast cancer and organochlorines obtained or factored in such information. Since age; family or personal history; reproductive factors, such as age at menarche, child birth and menopause; obesity; and socioeconomic and education level, fall into the 20-30% of known risk factors for mammary cancer, the results of those studies that failed to factor in all of these known causes of breast cancer should be read with caution.

The remaining 70-80% of risk factors still are being debated. However, those with the most compelling evidence in influencing development of the disease, such as diet and residence, should be calculated into the test results. As breast feeding is known to reduce concentrations of organochlorines in the adipose tissue of the breast, those studies that failed to obtain and factor information regarding lactation into the results should also be read with prudence. Other potentially important factors to question subjects about are alcohol consumption history and silicone breast implants.

This limited research cannot, with certainty, be extrapolated to apply to the general populous of women. There remains a great deal to learn about the 70-80% of unknown or unrecognized risk factors. Without knowledge of at
least the majority of risk factors, all studies should be interpreted with caution since calculating those factors into a study's results would probably have great impact.

Only two of the six studies, at best, factored all recognized breast cancer risk factors into their findings. This leaves less than six known epidemiological test results, with the greatest number of subjects being 150, on which to base the hypothesis of organochlorines being a risk for mammary carcinogenesis. In short, there have not been enough adequate studies with a sufficient number of subjects to conclusively determine the existence of a risk between organochlorines and breast cancer.

The following is a table comparing whether or not the established 20-30% of risk factors were factored into each study (see Table 7). Also compared is whether or not other highly suspected risk factors were calculated into test results. Occupation, education, and socioeconomic level will be treated as being interconnected for the purposes of this table. Also height and weight together will appear under the obesity category.
Table 7.

Analysis of Studies Linking Breast Cancer to Pesticides with Respect to Taking into Account Known Breast Cancer Risk Factors and Those Considered Likely to Attribute to Breast Cancer Development

<table>
<thead>
<tr>
<th>Researcher: Unger et al.</th>
<th>Asked</th>
<th>Adjusted for, or, case &amp; controls were matched</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Known Risk Factors (20-30%)</strong>:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>Yes</td>
<td>Yes (1)</td>
</tr>
<tr>
<td>Personal/Family History</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Age Menarche</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Parity</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Age Menopause</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Obesity</td>
<td>(2)</td>
<td>Yes (1, 2)</td>
</tr>
<tr>
<td>Occupation/Education/</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Socioeconomic Status</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Potential Risk Factors (70-80%)</strong>:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Breast Feeding</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Residential History</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Diet</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Smoking History</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Researcher: Mussalo-Rauhamaa et al.</th>
<th>Asked</th>
<th>Adjusted for, or, case &amp; controls were matched</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Known Risk Factors (20-30%)</strong>:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>Yes</td>
<td>Yes (4)</td>
</tr>
<tr>
<td>Personal/Family History</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Age Menarche</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Parity</td>
<td>Yes (5)</td>
<td>Yes</td>
</tr>
<tr>
<td>Age Menopause</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Obesity</td>
<td>Yes</td>
<td>No (4)</td>
</tr>
<tr>
<td>Occupation/Education/</td>
<td>Yes (6)</td>
<td>No</td>
</tr>
<tr>
<td>Socioeconomic Status</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Potential Risk Factors (70-80%)</strong>:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Breast Feeding</td>
<td>Yes (7)</td>
<td>No</td>
</tr>
<tr>
<td>Residential History</td>
<td>Yes (6,8)</td>
<td>No</td>
</tr>
<tr>
<td>Diet</td>
<td>Yes (9,10)</td>
<td>No</td>
</tr>
<tr>
<td>Smoking History</td>
<td>Yes (10)</td>
<td>No</td>
</tr>
</tbody>
</table>
Table 7., Cont.

Analysis of Studies Linking Breast Cancer to Pesticides with Respect to
Taking into Account Known Breast Cancer Risk Factors and Those
Considered Likely to Attribute to Breast Cancer Development

<table>
<thead>
<tr>
<th>Researcher: Falck et al.</th>
<th></th>
<th>Adjusted for, or, case &amp; controls were matched</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Known Risk Factors (20-30%):</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Personal/Family History</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Age Menarche</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Parity</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Age Menopause</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Obesity</td>
<td>Yes</td>
<td>No (13)</td>
</tr>
<tr>
<td>Occupation/Education/</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Socioeconomic Status</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Potential Risk Factors (70-80%):</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Breast Feeding</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Residential History</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Diet</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Smoking History</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Researcher: Wolff et al.</th>
<th></th>
<th>Adjusted for, or, case &amp; controls were matched</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Known Risk Factors (20-30%):</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>Yes</td>
<td>Yes (3)</td>
</tr>
<tr>
<td>Personal/Family History</td>
<td>Yes</td>
<td>Yes (1)</td>
</tr>
<tr>
<td>Age Menarche</td>
<td>Yes</td>
<td>Yes (1)</td>
</tr>
<tr>
<td>Parity</td>
<td>Yes</td>
<td>Yes (1)</td>
</tr>
<tr>
<td>Age Menopause</td>
<td>Yes</td>
<td>Yes (3)</td>
</tr>
<tr>
<td>Obesity</td>
<td>Yes</td>
<td>Yes (1)</td>
</tr>
<tr>
<td>Occupation/Education/</td>
<td>Yes</td>
<td>No (13)</td>
</tr>
<tr>
<td>Socioeconomic Status</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Potential Risk Factors (70-80%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td>Yes</td>
<td>Yes (1)</td>
</tr>
<tr>
<td>Breast Feeding</td>
<td>Yes</td>
<td>Yes (1)</td>
</tr>
<tr>
<td>Residential History</td>
<td>Yes (6)</td>
<td>No</td>
</tr>
<tr>
<td>Diet</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Smoking History</td>
<td>Yes</td>
<td>Yes (1)</td>
</tr>
</tbody>
</table>
Table 7., Cont.

Analysis of Studies Linking Breast Cancer to Pesticides with Respect to Taking into Account Known Breast Cancer Risk Factors and Those Considered Likely to Attribute to Breast Cancer Development

<table>
<thead>
<tr>
<th>Researcher: Dewailly et al.</th>
<th>Known Risk Factors (20-30%):</th>
<th>Asked</th>
<th>Adjusted for, or case &amp; controls were matched</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Age</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Personal/Family History</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Age Menarche</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Parity</td>
<td>Yes</td>
<td>No (13)</td>
</tr>
<tr>
<td></td>
<td>Age Menopause</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Obesity</td>
<td>Yes (11)</td>
<td>No (11, 13)</td>
</tr>
<tr>
<td></td>
<td>Occupation/Education/</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Socioeconomic Status</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Potential Risk Factors (70-80%):</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Race</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Breast Feeding</td>
<td>Yes</td>
<td>No (13)</td>
</tr>
<tr>
<td></td>
<td>Residential History</td>
<td>Yes (6, 8, 12)</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Diet</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Smoking History</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Researcher: Kreiger et al.</th>
<th>Known Risk Factors (20-30%):</th>
<th>Asked</th>
<th>Adjusted for, or case &amp; controls were matched</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Age</td>
<td>Yes</td>
<td>Yes (3)</td>
</tr>
<tr>
<td></td>
<td>Personal/Family History</td>
<td>(14)</td>
<td>(14)</td>
</tr>
<tr>
<td></td>
<td>Age Menarche</td>
<td>Yes</td>
<td>Yes (1)</td>
</tr>
<tr>
<td></td>
<td>Parity</td>
<td>Yes (15)</td>
<td>Yes (1, 15)</td>
</tr>
<tr>
<td></td>
<td>Age Menopause</td>
<td>Yes</td>
<td>Yes (1)</td>
</tr>
<tr>
<td></td>
<td>Obesity</td>
<td>Yes</td>
<td>Yes (1)</td>
</tr>
<tr>
<td></td>
<td>Occupation/Education/</td>
<td>Yes</td>
<td>(13,14)</td>
</tr>
<tr>
<td></td>
<td>Socioeconomic Status</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Potential Risk Factors (70-80%):</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Race</td>
<td>Yes</td>
<td>Yes (3)</td>
</tr>
<tr>
<td></td>
<td>Breast Feeding</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Residential History</td>
<td>Yes (6)</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Diet</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Smoking History</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>
Table 7., Cont.

Analysis of Studies Linking Breast Cancer to Pesticides with Respect to Taking into Account Known Breast Cancer Risk Factors and Those Considered Likely to Attribute to Breast Cancer Development

Key:

1: This criterion was adjusted for in the results.

2: Fat percentage, of mammary biopsy extracted only, was factored into results.

3: Case and control subjects were matched for this criterion.

4: No statistical difference between subjects and controls.

5: Unknown for two cases and nine controls.

6: Current only.

7: Case patients only.

8: Not specified city or suburbs.

9: Fish eating habits only.

10: Obtained only from 18 controls.

11: As to weight loss over previous year only.

12: With the exception of two subjects.

13: Similarity exists between case and controls; however, no specific mention is made as to whether or not this similarity is statistically significant.

14: These researchers state data was obtained as to a subject's breast cancer risk factor profile, based on well-established risks, but did not specify what they consider risk factors.

15: Age at first pregnancy was unknown for nearly 40% of women who were ever pregnant.
Articles Commenting on Research

Numerous articles have been written about the epidemiological studies and their results. Different articles citing the same study often have divergent interpretations. Reviewing related literature suggesting a link between breast cancer and pesticides reveals the need to base such research on primary versus secondary sources and to interpret studies carefully.

One article entitled, "Organochlorines in the environment and breast cancer," combined the findings of all six epidemiological studies and concluded, "Women with breast cancer had slightly higher concentrations of DDE than controls, but the difference was not statistically significant" (Key & Reeves, 1994, p. 11). These authors did not take into account that they were not comparing similar studies. Some of the studies took into account some of the known breast factor risks, while two studies, at most, factored all known risk factors into their findings.

There are a number of highly suspected risk factors that comprise the 70-80% unofficially recognized risks in breast cancer development. Diet, for instance, is considered a likely risk, as is breast feeding history, and smoking history; however, few of the studies took these factors into account. Combining these studies, if done at all, must take into consideration their differences and the fact not every study took into account all known or those most highly suspected risk factors.
Another article states, "Important new research has linked organochlorines to breast cancer risk among women from the general population-those with no unusual chemical exposures" (D'Argo, Weinberg, Finaldi, Thorpe, Bogart, & Stairs, 1993, p. 10). While three of the six epidemiological studies concluded to having found a potential link between organochlorines and breast cancer, the remaining three studies found there to be no link. Not all were performed by the time this article was written; however, there was still debate over the results of the studies in 1993, as not all found a link to exist at that time. Thus, this particular article by D'Argo et al., seems to come to a hasty conclusion by its suggestion that a link was found. It may have been preferable for these authors to conclude a link was potentially found.

This article also mentioned the women in the epidemiological studies had "no unusual chemical exposures" (p. 10). None of the studies conducted specifically asked whether or not a subject had unusual chemical exposure. Consequently, since such information was not obtained, it was not represented as a factor in the test results. For instance, no question was posed as to whether or not a subject lived near a hazardous waste site in previous years or at the time of the study. Nor did the studies specifically ask if a subject worked with chemicals in the capacity of chemist, farmer, fruit picker, or any other. To assume that these women had no unusual chemical exposure seems to be unfounded.
While no specific studies were named, this article stated, “Seen in such a framework, the studies presented in this report indicate that organochlorines are likely to contribute to breast cancer rates in the general population” (D'Argo et al., 1993, p. 12). Again, this is a hasty conclusion. Debate continues over the studies and their results and to draw such a conclusion, is an oversight of some of the conducted whose results stated no such link exists. Further, none of the studies factored all known risk factors for breast cancer into their results, thus, their findings must be interpreted with that information in mind.

Influences on Interpreting Research

Authors have responsibilities to several people. There is a responsibility to the reader. This duty entails keeping information in context and not misrepresenting facts or figures. Authors also have a responsibility to maintain credibility to themselves and to their school of thought. According to McMillan and Schumacher (1993, p. 157), credibility refers to the extent to which the results approximate reality and are judged to be trustworthy and reasonable. Credibility is enhanced when the research design takes into account potential sources of bias that may distort the findings. Bias is a form of systematic error, a factor that influences the results and undermines the quality of research. The goal of good research design, then, is to provide a credible answer to a question, and bias reduces the credibility of the results. By carefully designing the study, the researcher can eliminate or at least reduce sources of error or
bias. Not every potential source of bias can be controlled completely in research, but there are principles for planning research to minimize such influences.

The issue of credibility can be examined by analyzing research suggesting a link between breast cancer and pesticides. Limited research and data are available on the subject. Some research seems to be better documented and to have a stronger foundation than other related research. Constraints, such as limited time, funding, and available resources, including subjects, are factors faced by many researchers. The studies examining a link between breast cancer and organochlorines vary in that some of the scientists were fortunate to have greater resources at their disposal than others did. Though their methods and findings may differ, all of these studies recognize the risk of breast cancer, the need to determine the remaining 70-80% of the unofficial risk factors, and none have said a link definitively does not exist.
CHAPTER FOUR

MAJOR PESTICIDE LEGISLATION

Understanding the history and laws available to protect our citizenry from pesticides is vital if we hope to invoke change. Pesticide regulation has developed through various federal legislative enactments which are enforced by several federal agencies. Each new statute helps to secure the foundation of its predecessors (see Table 8).

The first of the building blocks that made pesticide legislation what it is today is the Commerce Clause of the United States Constitution. The Commerce Clause serves as broadly defined Congressional power to regulate environmental legislation (Kubasek & Silverman, 1994, p. 27). However, the 1910 Insecticide Act marks the first statute directed specifically at pesticide regulation. This Act was also important because it marked the commencement of labeling standards for pesticides (Rodgers, 1994, pp. 413-414).

In 1947 the Insecticide Act was repealed and the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) took its place. The 1947 Act was significant in that it required pesticides shipped interstate to be registered. The same year, the Federal Environmental Pesticide Control Act was passed. This law addressed labeling of pesticide products. These Acts were followed by the 1954 Miller Amendment which further established stringent standards by
allowing tolerance limits for pesticide residues to be set (Kubasek & Silverman, 1994, p. 175; Rodgers, 1994, pp. 414 & 419).

The Delaney Clause was the next major building block in pesticide legislation. Enacted in 1958, Delaney prohibits the FDA from approving any food additive, including pesticides, found to be carcinogenic (D’Argo & Thorton, 1993, p. 2). This Clause continues to be in effect, though it currently is under scrutiny and may be the subject of amendment or repeal.

FIFRA was amended in 1959 and again in 1964. In 1959, new types of pesticides fell under its authority. The year 1964 marked the first time administrators had authority to deny pesticide registration applications (Rodgers, 1994, p. 420).

The National Environmental Policy Act was passed in 1970. This legislation is important because it requires federal agencies to prepare an environmental impact statement prior to the commencement of a project (Cohen & O’Connor, 1990, p. 203).

The Federal Environmental Pesticide Control Act was amended in 1972. It specified registration procedures. At that time exemptions for experimental use and emergency permits were developed. Also, the distinction was made between restricted and general use of pesticides.

Each of the aforementioned statutes represents growing strengthening of pesticide regulation in an effort to protect the environment and humans. Although the United States Constitution does not specifically address the issue
of environment, the Commerce Clause first provided the means to enact environmental legislation. Since its inception, numerous agency and Supreme Court decisions, as well as Congressional enactments, have been passed concerning pesticides.

The Commerce Clause

Environmental law finds its roots in the Commerce Clause of Article I of the United States Constitution. The Commerce Clause provides authority for Congress to pass most federal environmental regulations. While the Commerce Clause is used to find justification for environmental law, it was not initially intended to function in that manner. In fact, there is no specific Constitutional right to environmental protection (Kubasek & Silverman, 1994, pp. 18, 27).

Commerce refers to trade or exchange of goods or services. This Clause empowers the legislature to "regulate Commerce with foreign Nations, and among the several States, and with the Indian Tribes." Depending upon the ideological makeup of the Supreme Court, interpretations of the specific boundaries of this clause vary. In determining whether Congress has the authority to enact legislation under the Commerce Clause, the Supreme Court asks whether there is any rational basis for Congress to find that the activity to be regulated affects interstate commerce. If so, the Court asks whether there is any reasonable connection between the ends asserted and the regulatory
scheme selected to achieve those ends. If both questions can be answered affirmatively, the legislation stands. Most environmental regulation by the federal government is now presumed to be constitutional (Kubasek & Silverman, 1994, pp. 18-20).

Insecticide Act of 1910

Whereas the Commerce Clause addresses environmental legislation in broad terms, the issue of pesticide use was initially addressed by the Insecticide Act of 1910. This 1910 Act was spawned by a general consensus that pesticide products required regulation. Specifically, it stemmed from grievances about chemical products that were both “too strong or too weak.” The 1910 Insecticide Act was an extension of the food and drug law enacted in 1906. The 1910 Act that emerged from the model of the food and drug legislation was a labeling measure covering all insecticides and fungicides. The Act forbade the manufacture or shipment of any adulterated or misbranded products (Rodgers, 1994, p. 413).

Adulteration was defined as deviation from product standards. A misbranded products, as defined in the Act, contained false or misleading information on the package or label or omitted required statements as to product ingredients. The remedies under the Act included criminal penalties and civil actions initiated by the government to condemn products in noncompliance with the legislation. The United States Department of
Agriculture (USDA) was empowered to examine specimens but no provision was made for registration or other government approval of pesticide products (Rodgers, 1994, pp. 413-414). The Insecticide Act of 1910 was a positive in that it protected the public by regulating products and creating labeling standards; however, increased protection was not secured until 1947 when pesticide registration was enacted.

The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA)-1947

The Insecticide Act of 1910 was repealed and replaced by the comprehensive Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) (Rodgers, 1994, p. 414). FIFRA was originally passed in 1947 and, then under the authority of the United States Department of Agriculture, further strengthened pesticide labeling requirements, and was the first law to mandate pesticide registration. FIFRA was limited, however, in that it required only pesticides shipped in interstate commerce to be registered (Boyd, 1992, p. 25). Elaborate provisions were included for violations and provisions were added authorizing the United States to go to court to seize and dispose of products that were adulterated, misbranded, or unregistered. Like its 1910 predecessor, the main thrust of the 1947 FIFRA was to protect consumers from ineffective products (Rodgers, 1994, p. 414).
The Federal Environmental Pesticide Control Act of 1947

In 1947, the Federal Environmental Pesticide Control Act was passed. This law was primarily concerned with pesticide labeling. It was later amended, at which time it added more stringent pesticide regulations.

The Miller Amendment-1954

Presently FIFRA remains one of the two major statutes concerning pesticides. The second federal law guiding major pesticide regulations is the Federal Food, Drug, and Cosmetic Act (FFDCA) (Boyd, 1992, p. 25).

FFDCA was enacted in 1938 and was originally under the authority of the Department of Agriculture. The Act did not initially regulate pesticides, but in 1954, the Miller Amendment to the Federal Food, Drug, and Cosmetic Act (FFDCA) authorized the Administrator of FDA, now the EPA, to establish tolerance limits for pesticide residues on raw agricultural commodities (United States Statutes at Large, 1938, pp. 1040-1043).

The manufacturer was required to include detailed data in a petition for a pesticide tolerance. The Administrator then was to set tolerances at a level "to the extent necessary to protect the public health." Food products containing residues in excess of tolerance levels (or for which no limits or exemptions are established) are "adulterated" under provisions of the Act, and subject to seizure by the FDA (Rodgers, 1994, p. 419).
The FFDCA aids in the regulation of pesticide use by requiring the Administrator of the EPA to establish tolerance levels for concentration of pesticide residues on commodities consumed in the United States (Kubasek & Silverman, 1994, p. 180). Under FFDCA, the FDA is directed to enforce the residue levels for food set by the EPA, to seize or condemn foods containing residues which exceed those levels, and to invoke criminal penalties when necessary (Boyd, 1992, p. 25).

The Delaney Clause-1958

The Delaney Clause is a section of the Food Additives Amendment (named after Representative James Delaney) to the Federal Food, Drug, and Cosmetic Act (FFDCA) (Miller, 1994, p. 218). Enacted in 1958, Delaney prohibits the FDA from approving any food additive, including pesticide residues, found to cause cancer in humans or test animals (D'Argo & Thorton, 1993, p. 2). This clause provides no consideration of economic or health benefits or risks. It is a precautionary approach that says no deaths will be allowed because of substances added to or finding their way into foods people eat (Miller, 1994, p. 218). The Delaney Clause is important since it is the only "zero tolerance" standard for carcinogens in United States law (D'Argo & Thorton, 1993, p. 2).

Until 1958, food processors wishing to use new additives were free to do so unless the FDA could prove the additive to be harmful to human health.
With the passage of the Food Additive Amendment containing the Delaney Clause enacted in that year, the situation was reversed. The manufacturers of proposed food additives needed to satisfy the FDA that the product was safe prior to its approval for use (Nadakavukaren, 1995, pp. 338-9).

Since many hundreds of food additives were already in widespread use at the time the Delaney Clause was passed, a portion of this legislation exempted such substances in use from the rigorous safety testing demanded for new food additives. Those additives already in common usage were designated “generally regarded as safe” and placed on what is referred to as the GRAS list. In order to remove a food additive from the GRAS list, the FDA must demonstrate that the substance in question is harmful (Nadakavukaren, 1995, p. 340).

Since 1958, some members of the food and pesticide industries have fought hard to have this law repealed or changed to allow balancing of health and economic benefits and risks (Miller, 1994, p. 218). Lobbyists for the food chemicals industry argue that the Delaney Clause should be replaced with a “one-in-a-million” cancer risk standard (D’Argo & Thorton, 1993, p. 2). The EPA is also lobbying to amend the law to allow continued use of pesticides that pose a less than one chance in a million of causing cancer, which is the current EPA standard (Miller, 1994, p. 218).

Some health scientists and environmentalists believe that instead of revoking or weakening the Delaney Clause, it should be strengthened. These
individuals want the Clause to ban substances in food that have been shown to cause mutations (mutagens), birth defects (teratogens), liver or kidney damage, or damage to the nervous, immune, or endocrine systems in test animals or humans (Miller, 1994, p. 218).

In 1992, the United States Supreme Court ruled that food-crop residues of pesticides shown to cause cancer in test animals must be banned from use. This ruling means that the EPA must ban about 50 pesticides whose active ingredients are shown to cause cancer in test animals or ask Congress to weaken the law (Miller, 1994, p. 218). In May of 1993, the EPA’s position was established when it announced it no longer will allow emergency exceptions for pesticides that violate the Delaney Clause (D’Argo & Thorton, 1993, p. 2).

FIFRA-1959 & 1964 Amendments

Amendments in 1959 to FIFRA brought several new types of pesticides under its authority. They included defoliants, desiccants, and plant regulators. In 1964, another Act of Congress provided the first administrative authority to deny registration applications for adulterated or misbranded products (Rodgers, 1994, p. 420).

The National Environmental Policy Act - 1970

Congress recognized pesticide regulation needed expansion due to their environmental effect, and it passed a law that called for an assessment of the
environmental impact of a project prior to its commencement. Enacted in 1970, the National Environmental Policy Act (NEPA) requires federal agencies to prepare an environmental impact statement (EIS) for all "major federal actions significantly affecting the quality of the environment." An EIS must study the range of environmental effects a proposed project will have, as well as alternatives to doing the proposed action (Cohen & O'Connor, 1990, p. 203).

The Federal Environmental Pesticide Control Act of 1972

At the heart of the amended FEPCA were registration provisions strongly featuring the cost-benefit balancing that is the distinctive mark of FIFRA today. The Act specified registration procedures, the criteria for approval, and the consequences of disapproval. The Act also developed exemptions for experimental use permits, emergencies perceived by federal or state agencies, and special local needs. Further, the Act distinguished between restricted and general use which gave rise to a state-controlled program for certified applicators (Rodgers, 1994, p. 421).

The FEPCA addressed exported and imported pesticide products. Also, it continued to strengthen the enforcement apparatus. Establishments producing pesticides were required to register with the federal Environmental Protection Agency (EPA). The Administrator of the EPA was given a number of powers to prescribe regulations requiring the maintenance of records in a form compatible with effective enforcement; to call for production of records; to
inspect establishments; to issue warnings and orders to stop selling or using a product; to seize adulterated, misbranded or unregistered pesticides; to initiate civil penalty proceedings; and to delegate to the state authority to cooperate in the enforcement of the Act. At that time testing pesticides on humans, unless they were fully informed and freely volunteered, was outlawed (Rodgers, 1994, pp. 423-424).

FIFRA-1972 Through Present

Amended in 1972, FIFRA shifted regulatory authority to the newly formed federal Environmental Protection Agency. Thereafter, this statute required that all pesticides used in the United States prior to the 1972 amendment be registered for specific uses on the basis of test results, including long and short-term toxicological data. All previously registered pesticides were to be tested and re-registered with these requirements (Boyd, 1992, p. 25). As of 1990, out of 40,000 pesticides on the market, fewer than 100 have been re-registered (Cohen & O'Connor, 1990, p. 194).

The amended FIFRA required the EPA to re-evaluate the 600 active ingredients approved for use in pesticide products before 1972 to determine whether any cause cancer, birth defects, or other health risks. The EPA was supposed to complete its analysis by 1975. Congress extended the deadline for completing this review to 1997 (Miller, 1993, p. 314).
Since 1972, the EPA has used this law to ban the use, except for emergencies, of over 50 pesticides because of their potential hazards to human health. The banned chemicals include most chlorinated hydrocarbon insecticides, several carbamates and organophosphates, as well as several herbicides, such as 2,4,5-T and Silvex (Miller, 1993, p. 314).

FIFRA was amended in 1978 and re-authorized in 1988. The key changes wrought by the 1988 Amendment address: a) reregistration, b) storage and disposal of banned pesticides, d) indemnity, and e) enforcement (Rodgers, 1994, p. 431). FIFRA requires that all commercial pesticides be approved for general or restricted use by the EPA and that a pesticide pose "no unreasonable risk" if used as directed (Boyd, 1992, p. 25). This law continues to be administered by the EPA and, along with the Federal Food, Drug and Cosmetic Act, is one of two federal laws that currently guide the major regulations of pesticides.
<table>
<thead>
<tr>
<th>Year</th>
<th>Law</th>
<th>Principal Characteristics</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1787</td>
<td>Commerce Clause</td>
<td>Provides authority for Congress to pass most environmental legislation</td>
<td>Kubasek &amp; Silverman, 1994, p. 27</td>
</tr>
<tr>
<td>1910</td>
<td>Insecticide Act</td>
<td>Labeling measure covering all insecticides and fungicides</td>
<td>Rodgers, 1994, p. 413</td>
</tr>
<tr>
<td>1947</td>
<td>Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA)</td>
<td>Stricter labeling standards and requires registration of pesticides shipped in interstate commerce</td>
<td>Rodgers, 1994, p. 414</td>
</tr>
<tr>
<td>1954</td>
<td>Miller Amendment to the Federal Food, Drug, and Cosmetic Act (FFDCA)</td>
<td>Authorizes the establishment of tolerance limits for pesticide residues on raw agricultural commodities</td>
<td>Rodgers, 1994, p. 419</td>
</tr>
<tr>
<td>1958</td>
<td>Delaney Clause</td>
<td>Prohibits the FDA from approving any food additives, including pesticides, found to cause cancer</td>
<td>D'Argo &amp; Thornton, 1993, p. 2</td>
</tr>
<tr>
<td>1959</td>
<td>FIFRA Amendment</td>
<td>New types of pesticides are placed under FIFRA's authority, including defoliants, desiccants, and plant regulators</td>
<td>Rodgers, 1994, p. 420</td>
</tr>
<tr>
<td>1964</td>
<td>FIFRA Amendment</td>
<td>Provides first administrative authority to deny pesticide registration applications for adulterated or misbranded products</td>
<td>Rodgers, 1994, p. 420</td>
</tr>
</tbody>
</table>
### Major Pesticide Legislation

<table>
<thead>
<tr>
<th>Year</th>
<th>Law</th>
<th>Principal Characteristics</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1970</td>
<td>National Environmental Policy Act (NEPA)</td>
<td>Calls for environmental impact statement (EIS) for major federal action significantly effecting the quality of the environment</td>
<td>Cohen &amp; O'Connor, 1990, p. 203</td>
</tr>
<tr>
<td>1972</td>
<td>FEPCA</td>
<td>Specifies registration procedures, criteria for approval, and consequences of disapproval; Allows for exceptions for experimental use, emergency and special needs; Distinguishes between restricted and general use; Requires manufacturers keep pesticide records</td>
<td>Rodgers, 1994, pp. 421-424</td>
</tr>
<tr>
<td>1972</td>
<td>FIFRA Amendment</td>
<td>Regulatory authority shifted to EPA; Requires EPA to evaluate 600 ingredients approved for use in pesticide products by 1975</td>
<td>Miller, 1993, p. 314; Boyd, 1992, p. 25</td>
</tr>
<tr>
<td>1988</td>
<td>FIFRA Amendment</td>
<td>Addressed reregistration; storage and disposal of banned pesticides; indemnity; and enforcement</td>
<td>Rodgers, 1994, p. 431</td>
</tr>
</tbody>
</table>
Other organochlorines not defined as pesticides

Not all organochlorines are pesticides. Pesticides fall into a special category of toxic substances (see Table 9). While pesticides are regulated by FIFRA and FFDCA, toxic substances used in commerce, such as PCBs, are regulated by the Toxic Substances Control Act as well as other environmental laws (Kubasek & Silverman, 1994, p. 167).

Generally, toxic refers to something that is directly poisonous to humans. However, nowhere in the Toxic Substances Control Act does Congress specifically define the term. In fact, in none of the acts that regulate potentially toxic substances is the term defined. Instead, some acts list certain substances that must be regulated as toxins, and other statutes focus on the risk of harm imparted by certain substances that makes them subject to regulation as toxins (Kubasek & Silverman, 1994, p. 167).
Table 9.

Environmental Laws Regulating Toxic Substances

<table>
<thead>
<tr>
<th>Statute</th>
<th>Regulated Substance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asbestos Hazard Emergency Response Act</td>
<td>Asbestos</td>
</tr>
<tr>
<td>Clean Air Act</td>
<td>Hazardous air pollutants</td>
</tr>
<tr>
<td>Clean Water Act</td>
<td>Hazardous water pollutants</td>
</tr>
<tr>
<td>Comprehensive Environmental Response, Compensation and Liability Act</td>
<td>Hazardous waste</td>
</tr>
<tr>
<td>Federal Food, Drug, and Cosmetic Act</td>
<td>Pesticide residues</td>
</tr>
<tr>
<td>Federal Insecticide, Fungicide, and Rodenticide Act</td>
<td>Pesticides</td>
</tr>
<tr>
<td>Marine Protection Research and Sanctuaries Act</td>
<td>Toxic waste</td>
</tr>
<tr>
<td>Occupational Safety and Health Act</td>
<td>Toxic substances in the workplace</td>
</tr>
<tr>
<td>Resource Conservation and Recovery Act</td>
<td>Hazardous waste</td>
</tr>
<tr>
<td>Safe Drinking Water Act</td>
<td>Pesticides &amp; other hazardous substances</td>
</tr>
<tr>
<td>Toxic Substances Control Act</td>
<td>Toxic substances used in commerce</td>
</tr>
</tbody>
</table>

(Kubasek & Silverman, 1994, p. 167)
Risk Assessment

The courts have not specified what degree of evidence of harm is necessary for a substance to be banned or regulated (Kubasek & Silverman, 1994, p. 168). FIFRA requires a pesticide pose “no unreasonable risk” if used as directed (Boyd, 1992, p. 25). Agencies such as the EPA and the Occupational Safety and Health Administration (OSHA) must determine acceptable risk. They generally do so by using the process of risk assessment and risk management (Kubasek & Silverman, 1994, p. 168).

A hazard is any substance or action that can cause injury, disease, economic loss, or environmental damage. Risk is the possibility of suffering harm from a hazard. It is expressed in terms of probability, which is a mathematical statement about how likely it is that something will happen. Risk assessment involves using data, assumptions, and models to estimate the probability of harm to human health or to the environment that may result from exposures to specific hazards (Miller, 1994, p. 208).

Risk assessment is generally defined as the process of characterizing the potentially adverse consequences of human exposure to an environmental hazard. Risk assessment is a necessary preliminary state before risk management, the process by which policy choices are made once risks are determined. Understanding the process agencies go through to make these assessments is helpful for examining the scientific basis for risk assessment (Kubasek & Silverman, 1994, p. 168).
One of the risks a potentially toxic substance may pose is that of carcinogenicity. In deciding whether to regulate a chemical in a manner that would sustain judicial scrutiny, an agency may undertake risk management. A four-step process, which was recommended in 1983, is described in the following paragraphs (Kubasek & Silverman, 1994, p. 169).

**Step One: Hazard Identification**

Four types of information are generally used at the hazard identification stage of risk assessment: comparisons of molecular structures, short-term studies, animal bioassay data, and epidemiological studies (Kubasek & Silverman, 1994, p. 169).

An initial step, that may lead to further identification of a potential carcinogen, is the comparison of a substance's physical and chemical properties with those of a known carcinogen. Short-term studies on the effects of the substance on single-cell animals may be the next step. If exposure causes mutation, this result is generally an indicator that a substance is likely to be carcinogenic, and thus further studies are warranted (Kubasek & Silverman, 1994, p. 169).

The most commonly used data to support regulation of a substance as a carcinogen are obtained from animal bioassays. To support a finding of carcinogenicity, scientists usually look for consistently positive results in both sexes and in several strains and species. Although animal bioassays are
important, they are viewed cautiously. There are several fundamental biological similarities among all mammals, and so we can except similarities in response to chemical toxicity. Usually, in cases where human and animal responses can be compared, these similarities are borne out. Thus far, all human carcinogens (except possibly arsenic) have also been shown capable of causing cancer in some (but not all) animal species. Usually, but not always, the same sites of the bodies of both humans and animals are most vulnerable to the carcinogen (Kubasek & Silverman, 1994, p. 169).

Epidemiological data that show a positive association between exposure to an agent and disease are considered the most convincing evidence about human risk. This evidence, however, is generally very difficult to obtain because the number of people exposed to any particular hazard may be low, exposures may be confounded by exposures to other substances, and the latency period may be uncertain (Kubasek & Silverman, 1994, p.169-170).

**Step Two: Dose-Response Assessment**

Once the hazardous substance has been identified, the next step is to ascertain the response of humans to various levels of exposure. Because epidemiological data are not generally available for most substances that are being assessed, dose-response assessment usually requires assessments of animals studies. One problem with these studies is that the amount to which the animals are exposed in the tests for hazard identification is much higher
than the doses to which humans would generally be exposed. However, human exposure may be coupled with exposure to other chemicals, which may lead to synergistic effects. Scientists have developed a number of mathematical models used to predict risks to humans exposed to lower doses. Adjustments must also be made to account for differences in size and metabolic rates (Kubasek & Silverman, 1994, p. 170).

**Step Three: Exposure Assessment**

This step in the process determines which populations would be exposed to the chemical and the dosages to which they would be exposed. Rarely, exposure data can be directly measured, but more often it must be estimated. When chemicals are present in food or absorbed when a consumer product is used, the exposure assessment becomes more complex because of people's different dietary and personal habits. Exposure of a group to a mixture of potential carcinogens is also a factor requiring consideration, although such calculations are nearly impossible to make (Kubasek & Silverman, 1994, p. 170).

**Step Four: Risk Characterization**

This is the final step, the estimate of the magnitude of the public health problem. This step requires no further scientific knowledge or concepts. At
this stage, value judgments of the assessors are likely to come into play
(Kubasek & Silverman, 1994, p. 170).

Pesticide Registration

The EPA works with the USDA in product registration (Rodgers, 1994, p. 410). When a pesticide is to be registered, data showing its impact are submitted to the EPA. The EPA registers a pesticide when four factors exist: a) the pesticide's composition is such as to warrant the proposed claims for it; b) its labeling complies with FIFRA; c) the pesticide will perform its intended function without unreasonable risk to people and the environment (taking into account economic, social, and environmental costs and benefits of pesticides); and d) when used in accordance with commonly used practice, the pesticide will not cause unreasonable environmental risk (Kubasek & Silverman, 1994, p. 175).

Registration of a pesticide lasts five years. If the EPA receives no request for renewal within 30 days prior to the end of registration, notice of impending cancellation is published in the Federal Register. The manufacturer has 30 days within which to protest the cancellation, or the registration terminates (Kubasek & Silverman, 1994, p. 176).

The EPA may not grant registration for five years, and instead, grant only conditional registration. Conditional registration is given when required data are not submitted and when two conditions exists: a) the pesticide and
proposed use are substantially similar to a currently used pesticides or differ in ways that would not substantially harm the environment, and b) no significant harm or risk of unreasonable adverse effects would result from the pesticide's use. If the active ingredient of the pesticide is not currently being used, conditional registration can be granted for time needed to generate and submit the required data, not to exceed one year (Kubasek & Silverman, 1994, p. 176).

Major Agencies Regulating Pesticides

Three major agencies share responsibility for the regulation of pesticides, the EPA, the USDA, and the FDA. These are the governmental bodies that implement the pesticide statutes granting them specific authority. These pesticide statutes are used at agency discretion (FDA, 1993, p. 1).

The EPA registers (approves) the use of pesticides and sets tolerances, which are the maximum level of pesticide residues in or on a food. Except for meat, poultry, and certain egg products, for which the Food Safety and Inspection Service (FSIS) of the USDA is responsible, the FDA is charged with enforcing tolerances in imported foods and in domestically produced food shipped in interstate-commerce (FDA, 1994, p. 1). Both the EPA and FDA inspect food for residue levels of pesticides (Kubasek & Silverman, 1994, p. 180). The following is a brief discussion of the EPA's and the FDA's role in pesticide residue enforcement.
The Environmental Protection Agency

The Environmental Protection Agency (EPA) was created in 1970 as an independent agency by a presidential reorganization order (Kubasek & Silverman, 1994, p. 78). It is a federal regulatory agency that Congress has delegated the authority to make rules governing the conduct of business and labor in certain areas (Kubasek & Silverman, 1994, p. 11). This new agency took over functions formerly carried out by the FDA, as well as functions of other agencies. Its mission is to control and abate pollution in the areas of air, water, solid waste, pesticides, radiation, and toxic substances (Kubasek & Silverman, 1994, pp. 78-79). When considering pesticides used on food crops, the EPA establishes an upper limit on the amount of residue that can remain on food, based on human tolerance levels (Cohen & O'Connor, 1990, p. 194). The established pesticide levels are enforced by both the EPA and the FDA. This ambiguous division of authority often leads to power struggles between the two agencies (Rodgers, 1994, p. 410).

The Food and Drug Administration

The Food and Drug Administration is required by the Federal Food, Drug, and Cosmetic Act (FFDCA) to enforce the EPA-established pesticide residue limits by monitoring imported and domestically produced foods shipped in interstate commerce and seizing foods whose residues are in excess (Cohen & O'Connor, 1990, p. 194; FDA, 1993, p. 1). The FDA also acquires
incidence/level data on particular commodity and pesticide combinations and carries out its annual market basket survey, which is the **Total Diet Study**.

One aspect of the FDA's monitoring program involves the sampling of individual lots of domestically produced and imported foods, including animal feeds, and analysis of the foods for pesticide residues. Domestic samples are collected as close as possible to the point of production; imported samples are collected at the point of entry into United State's commerce. Emphasis is on the raw agricultural product, which is analyzed as the unwashed, whole commodity, i.e., with the peel or skin intact. Processed foods are also included (FDA, 1993, pp. 1-2).

Food samples collected are classified as either "surveillance" or "compliance." Most samples the FDA collects are the surveillance type, i.e., there is no prior knowledge or evidence that a specific food shipment contains illegal pesticide residues. Compliance samples are taken as follow-up to the finding of an illegal residue or when there is other evidence of a residue problem (FDA, 1993, p. 1).

If illegal residues are found in domestic samples, including those above EPA tolerance or no tolerance, for a particular food and pesticide combination, the FDA can invoke sanctions, such as seizure or injunction. For imports, shipments may be stopped at the point of entry when illegal residues are found. "Automatic detention" may be invoked for imports based on the finding of one
violative shipment if there is reason to believe that the same situation will exist in the future (FDA, 1993, p. 1).
CHAPTER FIVE

POTENTIAL SOLUTIONS

Reviewing the breast milk contamination data makes clear the need to establish international protocols for the collection, measurement and biomonitoring of pesticides and other xenobiotics in human breast milk. Cross-cultural comparisons within and between different countries are valuable epidemiological tools in the study of the health of women and children of all ages and races (Moses, 1993, p. 3).

It has been stated that if we know how cancer changes cells, and what the basic mechanism of actions is, then we can figure out how to stop it. Thus the exposure to a carcinogen would not matter. While this may be true for cancer, it ignores the fact that carcinogenicity is only one aspect of toxicity. In the case of pesticides, important non-cancer endpoints are neurotoxicity (poisonous or destructive to nerve tissue), teratogenicity (causing production of physical defects in the developing embryo), infertility, sub-fertility and immunotoxicity among others. Reliance on a single endpoint, cancer, to determine health risks of pesticide exposure is inappropriate as a basis of regulatory or public health policy (Moses, 1993, p. 3).

Education is another important measure to be taken. The public needs to be informed about the potential link between breast cancer and pesticides. Hopefully, educating the public will foster the populous to put pressure on the
government, calling for stricter regulation of pesticides allowed in the United States and on imported foods. Educating the public may also put pressure upon the government to conduct more research into whether or not any link between breast cancer and pesticides does exist.

There are numerous measures by farmers or gardeners can take to reduce pesticides use. Crop rotation, which involves changing the type of crop planted each year, is a nonchemical means to help reduce pests. Another cost-effective and health-wise method is to change from a monoculture to a polyculture. This uses diversity to reduce losses to pests. Using natural enemies (predators, parasitic and disease-causing bacteria, and viruses) can be an effective way to reduce pest population (Miller, 1994, p. 202).

Integrated Pest Management (IPM), also known as “Low Impact Pest Control” or “Low Impact Sustainable Agriculture,” is another viable alternative to reduce pesticide use. After ascertaining a pest problem exists, IPM practitioners combine various compatible methods to obtain the best control with the least possible environmental disruption. While IPM emphasizes utilizing natural controls such as predators, food deprivation, or weather to increase pest mortality, it can include pesticide application, but only after careful monitoring of pest population indicates a need. Unlike the total chemical control approach, IPM recognizes the adaptability of insects and does not attempt to eradicate a particular pest entirely, but rather is aimed at
keeping pest populations below the threshold level, where damaging economic losses can occur (Nadakavukaren, 1995, p. 317; Postel, 1988, p. 24).

When approving pesticides for use on crops, the EPA does not screen them for chemical properties that imitate estrogen. While present research linking estrogen-mimicking substances to breast cancer is still debated, it is strong enough to warrant cessation of those chemicals in question until a definite conclusion is drawn. Further the EPA's pesticide registration only considers the action of pesticides individually and does not examine synergistic or additive effects (McCarthy, 1993, p. 25). The EPA should instead expand its analysis of pesticides to take account of exposure from multiple sources.

Even though certain pesticides have been banned, severely restricted, or never approved in the United States, pesticide companies can make and export to other countries those very same pesticides they are forbidden to sell domestically. Residues of some of these chemicals return to the United States on imported items such as coffee, cocoa, pineapples, and out-of-season melons, tomatoes, and grapes, since more than one-fourth of the produce (fruits and vegetables) consumed in the United States is grown overseas (Miller, 1994, p. 202). Pressure needs to be put on our government to pass legislation forbidding both the exportation of pesticides not approved in our country and the importation of produce that has residues deemed legally unacceptable in our country.
NEED FOR FURTHER RESEARCH

Undoubtedly, further research is essential relative to the issue of breast cancer and pesticides. In breast cancer research, pesticides are only one of several environmental exposures being considered as risk factors for the disease. But it is important to look at what we are doing now and what current pesticide exposures may put pre-adolescent girls, in particular, at greater risk.

Most pesticides being used in the United States are not persistent and are not stored in the body. Tissue and blood levels will not be useful for finding markers (such as DDE) of past exposure. For this very reason it is important to set up comprehensive monitoring programs, including tissue and other specimen banks for archiving and testing samples, as part of the study of environmental causes for human cancer and other chronic diseases. Good candidates to include, along with blood and urine, are tissues routinely discarded such as placenta and liposuction fat. Evidence suggests fat itself does not cause breast cancer, but probably that the cancer results from carcinogenic pesticides, containing estrogen, that both accumulate and are biologically amplified in the fat (Epstein, 1992, p. 16).

Although the current focus is on breast cancer, we must broaden our vision in the case of pesticides to include other cancers, especially in children, because of placental and breast milk transfer, and the ubiquity of environmental exposure to pesticides, in the home, workplace, and community (Moses, 1993, p. 4). There is a need to research the impact of manufacturing
DDT regarding its effect on the manufacturers and the surrounding environment of the chemical plants.

Our goal should not be to replace old chemicals, but rather to seek non-chemical alternatives to meet the demands placed on agriculture and industry to meet society's needs (Feldman & Schubert, 1993, p.1). Integrated Pest Management (IPM) is an excellent first step. This system is attractive because it is less toxic and a cost-effective alternative to the traditional pesticide application used since World War II.

Undoubtedly, further research linking breast cancer to organochlorines is necessary. The research should factor into its results all recognized breast cancer risks factors, as well as diet, race, specific type of residence and employment, and breast feeding history. Also, further research should include larger numbers of subjects to ensure optimum results.

CONCLUSION

In virtually every nation in the world, age-adjusted incidence rates for breast cancer are rising, especially among older women (D'Argo et al., 1993, p. 8; Hunter & Kelsey, 1993, p. 598). The incidence of mammary cancer has been linked to age, family history, reproductive factors, obesity, education, and socioeconomic status (Cancer facts and figures - 1994, 1994, p. 10; California cancer facts and figures - 1995, 1994 p. 18). Industrialized countries are the
prime target of breast cancer; however, incidence is growing in developing countries as well.

Given this incompletely understood secular trend in breast cancer rates, more research is necessary (Hunter & Kelsey, 1993, p. 598). The possibility of carcinogenic hazards of environmental pollution, including organochlorine pesticides, raises concern over the need to consider other risk factors in breast cancer development, such as the environment, fat as a storage house for fat-soluble chemicals, and estrogen.

Research has shown that certain pesticides are stored in the adipose tissue of humans. Since fat tissue contains high levels of the fat-soluble organochlorine compounds, such as DDE and PCBs, it would be permissible to suggest a relationship between these compounds and mammary cancer (Unger et al., 1984, p. 24).

Studies have also indicated that pesticides can act like estrogen and alter estrogen activity and production. Such an effect on estrogen has been considered carcinogenic. Further, tests with human breast cancer cells and estrogenic pesticides indicated pesticides accelerated the reproduction of breast cells.

Blood serum and adipose tissue samples taken from some studies showed significantly higher levels of certain pesticides in the patients with breast cancer. Other studies have found breast milk to be contaminated with xenoestrogenic and carcinogenic pesticide residues.
The organochlorine compounds such as PCBs, have been demonstrated to be toxic, oncogenic, teratogenic and cocarcinogenic in experimental animals. The toxic effects have also been shown in long-term animal experiments after administration of parts per million range doses to nonhuman primates (Unger et al., 1984, p. 24). Whether the impact on rats and humans is similar is still open to discussion. However, some pesticides were linked to mammary cancer in rats.

The short-term advantages we gain from the use of pesticides are not a reason for us to overlook the possibly detrimental long-term effects that pesticides may have upon our health and that of our environment. While a link between pesticides and breast cancer is still open to debate, the studies performed suggest that such a link may exist.

As citizens, this potential link indicated by limited research should be a call to action. The necessary action taken should include education regarding alternatives to pesticide use, further research, and adherence by our government to strict regulation of each chemical that is put into our environment, as well as the combination of chemicals and their combined reactions.
REFERENCES


Pesticide and toxic chemical news, 21, (52), 17-20 (1993, October 27). Scientists say pesticides estrogenic, may cause breast cancer. (No author or editor noted).


