

THIRD EDITION

2004



State of the Evidence

**What Is the Connection Between
the Environment and Breast Cancer?**

Edited by Nancy Evans, Health Science Consultant, Breast Cancer Fund



*Dedicated to our founders,
pioneers in breast cancer and environmental health*



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Cover Illustration: *Book of Flowers IX*, by Lynda Fishbourne, 1997, "Art.Rage.U.s; Art and Writing by Women with Breast Cancer"

After I finished chemotherapy and started radiation treatments every day, I also found a new medium, encaustic (wax). It felt like a rebirth in a way. As a reward to myself for my daily hospitals visits, I painted in encaustic every day before leaving for my appointment. A series of these paintings resulted. The darker side has petals falling, and the background is etched with counting; it shows what I was leaving behind. The lighter, sunnier side contains written thoughts as well as flowers and leaves from my walks in nature. It reflects the more positive feelings I was having.

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Breast Cancer Fund and Breast Cancer Action are solely responsible for the content of this document. Some of the elements included may not reflect the opinions of these experts, nor should their assistance with this document imply endorsement by their institutions.

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Executive Summary

Less than one out of every 10 cases occurs in women born with genetic predisposition for the disease.

Breast cancer rates have been climbing steadily in the United States and other industrialized countries since the 1940s, amounting to more than one million cases per year worldwide. In 2004, in the United States alone, an estimated 215,990 women will be diagnosed with invasive breast cancer and more than 55,390 women will be diagnosed with in situ breast cancer, meaning the tumor is confined to its original location in the breast. This year, breast cancer is expected to kill more than 40,000 American women and more than 370,000 women worldwide. Billions of dollars have been spent in an effort

to stem this unrelenting tide, yet as many as half of all breast cancers occur in women who have no known risk factors for the disease. Less than one out of every 10 cases occurs in women born with genetic predisposition for the disease.

Research indicates that breast cancer arises for four primary reasons: genetic mutation, altered gene expression, altered cell interaction or from exposure to agents that alter the body's natural production of estrogen and other hormones. Not everyone exposed to a carcinogen will develop breast cancer, however. In fact, the development of breast cancer and other cancers is a multi-step process that most commonly results from more than one exposure over time. For example, one exposure might occur prenatally, another during childhood and a third during adolescence. Each of these exposures increase the risk of breast cancer in later life. Depending on the individual, cancer might develop after just two exposures, perhaps after dozens more, or may not develop at all.

Ionizing radiation is the best-established environmental cause of human breast cancer. A growing body of evidence also implicates non-ionizing radiation (electromagnetic fields and radio-frequency radiation) as a possible contributor to the development of breast cancer. In addition, compelling scientific evidence points to some of the 85,000 synthetic chemicals in use today as contributing to the development of breast cancer, either by altering hormone function or gene expression. As with ionizing radiation, some synthetic chemicals (called mutagens) also can cause gene mutations that lead to breast cancer. While there is no simple method for linking chemical exposures to breast cancer, several types of research—experimental, body burden and epidemiological studies—yield evidence that such a link exists.

For women born without genetic predisposition for breast cancer, events during their lifetimes contribute to producing the disease. But genetic predisposition does not cause breast cancer. Rather, it means that women

with inherited predisposition are more sensitive to the effects of breast carcinogens than those without a genetic predisposition.

There is broad agreement that exposure over time to estrogens that are naturally produced in the body increases the risk of breast cancer. Thus, the earlier in life a woman's menstrual cycle begins and the later it ends, the higher her risk of breast cancer. Hormones administered as pharmaceuticals also increase this risk. The Women's Health Initiative study on Hormone Replacement Therapy (HRT) was halted when it became clear that women who regularly took HRT had significantly higher rates of breast cancer (as well as other potentially life-threatening diseases). The National Toxicology Program now lists steroidal estrogens as known human carcinogens.¹ Since 1987, the International Agency for Research on Cancer (IARC) has categorized nonsteroidal estrogens as known human carcinogens. Other compounds with estrogenic activity, including drugs such as diethylstilbestrol (DES) and pesticides such as dieldrin, are understood to increase the risk of breast cancer. In addition, plastic additives such as bisphenol-A (BPA), polyvinyl chloride (PVC, which is found in many consumer products) and gasoline additives such as benzene, solvents and degreasing agents may be linked with increased risk of breast cancer due to their estrogenic activity.

Experimental studies have identified a number of synthetic chemicals that induce mammary cancer in rodents. These include: organic solvents (used in many manufacturing processes, including the manufacture of computer components); polycyclic aromatic hydrocarbons (PAHs, produced from combustion of gasoline, diesel, heating oil, cigarettes and other tobacco products, or by grilling meats and fish at high temperature); and 1,3-butadiene, which is both an air pollutant created by internal combustion engines and petroleum refineries, as well as a chemical used in the

manufacture and processing of synthetic rubber products and some fungicides.

There also is experimental evidence that certain chemicals can disrupt hormone function and thereby may increase the risk of breast cancer. These chemicals include the insecticide heptachlor, the herbicide atrazine and ingredients in some sunscreens. Others include certain phthalates, which are compounds used to make plastic soft and flexible, and parabens, which are chemicals that act as preservatives. Both phthalates and parabens are widely used ingredients in personal care products.

Body burden studies measure the presence of chemicals in people by analyzing blood, urine, body fat or breast milk. Also called biomonitoring, this type of research is used to study possible con-

nections between chemicals and breast cancer. These studies cannot establish cause but can reveal the internal contamination of women's bodies. Studies by the Centers for Disease Control and Prevention (CDC) show that Americans of all ages carry a body burden of at least 116 chemicals, some of them banned for more than two decades because of toxicity.²

Public health studies that have followed the development of breast cancer in women over time have identified a number of other compounds as likely contributors to the development of the disease, although the evidence remains incon-

Studies by the Centers for Disease Control and Prevention (CDC) show that Americans of all ages carry a body burden of at least 116 chemicals, some of them banned for more than two decades because of toxicity.

sistent. These chemicals include: dioxin, created when chlorinated materials such as plastics are burned; the pesticide DDT (dichloro-diphenyl-trichloroethane) and its metabolite and environmental breakdown product DDE; and some forms of PCBs (polychlorinated biphenyls), once widely used in the manufacture of electrical equipment, carbonless paper and other industrial and consumer products.

We clearly have major gaps in our current knowledge about the links between breast cancer and the environment. Research efforts should be focused, therefore, in areas most likely to provide useful information for shaping public policies around environmental exposures and public health. The types of research most likely to produce useful evidence will be those examining: (1) the interplay between the timing of exposures (especially periods of vulnerability), multiple exposures and chronic exposures (including occupational exposures and secondhand smoke); (2) disparities in health outcomes and differences in exposures among racial groups; (3) human contamination, measured by biomonitoring; and (4) public health studies examining unexplained patterns of breast cancer.

To reduce the burden of breast cancer in our society, public officials and the scientific and corporate communities must act based on what is already known about agents that increase the risk of breast cancer. More research on avoidable causes of the disease is also required. Studies that ask tough and honest questions about the underlying causes of breast cancer, including research based on recommendations from the first International Summit on Breast Cancer and the Environment, must be pursued. This 2002 summit was sponsored by the CDC. While this research proceeds, fundamental changes are needed in both the public and private sectors regarding the

production, use and disposal of chemicals found to increase the risk of breast cancer, specifically controlling or removing many of these substances from the environment and reducing exposure to both ionizing and non-ionizing radiation.

Considerable resources are spent encouraging women to make changes in their personal lives that might reduce their risk of breast cancer. But many factors that contribute to the disease lie far beyond an individual's personal control and can only be addressed by government policy and private sector changes. Breast cancer is not just a personal tragedy; it is a public health crisis that requires political will to change the status quo.

This crisis must be addressed by implementing the precautionary principle as a matter of public policy. Under this principle, evidence of harm, rather than definitive proof of harm, becomes the trigger for policy action. In addition, the precautionary principle mandates that proponents of chemicals and radiological products and processes assess their health, safety and environmental impacts before introducing them to the marketplace, and make that information publicly available. The burden to provide such information thus lies with manufacturers and sellers, not with the public. An obligation exists for manufacturers to examine a full range of alternatives to toxic ingredients and to select the alternative with the least potential impact on human health and the environment, including the alternative of not bringing questionable products to the market at all. The precautionary principle rests on the democratic principle that government officials are obligated to serve the public interest by protecting human health and the environment. Decisions applying the precautionary principle must be transparent, participatory and informed by the best available information.

Six-point Plan to Help Reduce the Risk of Breast Cancer and Ultimately End the Epidemic

1. Phase out chemicals known to cause cancer or genetic harm. Test all other chemicals currently in use and proposed for market to determine the effects on human health and the environment. Make this information available to the public.

2. Educate the public about the health effects of radiation and on how to reduce exposure to both ionizing and non-ionizing radiation.

3. Monitor the chemical body burden and resultant health outcomes in humans using biospecimens (blood, urine, fat and breast milk). Establish a comprehensive community program to detect synthetic chemicals and their metabolic products in people, document any geographic distribution patterns and health outcomes, and initiate a plan to eliminate these contaminants.

4. Hold corporations accountable for hazardous practices and offer incentives for clean, green practices.

5. Enact “sunshine” laws and enforce existing environmental protection laws.

6. Practice “healthy purchasing,” with local, state and federal governments leading the way in purchasing environmentally preferable products, so as to create an example for corporations and individuals to follow.

Implementing this plan depends on collaboration and cooperation among individuals and organizations with varying agendas. There are well-established networks of experienced environmental and health organizations that can act as resources to move this effort forward.

Increasing evidence that chemicals and radiation are contributing to the rising tide of breast cancer must not be ignored. Government and the private sector have an obligation to act on this evidence by supporting and implementing public policies that put health first. Now is the time to change the dangerous course we are on.

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Introduction

Breast cancer now strikes more women in the world than any other type of cancer except skin cancer. During the past half-century, the lifetime risk of breast cancer more than tripled in the United States. In the 1940s, a woman’s lifetime risk of breast cancer was one in 22. In 2004, it is one in seven. Breast cancer is the leading cause of death in American women ages 34 to 44.^{3,4} Although breast cancer in men accounts for less than one percent of the disease, in the United States the incidence has increased by 25 percent in the past 25 years.⁵ An estimated 1,600 men are expected to be diagnosed with breast cancer this year.⁶

Once a disease almost exclusively of postmenopausal women, breast cancer now strikes women in their 20s and 30s. Of the estimated 211,000 women in the United States diagnosed with breast cancer in 2002, approximately 10,500 were women under 40.⁷

More American women have died of breast cancer in the last 20 years than the number of Americans killed in World War I, World War II, the Korean War and the Vietnam War combined.

Several factors associated with elevated risk of breast cancer exist. They include alcohol consumption,^{8,9} personal characteristics such as early puberty, late menopause and a woman’s age at her first full-term pregnancy, and social factors such as higher income. Even when all known risk factors and characteristics including family history and genetics are aggregated, however, as many as 50 percent of breast cancer cases remain unexplained.^{10, 11}

Purpose Of This Report

The effort to understand and explain the major reasons for today’s high incidence of breast cancer has produced an ongoing, unsettled debate with differing findings in existing epidemiological and biological research. A significant body of evidence indicates, however, that exposure to radiation and synthetic chemicals must be understood as contributing to the increased incidence of breast cancer.

This report summarizes that evidence—based on experimental, body burden and epidemiological studies—and recommends new directions for future research. It also outlines a six-part plan to act on the evidence

A Woman’s Lifetime Risk of Breast Cancer



and reduce the burden of synthetic chemicals in our environment and in our bodies, and reduce our exposure

to radiation. This plan is based primarily on the precautionary principle,¹² which states that evidence of harm rather than proof of harm should be the trigger for action.

History Of This Report

On February 20, 2002, Breast Cancer Fund and Breast Cancer Action introduced *State of the Evidence: What Is the Connection Between Chemicals and Breast Cancer?* at the first informational hearing on breast cancer and the environment of the California State Senate Health and Human Services Committee in Sacramento, Calif. The hearing was sponsored by Sen. Deborah Ortiz. Since then, previous editions of the report have been widely distributed to scientists, advocates, policymakers, the public and the media.

State of the Evidence also served as a core document for participants at the first International Summit on Breast Cancer and the Environment, convened in Santa Cruz, Calif. from May 22-25, 2002. Sponsored by the U.S. Centers for Disease Control and Prevention (CDC) and the University of California Berkeley School of Public Health, the Summit brought together more than 100 scientists, advocates and community representatives to create a new agenda for breast cancer research and public policy. The primary policy recommendation from the Summit was to establish a national program of biomonitoring, using breast milk and other biospecimens as markers of community health. A report on the Summit was submitted to the CDC on January 23, 2003.¹³

On October 23, 2002, *State of the Evidence* was distributed at a joint informational hearing of the California State Senate Health and Human Services Committee and the State Assembly Health Committee, held in San Francisco. State Sen. Deborah Ortiz and Assemblymember Dario Frommer co-chaired the hearing. At this hearing, scientists, advocates and physicians presented testimony on breast cancer and the environment,

including research and policy recommendations that emerged from the International Summit. The Healthy Californians Biomonitoring Program legislation was introduced in two successive sessions of the California state Legislature and progressed significantly in each effort. The legislation will be reintroduced in the 2005 session amid growing support from the public, legislators, California Department of Health Services and non-governmental organizations across the state. A state-wide public opinion poll conducted by Lake Snell Perry & Associates showed that nearly 80 percent of California voters voiced strong support for such legislation and 97 percent agreed that industrial pollutants can cause health problems and disease.

New In This Edition

This edition includes expanded coverage of radiation, both ionizing and non-ionizing radiation, to broaden and deepen discussion of the environmental causes of breast cancer.

Previous editions have acknowledged ionizing radiation as a known cause of breast cancer. The continued aggressive promotion of mammography screening as “an important part of preventive care,”¹⁴ however, suggests the need for clarification and a more thorough examination of the role of radiation in carcinogenesis. The evidence that ionizing radiation causes breast cancer is indisputable.^{15,16} This edition includes a more detailed presentation on ionizing radiation and the decades of research that established radiation exposure as a major factor in the current

More American women have died of breast cancer in the last 20 years than the number of Americans killed in World War I, World War II, the Korean War and the Vietnam War combined.

epidemic of breast cancer (see page 20). As science editor Peter Montague wrote, “Radiation is a known cause of breast cancer in women; it is not speculative or uncertain. It is widely accepted. It just is not widely discussed.”¹⁷

In addition, there is evidence that non-ionizing radiation such as electromagnetic fields (EMFs) and radio-frequency radiation also increases the risk of breast cancer. Scientific research on this issue is incomplete but important to pursue, given that even a small increase in risk for such a common cancer will result in a significant increase in the number of cases.

Exposure to non-ionizing radiation is chronic, ubiquitous and increasing throughout the industrialized world. Health effects of EMF exposure are difficult to study because there is no unexposed population, i.e., no control group, and, unlike many chemicals, exposure to non-ionizing radiation cannot be traced through biomonitoring. Therefore, the differences in health effects between workers who have chronic occupational exposure to EMF and people without occupational exposure may be merely twofold. Nonetheless, numerous research studies have shown an association between EMF exposure and increased risk of breast cancer, other cancers and other chronic health conditions.

Three recent studies on EMF and breast cancer are cited below and discussed on p. 37.

New Research Highlights



Since publication of the second edition of *State of the Evidence* in 2003, several pertinent research studies have been completed. This third edition reports on those studies to further our understanding of environmental links to breast cancer and the implications for research and public policy.

Germane research published since February 2003 includes the following studies, some of which are discussed in this document:

- All types of **postmenopausal hormone replacement therapy (HRT)** were shown to **significantly increase the risk of breast cancer** in the Million Women Study in the United Kingdom. The risk was greatest among users of estrogen-progestin combination therapy.¹⁸ This study confirmed the findings relevant to HRT in the Women's Health Initiative Study, reported in 2002 (see page 24). However, the findings about estrogen-only replacement therapy (ERT) differed in these two large studies. The Million Women Study found an increased risk of breast cancer among estrogen-only users whereas the Women's Health Initiative study found no increase in risk with estrogen-only users.
- In a Swedish trial, use of **HRT** after previously being diagnosed with breast cancer **tripled a woman's risk of recurrence** or development of a new breast tumor, causing researchers to halt what had been planned as a five-year study after only two years.¹⁹
- **Chlorinated chemicals were associated with elevated risk of breast cancer** in three new studies. Taiwanese electronics workers exposed to chlorinated solvents were found to have an increased risk of breast cancer;²⁰ Massachusetts women exposed to perchlorethylene-contaminated drinking water were found to have a small to moderate increased risk of breast cancer;²¹ A biomonitoring study in Belgium found higher

levels of DDT and hexachlorobenzene (HCB) among breast cancer patients than in women without the disease.²² (See pages 32-33.)

- The solvent **ethylene glycol methyl ether (EGME)** and its metabolite, 2-methoxyacetic acid (MAA) were found to **sensitize breast tissue cells** to the effects of estrogens and progestins, thereby increasing the risk of breast cancer. EGME is used in the semiconductor industry and is also a component in varnishes, paints, dyes and fuel additives.^{23, 24}
- **Polychlorinated biphenyls (PCBs)** were **implicated in breast cancer recurrences** in a study of 224 women on Long Island, N.Y.²⁵
- Several metals, including **cadmium, copper, cobalt, nickel, lead, mercury, tin and chromium demonstrated estrogen-like activity in MCF-7 breast cancer cells**, according to Georgetown University researchers.²⁶ An animal study by the same researchers found that in utero exposure to cadmium caused early puberty and altered mammary gland development in female offspring.²⁷ The presence of both cadmium and mercury in women's bodies has been confirmed through several breast milk monitoring studies.^{28, 29, 30, 31}
- **Zeranol**, a hormone **used to help fatten beef cattle more quickly, caused breast cancer cells to proliferate** even when exposed to much lower levels of the hormone than the FDA has approved as safe, according to a study at Ohio State University School of Medicine (see page 41).³²
- **Flight attendants** were found to have varying degrees of **increased incidence of breast cancer** in studies in Iceland, Sweden and California.^{33, 34, 35} These findings confirm earlier studies showing similar results.
- Two occupational health studies, one from Yale University, the other from Mt. Sinai School of Medicine, found **increased breast cancer risk among teachers and librarians**.^{36, 37} The Mt. Sinai study, which looked only at women ages 20 to 44, also found **elevated risk among computer equipment operators** (which includes persons operating input/output devices such as tape drives, disk drives and printers). (See page 44.)
- **Exposure to ethylene oxide** was linked to **increased incidence of breast cancer** among female workers in commercial sterilization facilities, according to scientists at the National Institute for Occupational Safety and Health.³⁸ (See page 35.)
- **Radiation treatment for Hodgkin's disease greatly increased the risk of breast cancer** in four new studies (see page 20).^{39,40,41,42}
- **Radiological technologists** were found to have an elevated risk of breast cancer, melanoma and thyroid cancer, based on a study by National Cancer Institute scientists.⁴³
- Both **residential and occupational EMF exposure** were **linked to increased risk of breast cancer** in Norwegian women. This population-based study used data from Statistics Norway and the Norwegian national cancer registry and found a higher incidence of estrogen-negative breast cancer in women of all ages.⁴⁴
- **EMF exposure from electrically heated bedding** (electric blankets, mattress pads and heated water beds) was associated with **increased risk of breast cancer among African American women** in a study by researchers at Walter Reed Army Medical Center and Meharry Medical College (see page 37).⁴⁵
- **EMF exposure was associated with increased breast cancer risk** in a study of **female radio and telegraph operators** by the Cancer Registry of Norway (see page 37).⁴⁶

What Does Environment Mean?

Federal spending on breast cancer research increased dramatically in the past decade, totalling \$6.8 billion since 1991.⁴⁷ Only a small percentage has been directed toward studying environmental connections to breast cancer, however. In 2002 and 2003, for example, just one of every nine research dollars spent on breast cancer at the National Cancer Institute was to examine environmental links to the disease.⁴⁸ The relatively few environmental studies that have been

undertaken often defined the environment to include nutrition, exercise and other lifestyle factors—i.e. broadly—and focused largely on voluntary exposures and individual behaviors. It is not surprising, therefore, that many questions about involuntary environmental links to breast cancer remain unanswered.

The authors of this report recognize that the environment includes the totality of living and working conditions as well as the physical, biological, social and cultural responses to these conditions. For the purposes of this report, however, we are concerned primarily with people's exposures to environmental agents beyond their control, such as pesticides, dioxin, secondhand tobacco smoke and other chemicals. Some of these agents may be present in air, food, water, medications and soil.

Radiation (both ionizing and non-ionizing) is also discussed as an environmental exposure, even

though some exposure to radiation is voluntary, as in the case of X-rays and other radiological procedures. Patients may choose whether to undergo these procedures; however, these are often uninformed choices since little or no specific information about radiation dose or potential risk usually is provided by health professionals. Exposure to non-ionizing radiation is largely involuntary and ubiquitous.

Environmental Exposures

- Environmental exposures can occur daily at home, at school, in the workplace, in health care facilities and in other settings.
- Environmental exposures can also occur in the womb, when chemicals in the mother's body or diet cross the placenta to the fetus.
- Environmental exposures are often influenced by social, economic and cultural factors such as employment, income, housing, access to food and the way food is produced and processed.
- These exposures may be chronic (from occupation or residence, for example) or acute (from an industrial accident, such as a release of radioactive materials or other hazardous substances).

In 2002 and 2003, for example, **only 1 of every 9** research dollars spent on breast cancer at the National Cancer Institute was to **examine environmental links** to the disease.

Types of Research

Three types of research have been used to study possible connections between breast cancer and environmental factors: experimental, body burden and epidemiological, and ecological. Each type has advantages and limitations, as explained below.

I. Experimental (Laboratory) Research

One method of investigating possible links between synthetic chemicals and breast cancer is laboratory experiments in which animals or human breast cancer cells are exposed to particular chemicals. Some of these compounds are eliminated quickly from the body, leaving no residue. Others are lipophilic (fat-seeking) and once they enter the body through diet or other means can remain in body fat for decades. Although studies of cancer in animals have not always provided information that can be extrapolated to humans, scientific research has consistently found that substances causing cancer in animals also cause cancer in humans. The International Agency for Research on Cancer (IARC) recommended that:

In the absence of adequate data on humans, it is biologically plausible and prudent to regard agents and mixtures for which there is sufficient evidence of carcinogenicity in experimental animals as if they presented a carcinogenic risk to humans.⁴⁹

“I wanted to increase and supplement the pitifully small federal budget for research, and understand what caused our cancers and how we could stop the disease from spreading.”

■ Andrea Ravinett Martin,
Founder, Breast Cancer Fund

The U.S. National Toxicology Program adheres to the same principle in evaluating chemicals and considers that, in the absence of human evidence of cancer causation, chemicals shown to cause cancer in animals as being “reasonably anticipated to be carcinogenic to humans.”⁵⁰

In addition, laboratory animals are generally exposed to one or two chemicals under controlled conditions, whereas humans are exposed to a complex array of chemicals in uncontrolled conditions, making it more difficult to prove cause and effect in cancer. Research on the health effects of chemical mixtures is limited due to the extreme difficulty they pose to researchers. Scientists have yet to develop a sound way to study the effects of mixtures on human health. While there is already a method to measure the additive effect of dioxin mixtures in “toxic equivalencies” (TEQs) and a method for measuring total xenoestrogen burden in “estradiol equivalents,” the need to study the effects of mixtures is recognized by scientists as essential to understanding the causes of cancer and other conditions.⁵¹

Studies of breast cancer cells, known as in vitro studies, allow scientists to observe how various chemicals affect many biological processes that are part of the normal functioning of the cell. Careful manipulation of the cellular environment enables scientists to learn how the cell responds to chemical stressors. In vitro studies permit researchers to closely observe the way in which normal cells develop abnormally and to investigate cell proliferation—a process essential to tumor

“A major focus of our organization is to influence the availability and prioritization of funds for medical research toward the prevention and cure of breast cancer.”

■ Elenore G. Pred,
Founder, Breast Cancer Action

formation—and other cellular phenomena that are part of the progression toward cancer. However, in vitro studies have a limitation in that the behavior of cells in a laboratory dish cannot duplicate the behavior of cells within a living organism. Each organism is a unique and living laboratory

with its own molecular, cellular, hormonal and genetic environment.

For nearly a century, most breast cancer researchers have operated on the premise that cancer (1) originates at the cellular level of biological organization and (2) is caused by mutations in the DNA of epithelial cells which, in turn, cause changes in the tissue architecture. This premise is termed the Somatic Mutation Theory. In the last decade, some researchers have challenged this theory, proposing that cancer occurs at the tissue level of biological organization and that carcinogens alter stromal-epithelial cell interaction, disrupting normal development. This newer approach, called the Tissue Organization Field Theory, assumes that cancer can occur without

DNA mutation and, conversely, that DNA mutation can occur without causing cancer.^{52,53,54,55,56} This new research is discussed further on page 48.

2. Body Burden (Biomonitoring) and Epidemiologic Research

A second method of studying possible connections between chemicals and breast cancer is epidemiological research, and in particular, biomonitoring. This measures and compares levels of suspect chemicals in the blood, urine, body fat or other biospecimens of women with breast cancer to levels in women without breast cancer. These methods are incapable of establishing cause but can point researchers toward important questions and concerns. The presence of chemicals in humans is referred to as “body burden.” Although body burden studies have their limitations, they provide an understanding of the internal contamination of women’s bodies and, in the case of breast milk, contamination of the breast itself.

Body burden studies may produce “false negative” effects because they only measure residues at a particular point in time, not when cancer may actually have begun to develop. Measuring the current body burden does not show whether the level of a chemical was always low or whether it was once high and simply declined over time, or perhaps was reduced by breastfeeding or changes in body weight. Similarly, biomonitoring cannot determine whether levels of a chemical have always been high.

Body burden studies are unable to show the timing of exposure to a chemical, which scientists now believe is as critical as the dose of that chemical.⁵⁷ The female breast is most vulnerable to chemical absorption during periods of significant development, including the prenatal period, adolescence, pregnancy and lactation.⁵⁸ Exposure at age 12 may well lead to cancer at age 32 or 42.

Body burden measurement at or near the time of diagnosis will not reflect levels at the time of exposure. In addition, some chemicals known to cause cancer, such as methylene chloride, benzene, chlorinated organic solvents and certain prescription drugs, do not linger in the body but are excreted without a trace.⁵⁹ Methods for measuring exposures to these chemicals are complex and expensive, and reveal only recent exposure, not past exposures that may be implicated in the development of breast cancer and other diseases.

Body burden studies are a tool that, combined with health outcomes data, help us understand whether environmental factors are linked to unusually high rates of disease in particular communities. Other measures such as total dioxin exposure and total xenoestrogen exposure could be even more relevant to understanding the rising incidence of breast cancer.

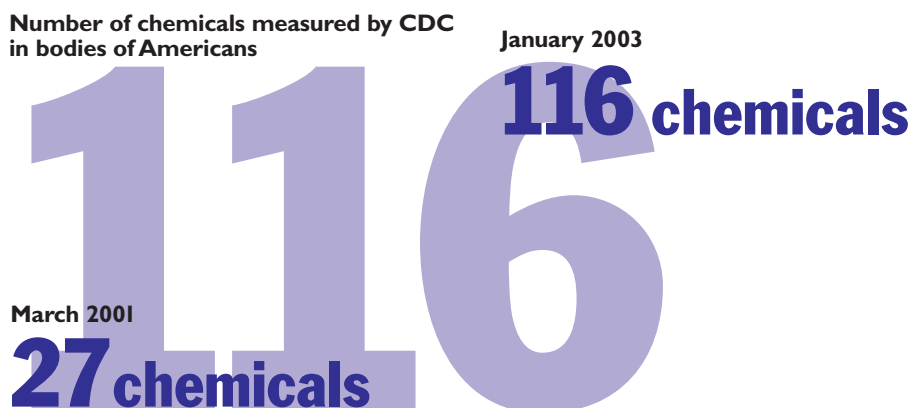
Despite these limitations, body burden studies show that human contamination with multiple chemicals is persistent, ubiquitous and often chronic. The First National Human Exposure to Environmental Chemicals report, released by the CDC in March 2001, revealed the presence of 27 chemicals in the bodies of Americans. The second CDC report, published in January 2003, measured body burden levels of 116 chemicals, some of them banned for two decades due to toxicity. Based on blood and urine samples from 8,000 people of all ages, the 2003 report includes chemicals associated with increased risk of breast cancer, such as polycyclic aromatic hydrocarbons (PAHs) and dioxin, as well as many compounds known to be endocrine disruptors.⁶⁰

3. Ecological Research

A third method of studying possible links between chemicals and breast cancer involves ecological studies. This type of research examines environmental and socioeconomic characteristics in geographic areas with a high incidence of breast cancer, and compares these findings with areas of low incidence. For example, a 2003 study by researchers at Silent Spring Institute found a correlation between a woman's length of residence on Cape Cod, Mass., and her risk of breast cancer.⁶¹ Ecological studies alone are not considered strong evidence of a causal link to breast cancer but are helpful for generating environmental or health hypotheses. They are often used to justify conducting analytical studies that measure individual exposure.

No research has found complete proof that synthetic chemicals are responsible for the current breast cancer epidemic. Yet experimental, body burden and epidemiological, and ecological research all have yielded compelling evidence that exposure to certain chemicals contributes to increased risk of breast cancer.

Silent Spring Institute found a correlation between a woman's length of residence on Cape Cod, Mass., and her risk of breast cancer.



National Human Exposure to Environmental Chemicals report, released by the CDC

Evidence that Timing of Exposure Matters

“I grew up in two of the most toxic regions in the country. Last year [2000], I learned that my blood is filled with residues of chemicals I was exposed to when I was just a child. I still carry those toxins with me; my body is a record of the environmental history of my life.”

■ Andrea Ravinett Martin,
Founder, Breast Cancer Fund

Two decades of research on laboratory animals, in wildlife and on cell behavior (in vitro)⁶² have shown the inadequacy of the long-held belief that “the dose makes the poison.” Scientists now know that the timing, duration and pattern of exposure are just as important as the dose. Low dose exposure to environmental chemicals—parts per billion or even per trillion—during a critical window of development can cause permanent damage to organs and systems. For example, fetal exposure of mice to low-dose bisphenol-A changed the timing of DNA synthesis in the epithelium and stroma of the mammary gland of the animals, and increased the number of terminal ducts and terminal end buds. According to Markey et al., these findings “strengthen the hypothesis that in utero exposure to environmental estrogens may predispose the developing fetus to mammary gland carcinogenesis in adulthood.”⁶³ Another study in laboratory animals showed that exposure to bisphenol-A caused earlier onset of puberty.⁶⁴

Two animal studies found that intrauterine exposure to TCDD dioxin predisposed offspring to mammary cancer. The first showed that dioxin exposure of the pregnant mouse caused proliferation of terminal end buds of the female offspring’s mammary gland, making the gland more vulnerable to carcinogen exposure.⁶⁵ The second study, on rats, showed that intrauterine exposure interfered with maturation of the mammary gland, widening the window of vulnerability to cancer.⁶⁶

Georgetown University scientists reported similar findings from a study of pregnant rodents exposed to cadmium. The female offspring experienced earlier onset of puberty and altered development of the mammary gland, increasing the risk of mammary cancer in adulthood.⁶⁷ The younger the organism, the more vulnerable the developing cells and tissues are to environmental exposures. The most critical windows of vulnerability for the developing breast, therefore, are the prenatal, prepubertal and adolescent periods, through to a woman’s first full-term pregnancy.

Evidence That Radiation Causes Breast Cancer

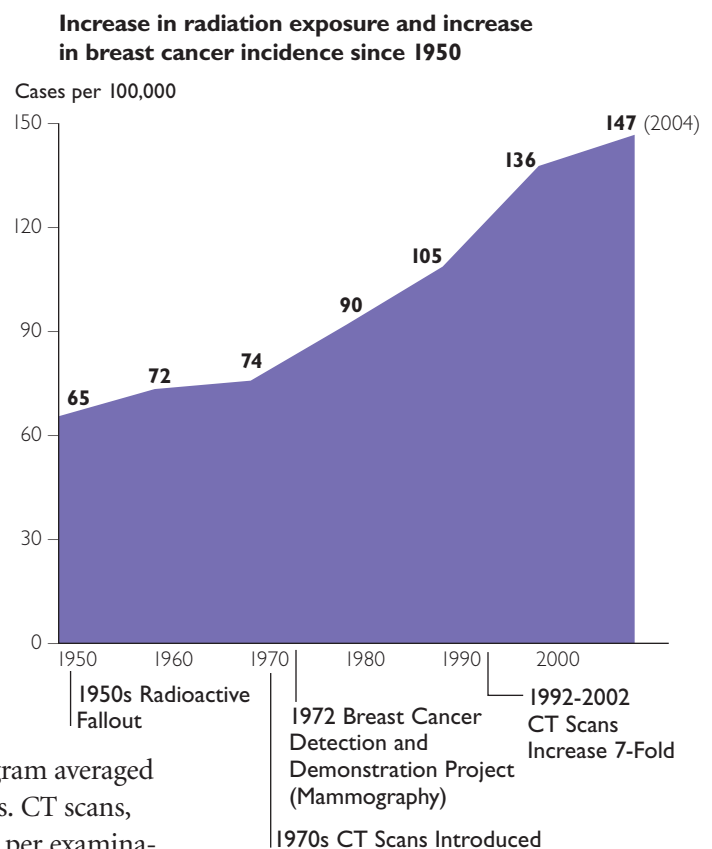
“More is known about the relationship between radiation dose and cancer risk than any other human carcinogen, and female breast cancer is the best quantified radiation-related cancer.”⁶⁸

Exposure to ionizing radiation is the best-established environmental cause of human breast cancer, and radiation damage to genes is cumulative over a lifetime.⁶⁹ Repeated low-dose exposures over time may have the same harmful effects as a single large-dose exposure. As noted earlier, however, exposure to a carcinogen does not mean that everyone exposed will develop cancer, only that the risk of developing cancer is increased.

Ionizing radiation is a form of radiant energy with enough power to break off electrons from atoms (to ionize the atoms) and energize the electrons, which then travel at high speed through body tissue, damaging genetic material.⁷⁰ X-rays and gamma rays are the only forms of radiant energy with sufficient power to penetrate and damage body tissue below the surface.

The ability of ionizing radiation to kill cells has made radiation therapy a standard of care following lumpectomy for breast cancer. Yet this cell-killing ability is sometimes overlooked or underestimated when screening or diagnostic radiation is prescribed and/or administered.

There are many sources of ionizing radiation, including X-rays, CT scans, fluoroscopy and other medical radiological procedures, nuclear fallout and radionuclides in drinking water. All Americans were exposed to nuclear fallout from above-ground testing in Nevada between 1951 and 1958.⁷¹ When annual mammography screening was first promoted in 1972, the radiation dose per mammogram averaged two rads, a dose 10 times greater than current mammograms. CT scans, introduced in the 1970s, greatly increased the radiation dose per examination compared with ordinary X-rays.⁷² According to the National Cancer Institute, CT scans “comprise about 10 percent of diagnostic radiological procedures in large U.S. hospitals,” but contribute an estimated 65 percent of the effective radiation dose to the public from all medical X-ray examinations.⁷³ Increased radiation exposure from multiple sources may have contributed to a rising incidence of breast cancer between 1950 and 1991. During that period, the incidence of breast cancer in the United States increased by 90 percent.⁷⁴



There is no safe dose of radiation:^{75,76,77,78} “A single X-ray photon is physically capable of causing irreparable and consequential damage to genetic molecules in a cell. Risk of such damage is proportional to dose, right down to zero dose.”⁷⁹

There is credible evidence that medical X-rays (including fluoroscopy and CT scans) are an important and controllable cause of breast cancer.^{80,81} Although X-rays have been a valuable diagnostic tool for more than a century, the radiation dose has not always been carefully

“This is not an individual woman’s personal tragedy; it is a tragedy for all women and together we have the power to change things.”

■ Elenore G. Pred, Founder,
Breast Cancer Action

controlled and sometimes has been higher than needed to obtain high quality images, particularly in the case of fluoroscopy and CT scans. Dose reduction can be achieved without sacrificing image quality. In mammography, for example, efforts to reduce the radiation dose to as low as reasonably achievable (ALARA)

levels have reduced the radiation dose from an estimated two rads in 1976 to 0.2 rads today.⁸²

One of the first physicians to recognize the association between medical radiation exposure and increased breast cancer risk was Ian MacKenzie, who studied 800 women who had undergone repeated fluoroscopy examination for tuberculosis.⁸³ His study, published in 1965, found that the irradiated women had 24 times the risk of breast cancer as other patients with tuberculosis who had not been radiated. Decades of research have confirmed the link between radiation and breast cancer in women who were radiated for many different conditions, including benign breast disease,⁸⁴ acute postpartum

mastitis,⁸⁵ enlarged thymus,⁸⁶ skin hemangiomas,⁸⁷ and Hodgkin’s disease.^{88,89,90,91,92}

The type of cancer that can result from radiation exposure depends on the area most directly exposed and the age at which an individual is exposed. Radiological examination of the spine, heart, lungs, ribs, shoulders, and esophagus also exposes parts of the breast to radiation. X-rays and fluoroscopy of infants constitute whole body irradiation.

Indeed, childhood exposure to radiation creates the greatest cancer risk while exposure after age 40 confers the lowest risk.⁹³ A study of 5,573 women who were radiographically examined for scoliosis before age 20 showed that breast cancer risk increased in direct proportion to the number of radiographic examinations. Patients who had 50 or more radiographic exposures had nearly four times the risk as those unexposed to radiation.⁹⁴ The link between radiation exposure and breast cancer also has been confirmed in atomic bomb survivors.^{95,96,97} Rates of breast cancer were highest among women who were under 20 when the United States dropped atomic bombs on Hiroshima and Nagasaki.⁹⁸

Computed tomography (CT) scans are of particular concern, especially in children, because (1) the radiation dosage is much greater than X-rays, (2) the use of CT scans increased about sevenfold between 1992 and 2002 and (3) children have a longer life expectancy and therefore a greater opportunity to develop a radiation-induced cancer.⁹⁹ For example, the same radiation dose given to a 40-year-old and a newborn is several times more likely to cause a cancer during the child’s lifetime than in the adult’s. In 2001, several researchers pointed out that many hospitals were using the same CT radiation exposure parameters for infants, children, adolescents and

adults, despite the extreme differences in body size.^{100,101,102,103} A CT scan of the chest may expose much of the chest to 10 times the dose from a mammogram.¹⁰⁴ Such a large dose of radiation delivered to a girl during the critical window of adolescence may dramatically increase her risk of breast cancer later in life. Experts estimate that CT radiation exposure can be cut by 50 percent during examinations of children without sacrificing diagnostic information.¹⁰⁵

Many physicians, especially non-radiologists, are not fully aware of the risks to the patient that radiological procedures involve. One small study in the United Kingdom revealed that no doctors interviewed knew the approximate dosage of radiation received by a patient during a chest X-ray. Asked to estimate the equivalent doses of radiation for various imaging examinations, all underestimated the actual doses involved—the average mean dose of radiation was 16 times larger than the doctors believed.¹⁰⁶

Patients who ask about the radiation dose involved in a procedure are often dismissed with the answer that it's similar to the exposure one would get in a cross-country plane flight. This is seldom true, however. An average radiation dose of one rad (or centigray) to the breast is equivalent to the breast irradiation received during about 3,300 hours of flying.¹⁰⁷ Thus a typical mammogram of 0.3 rads would equal the radiation dose received by the breast in 1,000 hours of flying, not a single trip.

Although the benefit of medical procedures involving radiation exposure most likely outweighs the risk, it is essential that physicians and the public recognize the inherent risk of radiation exposure and where feasible and practical, seek alternative diagnostic and therapeutic methods.

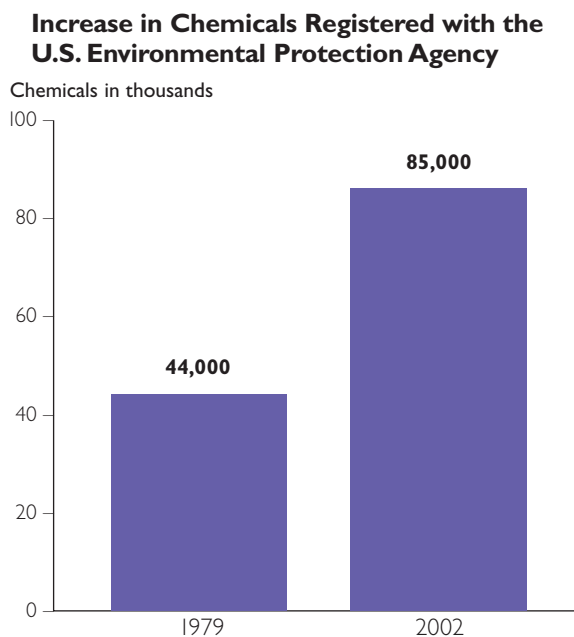
Radiation is not the sole cause of breast cancer, only the best-established cause. Other potential contributors to increased breast cancer risk include genetic predisposition, electromagnetic fields, chemicals, and hormones. Many of the environmental exposures discussed in this report may interact to increase the risk of breast cancer. Radiation is a mutagen as well as a carcinogen; the same is true of some chemicals. Indeed, radiation may enhance the ability of hormones or other chemicals to cause cancer.^{108,109}

Increased radiation exposure from multiple sources may have contributed to a rising incidence of breast cancer between 1950 and 1991. During that period, the incidence of breast cancer in the United States increased by 90 percent.

Evidence That Chemicals Cause Breast Cancer

The scientific evidence connecting chemicals and breast cancer does not, in most cases, constitute proof of cause and effect but it is nonetheless powerful. A cause-effect link is very difficult to establish since it is a life history of exposure, not only to ionizing radiation or to a single chemical but to complex mixtures of agents, including endogenous hormones, that counts. For example, researchers at Tufts University showed in 1994 that xenoestrogens acted additively with each other.¹¹⁰ In 2002, scientists in London demonstrated that weak estrogens act additively with steroidal estrogens.¹¹¹

Breast cancer rates continue to rise around the world.¹¹² Within this broad demographic picture, there is a discernible relationship between the rates of breast cancer and the widespread use of man-made chemicals. The highest rates of breast cancer are found in the industrialized nations of North America and northern Europe, while the lowest rates are in



Asia and Central Africa. In northern Africa, as in many countries either developing or in transition,^{113,114,115,116,117,118} breast cancer rates are escalating sharply.¹¹⁹ In Tunisia, for example, the rate has increased by a third, from 15 cases per 100,000 in 1994¹²⁰ to 20 cases per 100,000 in 2000.¹²¹

The increasing risk of breast cancer and other cancers has paralleled the proliferation of synthetic chemicals since World War II. An estimated 85,000 synthetic chemicals are registered for use today in the United States. Another 2,000 are added each year. Complete toxicological screening data is available for just seven percent of these chemicals. More than 90 percent have never been tested for their effects on human health.¹²² Many chemicals persist in the environment, accumulate in body fat, and remain in breast tissue for decades. Studies of

women's chemical body burden show that all of us carry pollutants in our bodies. Some of these pollutants, commonly used as fuels, solvents and other industrial applications, have been linked to mammary tumors in animals.^{123,124} (See Appendix, page 56, for a complete listing of chemicals shown to induce mammary tumors in animals.)

Groups of people who move to industrialized countries from countries with low breast cancer rates soon develop the higher rates of the industrialized country. For example, women who emigrate to the United

States from Asian countries, where the rate is four to seven times lower, experience an 80 percent increase in risk within one generation.¹²⁵ A generation later, the rate for their daughters approaches that of U.S.-born women. This change in risk over two generations suggests that in utero exposures, such as nutrition, affect subsequent disease risk. As immigrants adopt a western diet, they may be increasing their—and their daughters’—breast cancer risk.

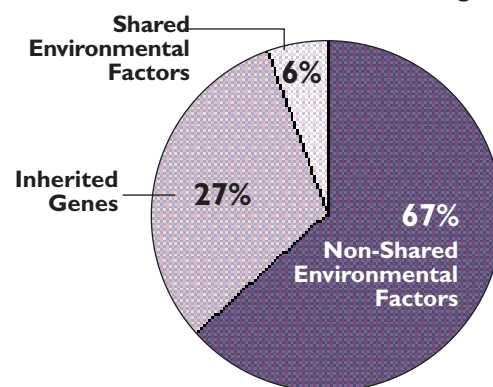
It is difficult to know, however, whether the dramatic increase in risk through dietary changes comes from nutritional content, contaminants, food additives or other factors. Emigration to the United States also may affect reproductive behavior, such as the use of oral contraceptives, as well as environmental exposures.¹²⁶

A person’s age at the time of emigration also affects cancer risk. A Swedish study of many different cancers showed that age at emigration determined whether the individual acquired the cancer risk of the country of origin or the country of destination. Researchers concluded that “birth in Sweden sets the Swedish pattern for cancer incidence, irrespective of the nationality of descent, while entering Sweden in the 20s is already too late to influence the environmentally imprinted program for the cancer destiny.”¹²⁷

Inherited genetic mutations have received much attention recently but they account for only a small fraction—five to 10 percent—of the breast cancer epidemic.¹²⁸ Women with an inherited mutation on the BRCA1 or BRCA2 genes have a 60 to 82 percent probability of getting breast cancer in their lifetime.¹²⁹ While these families are devastated by cancer, all families share more than genetic mutations. They also share a common environment. A study in 1988 found that adopted children whose adoptive parents died of cancer were five times as likely to get the same disease,¹³⁰ revealing a connection to common exposures and lifestyles independent of inherited genes.

In the largest study ever conducted among twins, researchers found that inherited genes contributed 27 percent of breast cancer risk, shared environmental factors six percent, and non-shared environmental factors 67 percent of the risk.¹³¹ In other words, most breast cancer is acquired, not inherited.

Contributors to breast cancer risk among twins



In the largest study ever conducted among twins, researchers found that inherited genes contributed 27 percent of breast cancer risk, shared environmental factors six percent, and non-shared environmental factors 67 percent of the risk.¹³¹

While the scientific community has undertaken relatively few research studies in humans aimed at identifying specific links between breast cancer and cancer-causing chemicals, there is strong evidence from laboratory studies that such links do exist. Tests performed on laboratory animals—a standard for public health research—implicate 45 chemical compounds in breast cancer formation.^{132,133,134} Other research has demonstrated that low levels of chemicals often found in the environment can act in synergy with ionizing radiation, creating a greater cumulative effect.¹³⁵

Scientists also recognize that testing one chemical at a time ignores the reality that we are all exposed to hundreds, if not thousands, of chemicals every day. Combinations of chemicals can produce multiplied effects, creating a more toxic chemistry.¹³⁶ Future research design must incorporate these insights.

The following sections examine the range of evidence that exists linking synthetic chemicals to breast cancer incidence and mortality. These chemicals include synthetic estrogens, progestins, solvents, polycyclic aromatic hydrocarbons (PAHs), 1,3-butadiene and aromatic amines.

I. Estrogens, Progestins and Breast Cancer

Although estrogens are necessary for childbearing, strong bones and healthy hearts, research has established that women who have prolonged exposure to estrogens are at higher risk for breast cancer. This includes women who begin to

Women who previously used oral contraceptives and later received HRT face an even greater risk than those who have not used either or have used only one.

menstruate before age 12, do not reach menopause until after age 55, have children late in life or not at all, do not breast-feed or who use hormone replacement therapy (HRT) after menopause. When

women's own estrogens are supplemented by oral contraceptives and/or HRT, hyperestrogeny (abnormally high levels of circulating estrogens) results, increasing the risk of breast cancer for some women.^{137,138,139} Women who previously used oral contraceptives and later received HRT face an even greater risk than those who have not used either or have used only one.¹⁴⁰ In 2002, the National Toxicology Program added HRT and steroidal estrogens, used in oral contraceptives, to the list of known human carcinogens.¹⁴¹ The International Agency for Research on Cancer (IARC) has listed steroidal estrogens as known human carcinogens since 1987.

In 2004, Swedish researchers halted a study of HRT in women with a history of breast cancer because of an unacceptably high rate of recurrence. Originally planned as a five-year study, the trial was stopped after just two years because women taking HRT had three times the rate of recurrence or new tumors compared to women who received other treatment for menopausal symptoms.¹⁴²

In 2003, researchers in the Million Women Study (MWS) in the United Kingdom reported that the use of all types of postmenopausal HRT¹⁴³ significantly increased the risk of breast cancer and that the risk was greatest among users of estrogen-progestin combination therapy. The study enrolled more than one million women ages 50 to 64. Researchers estimated that women who used estrogen-progestin HRT for 10 years were almost four times more likely to develop breast cancer as women who used estrogen-only HRT (19 additional breast cancers per 1,000 women compared to five per 1,000). Researchers concluded: "Use of HRT by women ages 50-64 in the UK over the past decade has resulted in an estimated 20,000 extra breast cancers, 15,000 of them associated with estrogen-progestin combination; the extra deaths cannot yet be reliably estimated."¹⁴⁴

The MWS study further confirms the link between HRT and breast cancer reported by the Women's Health Initiative (WHI) study in 2002. The WHI study enrolled more than 16,000 women ages 50 to 79 years of age. Half the women took Prempro, a combination of estrogen plus progestin. The other half took a placebo. The trial was halted at the end of five years when researchers saw a 26 percent increase in the risk of breast cancer, in addition to significant increases in the risk of heart disease, stroke and blood clots.¹⁴⁵

During the course of the WHI study, 42 percent of women withdrew. When the researchers reanalyzed the data, based on the number of women actually treated with HRT, the risk of breast cancer increased from 26 percent to 49 percent. Other health risks also increased in the women taking HRT. These two large studies confirm the decades of research indicating that HRT increases the risk of breast cancer and other life-threatening conditions. Furthermore, it indicates that both endogenous hormones and exogenous substances that act like hormones increase the risk of hormone-related cancers such as breast cancer.

Prior to the WHI trial, two other studies found that HRT that included progestins (EPRT) increased the risk of breast cancer by 24 percent for each five years of use. This effect was more than twice as great as the effect of estrogen replacement therapy (ERT).¹⁴⁶ Progestins are often combined with estrogen in HRT to help decrease the known risk of endometrial cancer from unopposed estrogen.

One predictor of higher risk for breast cancer is the amount of body fat in women who have completed menopause. Studies of postmenopausal women have found a correlation between a higher proportion of body fat, higher amounts of free circulating estrogens and an increased risk of the disease.¹⁴⁷ An international analysis of data from eight prospective studies confirmed this link.¹⁴⁸ Moreover, body fat becomes a reservoir for many synthetic lipophilic (fat-seeking) chemicals, such as organochlorines. Some of these lipophilic chemicals mimic the effects of natural estrogens. Breasts are composed primarily of fat, making them repositories for these contaminants.

Breast cancer in men also implicates estrogen as a contributing factor. Although breast cancer is a rare disease among men, those who develop the disease have been found to have higher than normal levels of estrogen.¹⁴⁹

The evidence linking estrogens and progestins to increased risk of breast cancer is undeniable. Clinical trials, epidemiological studies and laboratory studies all point to estrogens and substances that behave like estrogens as contributors to the breast cancer epidemic. The most fundamental biological evidence is seen in animal studies in which chemicals known to cause breast cancer in animals only do so if estrogens are present. If no estrogens are present, no abnormal lesions appear. Estrogens are necessary for tumor development because they affect tissue organization, including cell proliferation.^{150,151} Such studies indicate that women are most vulnerable to harm from estrogens or substances that behave like estrogens.

Clinical trials, epidemiological studies and laboratory studies all point to estrogens and substances that behave like estrogens as contributors to the breast cancer epidemic.

2. Synthetic Estrogens (Xenoestrogens)

In 1991, researchers at Tufts University discovered that a chemical leaching from polystyrene laboratory tubes was causing breast cancer cells to grow, even though no estrogens had been added to the culture medium. Subsequent investigation showed that the substance leached was p-nonylphenol, an additive commonly used in plastics.¹⁵²

This landmark study created widespread interest in xenoestrogens among scientists and the breast cancer community. Xenoestrogens are synthetic agents that mimic the actions of estrogens and are

contained in many pesticides, fuels, plastics, detergents and prescription drugs.¹⁵³

In 1993, a team of researchers developed the hypothesis that xenoestrogens played a role in some significant portion of breast cancer cases.¹⁵⁴ Because xenoestrogens mimic naturally occurring estrogens, they may also cause breast cells to pro-

liferate, increasing the risk of breast cancer. Since many of the personal characteristics associated with breast cancer (early puberty, late menopause, delayed childbearing or no children) were related to increased total lifetime exposure to estrogens, scientists reasoned

that environmental chemicals that affected estrogen metabolism also contributed to the disease.

The research on xenoestrogens intensified in 1994 when the Tufts University researchers identified certain pesticides as xenoestrogens because they caused breast cancer cells to proliferate in culture.¹⁵⁵ By 1997, a number of studies from other laboratories reported on compounds that act like estrogens when put in contact with breast cancer cells in tissue culture and may, therefore, act as estrogens in humans.^{156,157,158} A recent study found that a number of metals, including copper, cobalt, nickel, lead, mercury, tin and chromium had estrogenic effects on breast cancer cells in the laboratory.¹⁵⁹ Other studies have found a broad array of chemicals in the environment that interfere with hormonal metabolism.¹⁶⁰

Researchers have theorized that chronic exposure to a number of widespread and persistent xenoestrogens—such as BPA—may help explain the increase in breast cancer in industrialized countries.

Meanwhile, on Cape Cod, where nine of 15 towns have breast cancer rates 20 percent above the Massachusetts state average, researchers at the Silent Spring Institute are engaged in a study that has raised suspicions about synthetic estrogens in the water.¹⁶¹ The vast sandy beaches of the Cape create a fragile ecosystem that allows contaminants to seep quickly through porous soil into underground aquifers. Pesticides used on forests, cranberry bogs, golf courses and lawns make their way into the water supply. In the first stage of the study, synthetic estrogens were found in septic tank contents, groundwater contaminated by waste and some private wells.¹⁶² In the second stage of the study, scientists measured synthetic estrogens in indoor air and house dust samples in 120 homes on Cape Cod. They found a total of 52 different compounds in air and 66 in dust, including phthalates, parabens, alkylphenols, flame retardants, PAHs, PCBs, banned and currently used pesticides and bisphenol-A.¹⁶³

Some of these endocrine disrupting chemicals (EDCs), sometimes called xenoestrogens, and the evidence linking them to breast cancer are discussed below.

a. Bisphenol-A (BPA)

Several studies have shown drastic changes in the development of the reproductive system and mammary glands when laboratory animals are exposed to xenoestrogens in utero. Researchers at Tufts University exposed mice in utero to low doses of bisphenol-A (BPA), a chemical commonly found in some types of plastic food containers, including some baby bottles. When researchers examined the mammary glands of the female animals at 10 days, one month and six months after birth, they found the development of the animals' mammary glands had been altered in ways associated with the development of breast cancer in rodents and in humans.¹⁶⁴ This evidence

suggests that fetuses and embryos, whose growth and development are regulated by the endocrine system, are the most vulnerable to and may have the most lasting effects from exposure to synthetic estrogens. Researchers have theorized that chronic exposure to a number of widespread and persistent xenoestrogens—such as BPA—may help explain the increase in breast cancer in industrialized countries. Studies also show that BPA may leach into food from containers made of polycarbonate plastics and from the lining of metal food cans.¹⁶⁵ A laboratory study from Spain suggests that BPA acts through all the same response pathways as natural estrogen (17-beta estradiol).¹⁶⁶ This enables low dose BPA to increase breast cell proliferation in vitro.

b. Polyvinyl chloride (PVC)

Polyvinyl chloride (PVC) is used extensively in the manufacture of food packaging, as well as in medical products, appliances, cars, toys, credit cards and rainwear. During the manufacture of PVC, vinyl chloride may be released into the air or wastewater. Vinyl chloride has also been found in the air near hazardous waste sites, landfills and tobacco smoke. Animal studies of long-term exposure to low levels of airborne vinyl chloride have shown an increased risk of mammary tumors.¹⁶⁷ Vinyl chloride has also been linked to increased mortality from breast and liver cancer among workers involved in its manufacture.^{168,169}

c. Pesticides

From the 1950s until 1970, the pesticides aldrin and dieldrin were widely used for crops such as corn and cotton. Because of concerns about damage to the environment and, potentially, to human health, the EPA banned all uses of aldrin and dieldrin, except for termite control, in 1975. In 1987, the EPA banned these pesticides altogether.¹⁷⁰ Thus most of the human body burden of this chemical comes either from long-past exposures or from lingering environmental residues.

One body burden study showed a clear relationship between breast cancer incidence and dieldrin.

Conducted by the Copenhagen Center for Prospective Studies

in collaboration with the CDC, the study examined a rare bank of blood samples taken prior to the development of breast cancer.¹⁷¹

During the 1970s, approximately 7,500 Danish women, ranging from 30 to 75 years of age, had blood samples

taken. Organochlorine compounds were detected in most of the 240 women who subsequently were diagnosed with breast cancer. Dieldrin, which has shown estrogenic activity during in vitro assays (studies of cells in a laboratory dish), was found in 78 percent of those women later diagnosed with breast cancer. Women who had the highest levels of dieldrin long before cancer developed had more than double the risk of breast cancer compared to women with the lowest levels. This study also showed that exposure to dieldrin made breast cancer more aggressive: higher levels of dieldrin were associated with higher breast cancer mortality.¹⁷²

By contrast, a Long Island study investigating organochlorines and breast cancer did not find an association between dieldrin levels and increased risk of breast cancer.¹⁷³ However, unlike the Danish study, dieldrin levels in Long Island women were measured near the time of breast cancer diagnosis and so the study did not show what the levels were at the time of initial exposure.

Compounds with estrogenic activity, including drugs such as diethylstilbestrol (DES) and pesticides such as dieldrin, are understood to increase the risk of breast cancer.

In the Massachusetts town of Newton, researchers at Silent Spring Institute have pointed to “hormone mimicking” compounds in pesticides as a possible explanation for why breast cancer risk is higher among affluent women. The researchers surveyed 1,350 residents living in areas that had both high and low breast cancer incidence. They found that women in high-incidence areas generally had larger disposable incomes and reported regular use of professional lawn services, termite treatments or home pesticides.¹⁷⁴

d. Household products

Chemicals that either mimic estrogen or are otherwise hormonally active (i.e., they interfere with normal hormone metabolism) can be found in many household products, particularly cleaning agents and pesticides. Spray paints and paint removers may contain methylene chloride, known to cause mammary cancer in laboratory animals.¹⁷⁵ Insecticides in current use include estrogenic compounds such as methoxychlor, endosulfan and lindane.¹⁷⁶

e. Diethylstilbestrol (DES)

The most convincing evidence that synthetic chemicals can act like hormones and produce delayed detrimental effects is the tragic experience with diethylstilbestrol (DES). Between 1941 and 1971, DES was prescribed for millions of pregnant women to prevent miscarriages. The drug was banned when daughters of women who took the drug were found to have higher rates of an extremely rare vaginal cancer than those who were not exposed to DES in the womb.^{177,178,179} Research indicates that DES may also have increased the risk of breast cancer in some women who took it during the 1950s.¹⁸⁰

Daughters of women who took DES during pregnancy, now age 40 or older, have been found to have more than twice the risk of breast cancer compared to women of the same age who were not exposed to DES in utero.¹⁸¹ This study adds to

the body of evidence that intrauterine exposures can have lifetime effects on cancer development.

3. The Phytoestrogens (Plant Estrogens) Hypothesis

The prevailing evidence against synthetic estrogens must also be understood alongside evidence about the effects of plant estrogens (phytoestrogens). Such foods as whole grains, dried beans, peas, fruits, broccoli, cauliflower and, especially, soy products are rich in phytoestrogens. Although scientific evidence suggests that humans may benefit from plant-based estrogens, these substances are not completely benign.

While some research indicates that phytoestrogens may counteract the effects of synthetic xenoestrogens, scientists continue to investigate the hypothesis that phytoestrogens are generally beneficial. Adding soy products to women’s diets has led to lower levels of harmful estrogens in their bodies than women who don’t eat soy products.¹⁸² Some human and laboratory studies suggest that plant-based estrogens may help reduce a woman’s risk of breast cancer, citing diets in certain Asian countries as evidence.¹⁸³ Women in Asian countries, who traditionally consume more soy products than American women, have both a higher concentration of phytoestrogens in their blood and urine and a lower risk of breast cancer. These findings need to be interpreted cautiously, however, because soy content is not the only difference between Asian and American diets. Asian diets generally include more fiber, different fatty acids and less meat than a typical American diet, all of which may contribute to protecting Asian women from breast cancer.

Both dosage and timing can also influence the effect of phytoestrogens. In laboratory research, high doses of genistein, a type of phytoestrogen found in most soy products, have been shown to inhibit the growth of isolated breast cancer cells.¹⁸⁴

Studies suggest a cautious approach to consumption of soy products, particularly in vegetarian diets and phytoestrogen-based HRT.

At low doses, however, genistein can stimulate the growth of cancer cells in vitro.¹⁸⁵ High doses of genistein correspond to the human exposure level for Asians and Caucasians who consume a high-soy diet.¹⁸⁶ These studies suggest a cautious approach to consumption of soy products, particularly in vegetarian diets and phytoestrogen-based HRT.¹⁸⁷

Timing of exposure to genistein has also been shown to have health implications in animal studies. One 1999 study showed that when pregnant female rats were injected with genistein late in the gestation period, the female offspring were more likely to develop carcinogen-induced mammary tumors at sexual maturity.¹⁸⁸ Another study showed a greater incidence of uterine cancer in newborn mice which were given genistein during the first five days of life than in mice given DES, a known carcinogen, during the same time period. These findings suggest that exposure to genistein during critical time periods may cause cancer.¹⁸⁹

Despite evidence from animal studies linking cancer susceptibility to intrauterine and newborn exposure to genistein, there are no epidemiological studies investigating the effects of maternal or fetal soy consumption on later development of breast cancer,¹⁹⁰ nor on the effects of soy-based infant formula consumption.

4. Solvents

Industrial use of organic solvents has increased over the last several decades, particularly in the manufacturing of computer components. Some solvents used in this industry (such as benzene, toluene, and trichloroethylene) have been shown to cause mammary tumors in laboratory animals.¹⁹¹ Such solvents are also used in other industries, including cosmetics manufacturing. Until recently, there were no studies of cancer rates among workers in the semiconductor industry.¹⁹² A 2003 Taiwanese study, however, showed an increased risk of breast cancer among electronics workers exposed to chlorinated organic solvents.¹⁹³ And a government study of cancer rates in a Scottish semiconductor plant showed a 30 percent increase in the rate of breast cancer among female workers.¹⁹⁴ In addition, Danish women ages 20 to 55 employed in solvent-using industries (fabricated metal, lumber, furniture, printing, chemical, textiles and clothing industries) had double the risk of breast cancer compared with women not employed in those industries, according to a study there.¹⁹⁵

It can be difficult to identify actual or probable carcinogenic occupational exposures, unless biomonitoring is coupled with both disease and hazard surveillance.¹⁹⁶ However, a 1995 study suggested an increased breast cancer risk associated with occupational exposure to styrene,¹⁹⁷ as well as with several organic solvents (carbon tetrachloride, formaldehyde).¹⁹⁸ These results have been validated by studies in Finland, Sweden and Italy.^{199,200,201,202}

Women who were exposed to perchloroethylene-contaminated drinking water on Cape Cod, Mass., were found to have a small to moderate increase in their risk of breast cancer. The contamination occurred between the late 1960s and the early 1980s when perchloroethylene, a solvent, leached from the vinyl lining of water-distribution pipes.²⁰³

Studies by Duke University and NIEHS researchers found that the solvent ethylene glycol methyl ether (EGME) and its metabolite, 2-methoxyacetic acid (MAA), act as hormone sensitizers both in vitro and in vivo, increasing cellular sensitivity to estrogens and progestins. EGME is used in the semiconductor industry and is also a component in varnishes, paints, dyes and fuel additives. The scientists found that exposure to EGME/MAA increased the activity of hormones inside cells as much as eightfold. The researchers

Plastic additives such as bisphenol-A (BPA), polyvinyl chloride (PVC, which is found in many consumer products) and gasoline additives such as benzene, solvents and degreasing agents may be linked with increased risk of breast cancer due to their estrogenic activity.

emphasized caution for women exposed to EGME while taking HRT, oral contraceptives or tamoxifen. These studies also found similar hormone-sensitizing effects with another compound, valproic acid, an anticonvulsant medication also prescribed for migraines and bipolar disorder.^{204,205} These provocative studies underscore the need for systematic evaluation of hormone sensitizers and their possible effect on breast cancer risk.

5. 1,3-butadiene

1,3-butadiene is an air pollutant created by internal combustion engines and petroleum refineries. It is also a feedstock chemical used in the manufacture and processing of synthetic rubber products and some fungicides. 1,3-butadiene is also found in tobacco smoke. According to the EPA health assessment for 1,3-butadiene, the substance is carcinogenic to humans by inhalation. Data from research on animals indicate that females may be more vulnerable to the carcinogenic effects of 1,3 butadiene,²⁰⁶ which is known to cause mammary and ovarian tumors in female mice and rats. Research shows this pollutant produces even greater toxic effects in younger rodent populations.^{207, 208}

6. Aromatic Amines

Aromatic amines make up a class of chemicals found in the plastic and chemical industries. They are also found in environmental pollution, tobacco smoke, and grilled meats and fish.²⁰⁹ There are three types of aromatic amines: heterocyclic, polycyclic and monocyclic. One type of monocyclic amine, o-toluidine, is known to cause mammary tumors in rodents.^{210, 211} Heterocyclic amines are formed, along with PAHs, when meats or fish are grilled or otherwise cooked at high temperatures. Since the female breast may be most vulnerable to carcinogens during a critical window of development between menarche and first full-term pregnancy, exposure to heterocyclic amines during adolescence may significantly increase the risk of breast cancer.²¹² Other sources of heterocyclic amines are polluted air and rivers, municipal wastewater, cigarette smoke, diesel exhaust and combustion of wood chips and rubber.

Evidence Indicating a Probable Link Between Chemicals and Breast Cancer

In addition to the experimental, body burden and ecological evidence indicating a strong link between certain types of chemicals and breast cancer, evidence also exists indicating a probable link between certain chemicals and breast cancer.

I. DDT/DDE and PCBs

Two types of chemicals known to disrupt hormone function are the organochlorine pesticide DDT (dichloro-diphenyl-trichloroethane) and polychlorinated biphenyls (PCBs) used in the manufacture of electrical equipment and many other industrial and consumer products.

Both DDT and PCBs have been banned in the United States since the 1970s, yet both can be found in the body fat of humans and animals, as well as in human breast milk.^{213,214} Levels of these organochlorines have declined significantly since they were banned, however.²¹⁵

For more than 30 years prior to the EPA's ban on domestic use of DDT in 1972, the pesticide was sprayed to control insects on farms and in swamps. An early version of DDT contained an estrogen-like form called o,p'-DDT. Today, DDT continues to reach many homes as a residue on food because it deteriorates very slowly in soil and much farmland is still contaminated. In fact, a 1995 study reported measurable levels of DDT residue in house dust in 82 percent of homes studied.²¹⁶ Although banned in many countries for agricultural use, DDT is still used for malaria control in 18 countries around the world.²¹⁷

Many of the highly toxic synthetic chemical compounds known as polychlorinated biphenyls (PCBs) have been identified as carcinogenic in a number of studies. Although new products containing PCBs were banned by the EPA in 1976, as many as two-thirds of all the insulation fluids, plastics, adhesives, paper, inks, paints, dyes and other products containing PCBs manufactured before 1976 remain in daily use. The remaining one-third has been discarded, eventually making its way into landfills and waste dumps. Environmental exposures are the most likely reason that measurable levels of PCBs are found in human and animal tissue.²¹⁸

One difficulty in studying the effect of PCBs on breast cancer is the diversity within this broad class of compounds. PCBs are classified in three types, based on their effect on cells. One type acts like an estrogen. A second type acts like an anti-estrogen. A third type appears not to be

“We have come through with advances in treatment, we are on the verge of exciting advances in detection, and we have pushed the envelope in terms of survivability. But now we need to turn our attention to cause and prevention: to our environment.”

■ Andrea Ravinett Martin,
Founder, Breast Cancer Fund

hormonally active, but can stimulate enzyme systems of animals and humans in a manner similar to certain drugs (such as phenobarbital) and toxic chemicals. Therefore, these compounds have the ability to alter normal metabolism, either by hormonal disruption or enzyme changes. Unfortunately, research studies generally have looked at total PCB levels without identifying individual types. In 1999, however, researchers showed

While there is no simple method for linking chemical exposures to breast cancer, several types of research—experimental, body burden and epidemiological studies—yield evidence that such a link exists.

that certain types of PCBs promote the proliferation of breast cancer cells in culture, by stimulating the production of key proteins or structures in the cancerous tissue.²¹⁹

Researchers have done more than 20 body burden studies involving DDT and PCBs since the mid-1980s. These studies have yielded conflicting results, depending on their design and methodology as well as the interpretation of the findings. For

example, some researchers measured only DDE, the principal metabolite and environmental breakdown product of DDT, some of which is stored in body fat, including breast fat.²²⁰ Other studies measured both DDE and several PCBs, but did not distinguish between estrogenic PCBs and other types of this contaminant.

While some studies have shown that women with breast cancer had higher levels of some chlorinated compounds compared to healthy women,^{221,222} most recent body burden studies have shown no relationship between organochlorine contaminant levels and breast cancer risk.^{223,224,225,226}

One widely-reported study from the multi-study Long Island Breast Cancer Study Project did not find an association between DDT/DDE, PCBs and breast cancer.²²⁷ Like many such studies, however, this project measured contaminant levels near the time that breast cancer was diagnosed, did not consider the effect of chemical mixtures and did not assess key metabolites. Levels of DDE in this recent negative study were more than 10 times lower than levels in the earlier positive studies.

A meta-analysis of five recent studies of women in the northeastern United States also failed to find an association between elevated risk of breast cancer and levels of PCBs present in blood.²²⁸ Although the original studies had suggested higher breast cancer risk from PCBs in certain groups of women grouped by reproductive and breast-feeding history, the combined data did not show a relationship between PCB levels and breast cancer. This does not mean that a connection between PCBs and breast cancer should be dismissed. Pooling data from different studies and combining data from premenopausal and postmenopausal women, in whom risk factors for breast cancer have a quantitatively different impact, can skew the results. In this case, combining the data may have affected the conclusion. For example, high bodyweight decreases breast cancer risk before menopause and increases it after menopause.

Despite studies that fail to show a connection between organochlorines and breast cancer, it appears some compounds may carry a higher risk for some women. For example, certain chemical compounds may make breast cancer more aggressive. A Canadian study measuring plasma concentrations of organochlorine compounds found that higher levels of DDE were associated with lymph node involvement and large tumors.²²⁹

A connection was also established by laboratory studies that found the estrogen-like form of DDT enhances the growth of estrogen-dependent (ER+) breast tumors,^{230,231} the most common type of breast cancer. Estrogen-dependent breast cancer has been increasing in the United States: Between 1973 and 1992, the percentage of ER+ tumors rose from 73 to 78 percent.²³²

Another Canadian study published in 2000 measured DDE and specific types of PCBs in breast biopsy tissue and showed that, compared with healthy women, premenopausal women with breast cancer had significantly higher levels of PCBs 105 and 118, while postmenopausal women with breast cancer had higher levels of PCBs 170 and 180. A 2004 Belgian case-control study of 120 women found significantly higher total blood levels of PCBs in women with breast cancer than in presumably healthy women, particularly PCB153, which has shown estrogenic activity in animal and in vitro studies.²³³

Researchers evaluating data from the Nurses' Health Study revisited the issue of PCBs and breast cancer risk. They had previously concluded: "Combined evidence does not support an association of breast cancer risk with plasma/serum concentrations of PCBs or DDE. Exposure to these compounds, as measured in adult women, is unlikely to explain the high rates of breast cancer experienced in the northeastern United States."²³⁴ Now, however, those researchers have reached a different conclusion, based on further study that took into account that individual genetic differences may affect their susceptibility to PCBs. In their 2002 study, the researchers wrote that, "The majority of studies have concluded that exposure to PCBs is unlikely to be a major cause of breast cancer but these findings indicate that further studies of genetically susceptible populations are warranted."²³⁵

PCBs were implicated in breast cancer recurrence among women with nonmetastatic breast cancer in a 2003 New York study. Women with the highest levels of one PCB congener in their adipose tissue were found to be almost three times as likely to have recurrent breast cancer as women with lower levels.²³⁶

In 2003, scientists in Belgium measured levels of DDT, DDE and hexachlorobenzene (HCB) in the blood of 159 women with breast cancer and 250 presumably healthy women. The results showed that levels of all three contaminants were significantly higher in women with breast cancer than women in the control group.²³⁷

A Swedish study of postmenopausal women also found higher residues of certain PCBs in women with breast cancer compared to women with benign breast disease.²³⁸ In Germany, researchers measured PCBs, DDT, DDD, DDE and hexachlorocyclohexane (lindane) in breast tissue samples from 65 women. Of the 65 women, 45 were diagnosed with breast cancer. After statistical adjustment for age differences, higher levels of all contaminants were detected in tissue from women with breast cancer than in tissue from those without breast cancer.²³⁹

A prospective nested-case-control study was performed in a population exposed to DDT during childhood and adolescence at the time of active DDT use in the United States. Blood was drawn at the time of exposure. In this study, increased risk of breast cancer paralleled increasing concentrations of serum DDT, and was significantly greater in women exposed before age 15 than after.²⁴⁰

2. Polycyclic Aromatic Hydrocarbons (PAHs)

Polycyclic aromatic hydrocarbons (PAHs), compounds found in soot and fumes from combustion of diesel and other fuels, appear to play a role in the development of breast cancer.

In August 2002, researchers reported that one study in the Long Island Breast Cancer Study Project had implicated PAHs as a risk factor for breast cancer.²⁴¹ PAHs create a distinctive type of damage on genetic material—that some call a

Four studies suggest that women who begin smoking cigarettes as adolescents face an increased risk of breast cancer.

“fingerprint”—where the compounds are directly bound up with the basic building blocks of DNA into what is called a DNA adduct. Women with the highest PAH body burdens had a 50 percent increased risk of breast cancer. The

Long Island study validated the earlier work of researchers at Columbia University who also found a close relationship between DNA damage from exposure to PAHs in breast tissue and increased risk of breast cancer.²⁴² In addition, some PAHs have shown estrogenic activity in laboratory studies and may cause estrogenic effects in addition to DNA damage.^{243,244}

Tobacco smoke also contains PAHs, which may explain a potential link between increased breast cancer risk and both active and passive smoking. A large study of California teachers revealed an increased risk of breast cancer among smokers, particularly those who began smoking during

adolescence, at least five years before their first full-term pregnancy, or who were long-time or heavy smokers.²⁴⁵ Four earlier studies also suggest that women who begin smoking cigarettes as adolescents face an increased risk of breast cancer.^{246,247,248,249}

Recent studies suggest that the breast cancer risk from exposure to secondhand smoke is also increased by about the same amount as active smoking.^{250,251} One possible explanation for the similar effects of active and passive smoking, despite the fact that nonsmokers receive a much lower dose of carcinogens in the smoke than do smokers, is that smoking acts as an anti-estrogen, which tends to blunt—but not fully eliminate—the effects of carcinogens in cigarette smoke. Passive smokers, in contrast to active smokers, do not get a large enough dose of smoke to depress estrogen levels whereas active smokers have depressed estrogen levels because of damage to their ovaries. In 2004, a draft report from the Air Resources Board of California EPA concluded:

Overall, the weight of evidence (including biomarker, animal and epidemiological studies) is consistent with a causal association between environmental tobacco smoke (ETS) in breast cancer, which appears to be stronger for premenopausal women.”²⁵²

Tobacco smoke also contains two known human carcinogens, polonium-210,²⁵³ a radioactive element, and vinyl chloride, as well as benzene, toluene and 1-3 butadiene, all of which are known to cause mammary tumors in animals.

3. Dioxin

When products containing polyvinyl chloride (PVC), PCBs or other chlorinated compounds are incinerated, among the chemicals released is dioxin, a known human carcinogen that mimics hormone activity. Dioxin is the name given to a group of toxic by-products of incineration and other industrial processes that use chlorine. One of these chemicals (2,3,7,8-tetra chlorodibenzo-para-dioxin-TCDD dioxin) has been classified by the International Agency for Research on Cancer (IARC) as a Group 1 carcinogen (i.e., known human carcinogen).²⁵⁴ Dioxin was officially declared a known carcinogen by the EPA in 2000 after more than a decade of controversy.

Of all toxic chemicals, dioxin may be the most prevalent. The body fat of every human being, including every newborn, contains dioxin. People are exposed to dioxin primarily through consumption of animal products: meat, poultry, dairy products and human breast milk.²⁵⁵ Dioxin enters the food chain when diesel exhaust or soot from incineration falls on grass which is later eaten by farm animals. It is then passed to humans through dairy and meat products. Until recently, only one study linked dioxin to increased risk of breast cancer, a UK study that implicated the toxin in the development of mammary tumors in laboratory mice.²⁵⁶ However, a new follow-up study on women exposed to a chemical plant explosion in 1976 in Seveso, Italy, makes a more compelling case for a connection between dioxin and breast cancer.²⁵⁷ Blood samples taken and stored at the time of the explosion were analyzed and the results correlated with cases of breast cancer. The scientists found that a tenfold increase in TCDD dioxin levels was associated with a more than doubled risk for breast cancer. Of the 981 women in the study, just 15 have developed breast

cancer to date, but the results are compelling because the stored samples allowed measurement of dioxin levels at the time of exposure. The study is continuing as the women age; there may yet be additional cases resulting from this past exposure.

Another recent study showed that intrauterine exposure to TCDD disrupted the development of the rat mammary gland in a way that predisposed offspring to mammary cancer. The mammary gland never fully matured, which prolonged the window of vulnerability to cancer-causing chemicals.²⁵⁸ This study validates findings by U.K. scientists, cited earlier, in which dioxin exposure of the pregnant mouse caused proliferation of terminal end buds of the female offspring's mammary gland, making the gland more vulnerable to carcinogen exposure.²⁵⁹

4. Ethylene Oxide

Ethylene oxide is a fumigant used to sterilize surgical instruments. It is also used in some cosmetics products.²⁶⁰ Ethylene oxide is a known human carcinogen and one of 45 chemicals that the National Toxicology Program identifies as causing mammary tumors in animals.

Scientists from the National Institute for Occupational Safety and Health studied breast cancer incidence in a group of 7,576 women exposed to ethylene oxide while working in commercial sterilization facilities. They found an increased incidence of breast cancer among these women in direct proportion to their cumulative exposure.²⁶¹

Evidence Indicating a Possible Link Between Electromagnetic Fields and Breast Cancer

Everyone in the industrialized world is exposed to electromagnetic fields (EMFs) every day. EMFs are a type of non-ionizing radiation, i.e., low frequency radiation without enough energy to break off electrons from their orbits around atoms and ionize (charge) the atoms. Microwaves, radio waves, radar and power frequency radiation associated with electricity are examples of non-ionizing radiation. Fluorescent lights, computers and other electric and electronic equipment all create electromagnetic fields of varying strength.

The International Agency for Research on Cancer (IARC) has classified EMFs as a possible human carcinogen. In 1998, a National Institute

Health effects of EMF exposure are difficult to study because there is no unexposed population, i.e., no control group.

of Environmental Health Sciences EMF Working Group recommended that extremely low frequency EMFs, such as those from power lines and electrical appliances, be classified as possible human carcinogens.²⁶²

In 1997, an international panel stated that EMF and environmental light may be considered potential risk factors for breast cancer.²⁶³ They concluded that “studies on human breast cancer from epidemiology, cell studies, animal studies and some human studies indicate a plausible biological mechanism for increased risk of cancer related to EMF and/or light exposure.”²⁶⁴

In 2001, a meta-analysis of 48 published studies on the association between EMF exposure and breast cancer found the data “consistent with the idea that exposures to EMF, as defined, are associated with some increase in breast cancer risks, albeit that the excess risk is small.”²⁶⁵

Health effects of EMF exposure are difficult to study because there is no unexposed population, i.e., no control group. Thus the differences in health effects between workers who have chronic occupational exposure to EMF and people without occupational exposure may be merely twofold.

The mechanism by which EMF exposure can affect health is not completely understood. Some research suggests that EMF exposure lowers the body’s level of melatonin, a hormone secreted by the pineal gland during darkness. Melatonin appears to have anti-cancer properties. For example, adding melatonin to cancer cells in a laboratory dish will cause them to stop growing. Placing the dish in an electromagnetic field will cause the cells to start growing again.²⁶⁶ In vitro studies have shown that EMF exposure interferes with the ability of tamoxifen to inhibit the growth of breast cancer cells in culture.²⁶⁷

Research has shown that exposure to light at night also decreases melatonin levels. This finding led to the hypothesis that working at night in a lighted environment may increase the risk of breast cancer by lowering melatonin levels. Although this hypothesis remains controversial, at least three studies suggest a link between night-shift work and increased risk of breast cancer, which may be related to the change in melatonin levels created by light at night.^{268,269,270}

The potential interaction of EMFs with the hormonal effects of night-shift work may help explain the elevated risk of breast cancer among flight attendants. Studies in Iceland, Sweden and California found varying degrees of increased incidence of breast cancer among flight attendants.^{271,272,273} The Icelandic study also found that length on the job affected breast cancer risk. Women who had been employed as flight attendants for five years or longer had twice the risk of breast cancer as women who had been flying for shorter periods. Flight attendants are also exposed to ionizing radiation from the sun and, until recently, were exposed to secondhand tobacco smoke.

Norwegian researchers reported an increased risk of breast cancer among female radio and telegraph operators exposed to radiofrequency and extremely low frequency EMF. Both premenopausal and postmenopausal women were studied. Premenopausal women showed an increased risk of estrogen-receptor-positive tumors and postmenopausal women had an increased risk of estrogen-receptor-negative tumors.²⁷⁴

Research on EMF exposure has shown increased mortality from breast cancer in women employed in the telephone industry.²⁷⁵ Further, premenopausal women appear to be at higher risk than postmenopausal women.²⁷⁶ Although breast cancer

is rare in men, research has shown links between EMF exposure and male breast cancer in electrical and telephone workers.^{277,278,279}

In a 2004 study, residential electromagnetic field (EMF) exposure from high voltage power lines was linked to a 60 percent increased risk of breast cancer in Norwegian women of all ages. This case-control, population-based study of more than 5,400 women used data from Statistics Norway and the national cancer registry, which minimized selection bias. Occupational exposure also increased risk but not as greatly as did residential exposure. Women under 50 who were exposed to EMF both at home and at work also had a modest increase in risk of breast cancer. Scientists also found a higher incidence of estrogen-negative breast cancer in women of all ages who were exposed to EMF both at home and at work.²⁸⁰ An earlier study found that premenopausal women are at higher risk for breast cancer related to residential EMF exposure.²⁸¹

A 2003 study suggests that EMF exposure from electric bedding (electric blankets, mattress pads and heated water beds) may increase the risk of breast cancer in African American women.²⁸² Researchers from Walter Reed Army Medical Center and Meharry Medical College compared 304 African American women with breast cancer to 305 African American women who did not have the disease. They found that the longer a woman used an electric bedding device, the greater her risk of cancer. Trends were similar in both premenopausal and postmenopausal women and in both estrogen-receptor-positive and estrogen-receptor-negative tumors. Most earlier studies on electric bedding use among Caucasian women did not show an association with increased breast cancer risk.

Evidence Indicating a Possible Link Between Chemicals and Breast Cancer

Finally, there are chemicals that affect how the body functions in ways that suggest a possible link to increased breast cancer risk. These include: heptachlor, an insecticide; atrazine, an herbicide; ingredients in some sunscreens; the group of chemicals known as phthalates, found in many plastics and other products; and food additives, including hormones used in milk and beef production.

I. Heptachlor

Heptachlor epoxide is a breakdown product of the insecticide heptachlor, now banned by the EPA but widely used throughout the 1980s and known to accumulate in fat, including breast tissue. Although heptachlor itself does not act like estrogen, it does affect the way the liver processes estrogen. Heptachlor also has been shown to disrupt cell-to-cell com-

munication in human breast cells in the laboratory.²⁸³

The body's cells need to communicate with each other to regulate their growth. By disrupting this growth regulation mechanism, heptachlor could increase the risk of breast cancer.

Heptachlor is one of many pesticides used on Hawaiian pineapple fields since the late 1950s, replacing mirex when that chemical was banned. After the fruit was harvested, the chopped up leaves, called "green chop," were sold to dairy farmers in Oahu to use in cattle feed, a practice that continued until 1982. Thus heptachlor contaminated the local milk and dairy supply for years. Between 1981 and 1984, heptachlor levels in milk and dairy products exceeded the FDA standard (0.3 ppm) ten-fold. Follow-up studies found that heptachlor levels in the breast milk of women who had consumed Oahu dairy products averaged 200 ppm and in some cases exceeded 400 ppm. Despite a 1988 EPA ban on heptachlor, its use continued until 1993 as growers were allowed to use up pre-existing stocks.²⁸⁴

Heptachlor continues to contaminate soil and crops such as cucumbers in some parts of Hawaii. It can also be found in the Continental U.S. in soil where it was used for termite control. Heptachlor still contaminates humans as well, nearly two decades after it was banned by the EPA.

Breast cancer rates in Hawaii are among the highest in the world and the rate of increase is greater than any other U.S. state. According to the International Agency for Research on Cancer (IARC), breast cancer incidence among Japanese women in Hawaii increased 42 percent between 1970 and 1985, while the increase in other U.S. states during that period did not exceed 20 percent.²⁸⁵

Heptachlor continues to contaminate soil and crops such as cucumbers in some parts of Hawaii. It can also be found in the Continental U.S. in soil where it was used for termite control. Heptachlor still contaminates humans as well, nearly two decades after it was banned by the EPA.²⁸⁶

2. Triazine Herbicides

Atrazine is one of the triazine herbicides, which also include simazine and cyanazine. All three have been shown to cause mammary cancer in animals. Triazines are the most heavily used agricultural chemicals in the United States. About 80 million pounds of atrazine are applied annually, primarily to control broadleaf weeds in corn and sorghum crops in the Midwest.²⁸⁷ The EPA re-registered atrazine as a permissible chemical after a lengthy and controversial risk assessment process; it is banned in the European Union. Elevated levels of atrazine are found each spring and summer in both drinking water and groundwater in the Midwest.

Atrazine is a known endocrine disruptor. Recent laboratory research has shown that atrazine exposure during gestation interferes with development of the rat mammary gland at puberty, leading to proliferation of terminal end buds.²⁸⁸ These biological structures have been shown to be sensitive to carcinogens. Thus atrazine exposure in utero widens the window of sensitivity to carcinogens in animals.

Simazine, another of the triazine herbicides, is widely used in Florida, California and the Midwest. It contaminates surface- and groundwater after being applied to farmlands. Research suggests that simazine also may contribute to breast cancer. In 1994, the EPA banned the use of simazine as an algicide in swimming pools, hot tubs and whirlpools, citing “unacceptable cancer and non-cancer health risks to children and adults.”²⁸⁹ Some lawn chemicals also contain simazine. One study reported an increase of breast tumors in female rats that were fed simazine.²⁹⁰

Although simazine-treated animals did not have elevated levels of estrogens, they did have elevated levels of prolactin, another hormone known to play a role in the development of breast tumors in animals.²⁹¹ Researchers are now trying to determine if simazine changes the levels of hormones in animals, resulting in breast tumor formation.

3. Sunscreens (UV screens)

Growing concern about ultraviolet (UV) radiation and the risk of skin cancer has led to widespread use of sunscreens, which are also added to cosmetics. Research has found that some chemicals in these products not only are estrogenic but also lipophilic. Studies show they are accumulating in wildlife and humans.²⁹² Swiss researchers who tested six frequently used UV screens found that five showed estrogenic activity in breast cancer cells and three showed estrogenic activity in laboratory animals.²⁹³

4. Phthalates (Endocrine Disrupting Chemicals in Plastics)

Phthalates, used to render plastics soft and flexible, are a group of chemicals used in common household products, some of which have hormone disrupting effects. Phthalates are found in soft plastic “chew toys” marketed for infants and also in some varieties of nail polish, perfumes, skin moisturizers, flavorings and solvents. Phthalates have also been found in indoor air and dust.²⁹⁴

Recent research indicates that phthalates increase levels of testosterone and estrogen in humans.²⁹⁵ Studies of circulating levels of estrogen, testosterone and other hormones and their relationship to breast cancer indicate that hormonal factors are central to breast cancer risk.^{296,297,298} Much remains to be learned about phthalates before a direct connection to breast cancer risk can be established. However, many phthalates are known to disrupt hormonal processes, raising concern about their implications for increasing breast cancer risk.²⁹⁹

5. Food and Food Additives (rBST and Zeranol)

Modern food-production methods open a major avenue of exposure to environmental carcinogens. Pesticides sprayed on crops, antibiotics used on poultry, hormones used in cattle, sheep and hogs, and to produce milk, expose us involuntarily to contaminants that become part of our bodies. Research suggests that some of these exposures may increase breast cancer risk.

Animal products such as meat also may hold inherent risks because they contain fat that may retain chemicals such as pesticides and other environmental toxicants. These lipophilic chemicals become more concentrated as they move from plants, to animals and finally to humans, who are at the top of the food chain.

a. Bovine Growth Hormone (rBGH)/ Recombinant Bovine Somatotrophin (rBST)

In 1993, the Food and Drug Administration approved Monsanto's genetically engineered hormone product, recombinant bovine growth hormone (rBGH), subsequently renamed recombinant bovine somatotropin (rBST) for injection in dairy cows to increase milk production. Since its introduction, rBST has proved controversial because of its possible link to increased risk of breast cancer and other cancers. Injecting a cow with rBST stimulates production of a naturally occurring hormone called Insulin Growth Factor 1 (IGF-1), which in turn increases milk production. IGF-1 is present in the bodies of both cows and humans, increasing cell division and decreasing cell death (apoptosis), changes that contribute to cancer risk.^{300,301} A prospective study of American women found that premenopausal women with the highest levels of IGF-1 in their blood (drawn before cancer developed) were seven times as likely

to develop breast cancer. No increased risk was noted in postmenopausal women.³⁰² Subsequent studies of IGF-1 also have linked elevated levels of IGF-1 with increased risk of breast cancer.^{303,304}

Physicians, scientists and consumer advocacy groups opposed FDA approval of rBST (its trade name is Posilac), which quickly found its way into the U.S. milk supply, and from there, into other dairy products such as ice cream, buttermilk, cheese and yogurt. Its use was not identified to consumers on labels, however. In September 2003, the FDA issued warning letters to four milk producers stating that their use of labels claiming "no hormones" and "hormone free" was false and misleading. The FDA letter also said there is no basis for claiming that milk from cows not treated with rBST is safer than milk from rBST-treated cows. In December 2003, Monsanto succeeded in a lawsuit against a Maine dairy, forcing it to add the FDA statement to their labels even though the dairy does not use milk from rBST-treated cows.³⁰⁵

Proponents of rBST argue that IGF-1 is harmless because it occurs naturally in humans, is contained in human saliva and broken down during digestion. However, digestion does not break down IGF-1 in milk because casein, the principal protein in cow's milk, protects IGF-1 from the action of digestive enzymes.³⁰⁶

Research continues to suggest that elevated levels of IGF-1 increase the risk of breast, prostate and colon cancers.³⁰⁷

The U.S. and Canadian beef, veal and lamb industry have used synthetic growth hormones since the 1950s to fatten animals faster. A study by researchers at Ohio State University suggests these hormones may also elevate the risk of breast cancer. Concern about this risk led the European Union to ban U.S. and Canadian beef since 1999.³⁰⁸

b. Zeranol

One of the most widely-used hormones in U.S. beef cattle is Zeranol, a nonsteroidal growth promoter with estrogenic activity. Ohio State University scientists found that Zeranol had estrogenic activity in normal breast epithelial cells and in breast cancer cell lines. The cell growth was significant even at Zeranol levels 30 times lower than the FDA has approved as safe.³⁰⁹ Researchers are continuing their investigation of Zeranol, measuring levels of the chemical in random samples of supermarket beef and in samples of normal and cancerous breast tissue from patients undergoing biopsy or surgical breast reduction.

Danish researchers compared the potency of Zeranol to other endocrine disruptors and concluded that “the very high potency of Zeranol... suggests that Zeranol intake from beef products could have greater impact on consumers than the amounts of the known or suspected endocrine disruptors that have been found in food.”³¹⁰

A recent study by Harvard researchers suggests there is reason for concern about the use of hormones in the meat industry. Scientists reported that premenopausal consumption of red meat may increase the risk of breast cancer later in life. This prospective analysis of dietary fat intake in 90,000 women found that the risk of breast cancer was one-third higher among women whose diets were highest in animal fat, primarily red meat and milk.³¹¹

Considerable resources are spent encouraging women to make changes in their personal lives that might reduce their risk of breast cancer. But many factors that contribute to the disease lie far beyond an individual’s personal control and can only be addressed by government policy and private sector changes. Breast cancer is not just a personal tragedy; it is a public health crisis that requires political will to change the status quo.

Moving Forward: Advancing the Research Agenda

It is essential, based on our knowledge of existing scientific evidence, to effect policy changes to reduce exposure to synthetic chemicals that are linked to increased breast cancer risk. Failing to act on the evidence summarized in this report would ignore the costly lesson learned from the relationship between tobacco and lung cancer in the 20th century.

Meanwhile, research into possible environmental causes of breast cancer must not only continue but expand, including testing and screening industrial chemicals and pesticides for their toxicity and hormone-mimicking effects, measuring and tracking the body burden levels of these chemicals in the public and investigating how girls and women are exposed to these chemicals.

Recommendations from the International Summit on Breast Cancer and the Environment serve as a useful guide to research approaches and methods to uncover the environmental causes of breast cancer and, ultimately, lead to prevention of the disease.

Two decades of research on DDT, PCBs and breast cancer have produced controversy in the scientific community, confusion in the public and strong opinions among all concerned. More research on genetically-susceptible populations may indeed show a link between PCB exposure and increased risk of breast cancer. This will not alter the fact, however, that all humans and other living things are contaminated with these compounds, which have been banned for decades. Increasing competition for research dollars will limit the resources available for breast cancer research. Thus research priorities must focus primarily on the effects of exposures to substances currently used in the United States and other industrialized countries.

One encouraging research development is the funding of four new breast cancer and environmental research centers by the National Cancer Institute and the National Institute of Environmental Health Sciences. The agencies have allocated \$5 million each year for seven years, beginning in 2004. The four sites include the University of California San Francisco, Fox Chase Cancer Center, University of Cincinnati and Michigan State University.

Recommendations from the International Summit on Breast Cancer and the Environment serve as a useful guide to research approaches and methods to uncover the environmental causes of breast cancer and, ultimately, lead to prevention of the disease.

The Summit also included public policy recommendations to implement needed changes in research.³¹²

The research recommendations include but are not limited to the following:

I. Study the interplay between timing of exposures, multiple exposures and chronic exposures (including occupational exposures and secondhand smoke)

Timing of Exposures (periods of vulnerability)

As Dr. Annie J. Sasco explained, “There is a crucial need to better define time windows of exposure. Vulnerability periods correspond to in utero life, as well as the prepubertal period both for girls and boys.”³¹³ Studies are also needed to evaluate childhood cancer, breast cancer in young women and major developmental and structural defects as combined indications of possible prenatal and early childhood exposures to hormone-mimicking chemicals.³¹⁴

The tragic legacy of DES combined with decades of animal research have shown that cancer can begin in the womb. The developing organism is very sensitive to hormonal influence. When any chemical disrupts normal development, the damage can be devastating and permanent. Thus scientists, policy makers and advocates must heed the comments of two EPA toxicologists in designing future research on environmental links to cancer:

All of these studies have demonstrated that prenatal exposure to EDCs [endocrine-disrupting chemicals] can alter the hormonal milieu, reproductive tissue development, and susceptibility to potential carcinogen exposure in the adult. These compounds are not genotoxic, yet can have significant adverse health outcomes.

We must ask the questions: Are the appropriate, sensitive animal strains being utilized to test for endocrinologically based diseases such as breast cancer? There have been epidemiological studies investigating the association of environmental chemicals, including both organochlorines, such as PCBs and atrazine, with breast cancer incidence. These particular studies have measured the levels of exposure of these chemicals in adult women who develop breast cancer. Could we be trying to correlate exposure and effect at the wrong time? If it is prenatal or early life stage exposure that is critical to disease susceptibility, why are we measuring environmental chemicals in people once they have developed breast cancer? The critical exposure window may have been much earlier.³¹⁵

Multiple Exposures

We urgently need breast cancer research methods and approaches that reflect the reality of human exposure to chemicals in the environment. We are all exposed to hundreds, perhaps thousands, of chemicals every day, many of which may interact. Studying one or two chemicals at a time will not yield meaningful results. The combined activity of the multi-chemical mixtures we are exposed to must be investigated.

Xenoestrogens offer an example of why research methods need to change. Scientists need to find a method to measure an individual’s total cumulative exposure to environmental xenoestrogens and determine how that total exposure relates to breast cancer risk. As a 1999 National Academy of Science report recommended, “Markers of total xenoestrogen exposure and chemical concentrations in blood or adipose tissue should be measured to provide an accurate

assessment of internal dose and, therefore, to identify groups experiencing different exposures.³¹⁶ Some scientists have begun that search and their work can serve as a model for future studies.^{317,318,319}

We clearly have major gaps in our current knowledge about the links between breast cancer and the environment. Research efforts should be focused, therefore, in areas most likely to provide useful information for shaping public policies around environmental exposures and public health.

Chronic (Occupational) Exposures

Since World War II, the number of women employed outside the home has increased steadily; today, women make up nearly half of the U.S. workforce (46%).³²⁰ This increased participation in the paid workforce parallels a steady increase in the risk of breast cancer. One of the earliest studies on workplace exposures found that more than half a million women were occupationally exposed to ionizing radiation and that tens of thousands were exposed to carcinogenic chemicals.³²¹ Despite these findings, however, relatively few recent studies have been carried out in the United States to identify occupational risk factors for breast cancer. Most occupational research on women comes from Scandinavia and Canada, and many of those report risk by job type rather than by specific exposures. The limited research evidence to date shows an increased risk of breast cancer among

two broad occupational categories: (1) those workers who regularly work with toxic chemicals, such as chemists, clinical laboratory technicians, dental hygienists, paper mill workers, meat wrappers and cutters, microelectronics and telephone workers and (2) professionals who are generally in higher socioeconomic groups such as school teachers, social workers, physicians, dentists and journalists.^{322,323,324}

Research shows that nurses too face increased cancer risk, particularly chemotherapy nurses and other healthcare workers who are exposed to drugs used to treat cancer, some of which are known carcinogens.³²⁵ However, one of the largest long-term studies of women's health, the Nurses Health Study at Harvard University, has only recently begun to examine the occupational hazards of the nursing profession. One epidemiologist described the Nurses Health Study as "really a study of women who happened to be nurses, rather than women as nurses or even as workers."

Two occupational health studies from Yale University³²⁶ and the Mt. Sinai School of Medicine³²⁷ found increased risk of breast cancer among teachers and librarians. The Mt. Sinai study also showed increased risk among computer and peripheral equipment operators (includes persons operating input/output devices such as tape drives, disk drives and printers). This was the first occupational study to focus on women ages 20 to 44 years of age.

A Canadian study of more than 1,000 women with breast cancer and an equal number of women who did not have breast cancer reported elevated breast cancer risk among women in a wide range of occupations. Occupational risk differed according to whether women had undergone menopause. Premenopausal women were at higher risk if they worked in electronic data-processing, as barbers

and hairdressers, in sales and material processing occupations, and in food, clothing, chemical and transportation industries. Postmenopausal women were at higher risk in teaching, medicine, health, nursing, dry-cleaning and the aircraft and automotive industries, including gasoline service stations. Elevated risk was noted for both pre- and postmenopausal women in crop farming, fruit and vegetable packing, publishing, printing and motor vehicle repair industries.³²⁸

Elevated breast cancer incidence among professional women is often explained by reproductive factors, primarily because of delayed childbearing or having no children. The role of reproductive factors as the sole reason for increased breast cancer risk among professional women has been challenged recently, based on an inadequate study of lifetime occupational exposures of these women.³²⁹ Future studies should address where women work and what risk factors are present in these environments, including the possibility that occupational exposures may play a role in increasing the risk of breast cancer.

Many women in the United States have two places of work: in the home and in the (paid) workplace. To accurately assess the environmental exposures that may increase the risk of breast cancer, researchers need to consider exposures at both sites, individually and collectively. A study by the Silent Spring Institute tested assessment methods to measure complex mixtures of widespread, hormonally-active agents in homes.³³⁰ Wider application of these methods in future research could offer new insights into the possible contribution of chemical mixtures to breast cancer risk.

a. Melatonin, light-at-night and non-ionizing radiation

A growing body of evidence (see pages 36-37) on the health impact of non-ionizing radiation (EMF) and night-shift work on melatonin levels indicates that more must be learned about these exposures and their possible link to breast cancer. However, there has been little federally-funded research in this area in the United States since 1998. Ongoing research in Sweden, Norway and other European countries continues to link EMF exposure to increased risk of breast cancer and other cancers. Until the actual cancer risk of EMF and light-at-night (LAN) can be confirmed or refuted by scientific evidence, research must continue in the United States without further interruption.

b. Solvents

It can be difficult to identify which organic solvents may be contributing to increased breast cancer risk in workers because industries often use combinations of solvents, many of which undergo frequent changes in formulation. This is particularly true in the electronics industry. Further study is needed to identify which solvents increase the risk of breast cancer and other cancers.

c. Household exposures, including personal care products

Homemakers face an increased risk of breast cancer.³³¹ Research is needed to determine what conditions and exposures may be linked to those increased breast cancer risks.

Personal care products used by women, including cosmetics, sunscreens and shampoos, may include endocrine-disrupting compounds (such as phthalates and parabens) that could increase breast cancer risk. Parabens are a group of compounds widely-used as anti-microbial preservatives in food, pharmaceutical and cosmetics products,

including underarm deodorants. Parabens are quickly absorbed through (intact) skin, and from the gastrointestinal tract and blood. Research has shown that parabens have estrogenic activity in human breast cancer cells in vitro^{332,333,334} and in vivo.^{335,336} U.K. researchers reported finding measurable concentrations of six different parabens in 20 human breast tumors.³³⁷ Larger studies are needed to determine whether the levels of these chemicals in breast tumors differ from levels in normal breast tissue and whether this ubiquitous group of xenoestrogens is contributing to increased risk of breast cancer.

2. Increase research on disparities in health outcomes and differences in exposures.

More studies are needed to explain disparities in breast cancer incidence, mortality and environmental exposures among women of color. For example, postmenopausal Hispanic women appear to be at significantly greater risk of breast cancer related to ERT than non-Hispanic white women.³³⁸ This difference could suggest greater sensitivity to environmental estrogens. Breast cancer rates are rising rapidly in Asian American women, particularly in Japanese American women.³³⁹ Research is needed to determine whether environmental exposures are contributing to these differences.

3. Develop and authorize less invasive, more effective breast cancer screening and diagnostic methods

Participants at the International Summit on Breast Cancer and the Environment called for breast cancer screening and diagnostic methods “that do not involve radiation exposure, such as blood testing or ultrasound.” Another policy recommendation from the Summit stated: “Radiation use in medicine should be reassessed

Recommending that women at high risk for breast cancer increase their exposure to the only proven cause of breast cancer highlights the urgent need for an alternative to mammography that does not involve radiation exposure.

by health professionals. Patients need better information about radiation risk and doses and better technology needs to be developed.”³⁴⁰

Ionizing radiation is the best-established environmental cause of breast cancer and other cancers; this is now commonly known thanks to decades of research. Despite this, mammography continues as a “gold standard” for breast cancer detection. The American Cancer Society and the National Cancer Institute now recommend that women begin annual mammographic screening at age 40, and even earlier if their family history, genetic predisposition or previous medical treatment puts them at high risk of developing breast cancer.

Recommending that women at high risk for breast cancer increase their exposure to the only proven cause of breast cancer highlights the urgent need for an alternative to mammography that does not involve radiation exposure. The recommended treatment for women who have already undergone radiation therapy for Hodgkin’s disease illustrates the contradiction in current medical practice. Four studies in 2003 found a greatly-increased risk of breast cancer among young women who had received radiation treatment for Hodgkin’s

disease.^{341,342,343,344} These studies confirmed findings from many earlier studies. Every year, 3,500 women are diagnosed with Hodgkin's disease and treated with radiation. The American Cancer Society suggests that these women consider undergoing annual mammograms as young as 30, ignoring the risk of 10 additional years of radiation exposure, in addition to the radiation exposure that has already put them at high risk. A similar recommendation is made for women with the BRCA1 and BRCA2 gene mutation. However, the Society's own "Guidelines for Breast Cancer Screening Update 2003"³⁴⁵ includes the following risk assessment:

"Overall risk from single and cumulative diagnostic exposures is small, but risk increases with the amount of exposure and with younger age at exposure...^{346,347} It has also been hypothesized that some women at increased inherited risk for breast cancer may also have increased radiation sensitivity, which could increase their risk for radiation-induced breast cancer. This hypothesis may be plausible because studies of BRCA1 and BRCA2 suggest that these genes code for functions related to repair of radiation damage to DNA."^{348,349,350,351,352}

Surely women at particularly high risk for breast cancer should not be repeatedly exposed to a known breast carcinogen as a "preventive" measure.

Women need a more effective method for breast cancer detection, one that works for women of all ages and does not expose them to radiation. Finding an alternative to mammography, a technology now more than half a century old, must be a top research priority. It is time to redirect scarce resources to answer this critical need.

Women also need better information about the benefits and harms of mammography screening. Researchers at the Nordic Cochrane Centre in Copenhagen, Denmark found the information provided by professional advocacy groups (including the American Cancer Society, the Susan G. Komen Foundation and Y-ME National Breast Cancer Organization) to be "severely biased in favour of screening. Few websites live up to accepted standards for informed consent."³⁵³ Web sites of the three consumer organizations studied (including Breast Cancer Action) mentioned the harms of screening, overdiagnosis and treatment, and were found to be "much more balanced and comprehensive than other sites."

The types of research most likely to produce useful evidence will be those examining:

- (1) the interplay between the timing of exposures, multiple exposures and chronic exposures;**
- (2) disparities in health outcomes and differences in exposures among racial groups;**
- (3) human contamination, measured by biomonitoring;**
- and (4) public health studies investigating unexplained patterns of breast cancer.**

Additional Research Recommendations

Dr. Annie J. Sasco, who commented on the Summit recommendations, also suggested the need to conduct studies in places “where there is an epidemiologic transition of breast cancer, i.e., going from low to higher incidence rates. This should allow us to capture the reasons for such a change and the discovery of new etiologic links is often far easier in low risk populations. In addition, there is an issue of equity. The rest of the world is also touched by breast cancer (more than 1 million new breast cancer cases each year) and deserves to get at least some investigation.”³⁵⁴ Studies in North African countries, where rates are now rising dramatically as the use of synthetic chemicals increases, may provide important insights into the causes of breast cancer.³⁵⁵

More research is needed on the Tissue Organization Field Theory, i.e., the role of the stroma and the extracellular matrix in the development of breast cancer and other cancers discussed on page 16. Under this theory, cancer can arise within the tissue without mutation or other direct damage to DNA. Two recent studies using animal mammary stroma supported this theory. In the first study, researchers exposed rodent mammary stroma to radiation, thereby initiating cancer in unirradiated epithelial cells.³⁵⁶ In the second study, researchers exposed rodent mammary epithelial cells to a known carcinogen, N-nitrosomethylurea (NMU) and implanted these cells into mammary gland stromata of five groups of rodents, some of whose stroma were exposed to NMU and some without NMU exposure. Only the rodents whose stroma was exposed to NMU developed epithelial cell tumors.³⁵⁷ Additional research into tissue organization could yield valuable insights into the development of carcinogenesis and perhaps lead to effective measures that would interrupt the development of the disease and ultimately lead to the prevention of breast cancer.

Policy Recommendations

Participants at the International Summit on Breast Cancer and the Environment identified major policy recommendations needed to implement the research recommendations and to improve the policies and strategies employed by legislators, government agencies, law enforcement, breast cancer advocacy groups and other affected communities, scientists, clinicians, research funders and industry. These policy recommendations are reflected in the Six Point Plan that accompanies this report. They include:

- **Establish a national biomonitoring program to track exposures, using breast milk and other biospecimens to assess community health**

Biomonitoring—using breast milk, fat, blood, urine and other biospecimens—affords an effective supplement to classical epidemiology by quantifying individual and community exposures to particular environmental chemicals. Although no systematic monitoring of chemical body burden in humans in the United States exists, a strong body of evidence indicates that many synthetic chemicals accumulating in Americans’ bodies are known carcinogens. Levels of such chemicals should be measured and changes over time should be identified. A research effort of this magnitude likely can only be accomplished with public support and funding.

Reports from the CDC have documented the presence of 116 environmental chemicals in the blood and urine of Americans of all ages and races.³⁵⁸ Many synthetic chemicals found in breast milk, fat, blood and urine are suspected breast carcinogens, having been found to cause mammary tumors in laboratory animals. It is essential that we study biospecimens to identify the contaminants in our bodies and make policy changes to eliminate these contaminants from the food chain.

Breast milk—once the purest food on the planet—has become unacceptably contaminated. This nourishment provided to 60 percent of newborns in the USA has been found to contain some 200 chemicals. Biomonitoring programs in Sweden and Germany have discovered PCBs, dioxins, DDT and other organochlorine compounds linked with increased breast cancer risk in human breast milk.³⁵⁹ Many organic solvents have also been found in breast milk.³⁶⁰ These include benzene and toluene, known to cause mammary tumors in animals.

The widespread presence of these contaminants in breast milk provides evidence of exposure of both mother and infant to potential harm. Women are faced with a dilemma when it comes to breast-feeding. Breast milk is a source of essential nutrients, many of which cannot be duplicated in infant formula. But infant formula poses problems, too: (1) it is more likely to be contaminated with lead³⁶¹ and (2) polycarbonate baby bottles may leach bisphenol-A, an endocrine disruptor, into the formula.³⁶²

Breast milk—which provides nourishment to 60 percent of newborns in the USA has been found to contain some 200 chemicals. However, scientists still consider it the best nutrition for infants because of the developmental, emotional, immunologic and neurological benefits.

Nevertheless, breast-feeding also transmits contaminants to infants. Whether these chemicals increase daughters' risk of breast cancer has yet to be determined. Despite contamination of breast milk, however, scientists still consider it the best nutrition for infants because of the developmental, emotional, immunologic and neurological benefits.^{363,364,365,366} All studies demonstrating the benefits of breast-feeding have been done since World War II, when the contamination of breast milk by industrial chemicals began.

An alliance of breast-feeding and environmental organizations stated in 2002:

“The contamination of breast milk is one symptom of the environmental contamination of our communities. The individual decision to breastfeed must be promoted and protected while we work collectively towards eliminating the chemicals that contaminate the food we eat, the water we drink, the air we breathe, and the products we use.”³⁶⁷

- **Track cancer incidence nationally**

Health tracking, using biomonitoring technologies, together with diligent surveillance of health outcomes, can increase understanding of the role of environmental exposures in breast cancer. Summit participants recommended that “all cancer registries should be adequately funded to cover the entire USA. With respect to breast cancer, registries should also track the incidence of ductal carcinoma in situ (DCIS).”

Current U.S. cancer incidence statistics are estimates based on data from 18 regional sites, calculated by the National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) program. These estimates are based on actual cancer cases in about 74 million people (26 percent of U.S. population).³⁶⁸

Scientists, Public Health Professionals and Activists Call for Change

Studies of the health effects of some of the 85,000 synthetic chemicals introduced since World War II are currently underway but will take decades to complete. For nearly 3,000 of those chemicals, more than one million pounds are produced annually. Yet little data is publicly available about even the basic toxicity of 75 percent of these high-production-volume chemicals, much less their effects on the development of breast cancer.

Evidence from the CDC shows that 116 chemicals have invaded the bodies of Americans without our knowledge or consent. Some of these chemicals, such as polycyclic aromatic hydrocarbons (PAHs), heptachlor

(an insecticide) and atrazine (an herbicide) are associated with increased risk of breast cancer.³⁶⁹ Many of them, such as atrazine, cadmium and various phthalates are known endocrine disruptors, which may put developing fetuses at greater risk of breast cancer in adulthood. The collective impact of this chemical mixture is unknown (some speculate it may be unknowable) but the uninvited presence of these chemicals in our bodies is unacceptable.

There is no shortage of advice for women about things they can do in their personal lives to reduce the risk of breast cancer. However, what many people see as personal choices are, in fact, imposed limitations and restrictions. Many people, for example, regardless of income or wealth, do not have access to a year-round supply of organic or chemical-free

produce or meat. This current consumer reality is a result of industrial and economic policy choices not made by consumers themselves.

Breast cancer is more than a personal issue; it is a public health crisis that demands action by society as a whole. A major public education campaign is underway to help people understand the mounting evidence linking synthetic chemicals with breast cancer and other cancers. Once informed, the public can be mobilized to action, using this evidence to support measures to protect human health and the health of future generations.

The public's health cannot and should not have to wait for absolute proof that certain chemicals cause breast cancer before moving to reduce the risk of such harm occurring. Too many people will suffer from this

The public's health cannot and should not have to wait for absolute proof that certain chemicals cause breast cancer before moving to reduce the risk of such harm occurring.

disease if we delay action until a “scientific standard” of proof is met. Such a standard requires a 95 percent certainty of cause and effect. While this strict standard is supported by industry when policy changes under consideration would have an impact on profits, in other settings less stringent standards are set. For example, legal remedies in a civil setting require only a “preponderance of the evidence”—a more than 50 percent likelihood—that a challenged action results from the behavior in question. And California’s Environmental Quality Act (CEQA) requires only “potential for significant impact”—10 to 30 percent likelihood—as a basis for action.

What may work for science and industry does not, in this case, work for the public’s health. The public deserves protection from environmental hazards based on a standard that acknowledges that some evidence—not conclusive proof—is sufficient. Public health policy based on the precautionary principle says that evidence of harm, rather than proof of harm, serves as the trigger for policy action. By that standard, there is ample evidence of the need to reduce or, in some cases, eliminate certain toxic chemicals. Understood by doctors as “first, do no harm,” the precautionary principle is sometimes abbreviated as “better safe than sorry.”

In addition, the precautionary principle mandates that proponents of chemicals and radiological products and processes assess their health, safety and environmental impacts before introducing them to the marketplace, and make that information publicly available. The burden to provide such information thus lies with manufacturers and sellers, not with the public.

As explained by the Science and Environmental Health Network, the principle provides that:

When an activity raises threats of harm to the environment or human health, precautionary measures should be taken even if some cause and effect relationships are not fully established. Implementing the principle requires exploring alternatives to possibly harmful actions... and using democratic processes to carry out and enforce the principle.

An obligation exists for manufacturers to examine a full range of alternatives to toxic ingredients and to select the alternative with the least potential impact on human health and the environment, including the alternative of not bringing questionable products to the market at all. The precautionary principle rests on the democratic principle that government officials are obligated to serve the public interest of protecting human health and the environment. Decisions applying the precautionary principle must be transparent, participatory and informed by the best available information.

To reduce the risk of breast cancer and ultimately end the epidemic, fundamental and immediate public policy changes must be made based on the precautionary principle. No longer can we afford to wait. The following six-point plan will help us accomplish this goal:

Understood by doctors as “first, do no harm,” the precautionary principle is sometimes abbreviated as “better safe than sorry.”

I. Phase Out Chemicals Known To Cause Cancer or Genetic Harm

There is ample evidence of the need to phase out unnecessary use of chemicals that cause cancer, or genetic harm, by requiring toxic-use-reduction planning and clean-production planning by all polluters and government agencies. Programs should be established to encourage, and, if necessary, require such planning by government agencies and companies doing business with them.

*“We must identify toxins
that are making us sick
and work with our allies
to eliminate them.”*

■ Andrea Ravinett Martin,
Founder, Breast Cancer Fund

Efforts should be advanced to implement the Persistent Organic Pollutants (POPs) treaty.³⁷⁰ This global treaty, negotiated under the auspices of the United Nations Environment Program,

targets hexachlorobenzene, endrin, mirex, toxaphene, chlordane, heptachlor, DDT, aldrin, dieldrin, PCBs, dioxins and furans. The agreement became legally-binding on May 17, 2004, when France became the 50th nation to ratify it. The first meeting of ratifying countries is to be held within a year from that date. Countries that ratify the treaty before the first meeting will be eligible to participate in discussions of how the treaty will be implemented and the process for deciding what additional POPs chemicals will be designated for elimination. Although the United States is a signatory, the U.S. Senate should now ratify this treaty and help lead the way in expanding the list of toxic chemicals to be phased out.

The European Union (EU), the world's second-largest economy³⁷¹ and largest chemical producer³⁷² is taking major steps to ensure that all chemicals released into the environment in EU countries are not linked to serious health consequences. The new policy proposed by the EU is known as REACH

(Registration, Evaluation and Authorization of Chemicals). The final draft of legislation was published on October 29, 2003, and is expected to become law in 2006.

REACH is a true precautionary approach to chemical regulation. Unlike current U.S. chemical policy, which makes the victim prove that a chemical has caused harm, REACH would make the manufacturer responsible. In many cases, such a policy would prevent harm from occurring.

REACH would apply not just to chemicals, but also to products that contain harmful chemicals, including cleaning solvents and cosmetics and personal care items.

In support of the REACH policy, members of the European Parliament, scientists, physicians, ethicists, and citizens from Europe, Canada, and the United States signed the International Declaration on Chemical Pollution Health Dangers in May, 2004, also known as the Paris Appeal. The Paris Appeal declares the following:

1. The development of numerous current diseases is a result of the deterioration of the environment.
2. Chemical pollution represents a serious threat to children and to mankind's survival.
3. As our own health, and that of our children and future generations, is under threat, the human race itself is in serious danger.

The signatories call on “national decision-makers, European Authorities, international organizations, and specifically the United Nations Organization (UNO)” to ban all products that are certainly or probably carcinogenic, mutagenic or contain reproductive toxins for humans, and apply the precautionary principle to all chemicals that are persistent and bio-accumulative. Other recommendations can be found on the following Web site: <http://appel.artac.info/anglais.htm>

Cancer prevention depends on reducing or eliminating exposures to substances and processes that cause cancer. A policy such as REACH would help reverse the epidemic of breast cancer and other cancers that now affect one in three women and one in two men in the United States.

2. Educate the Public About the Health Effects of Radiation and on How to Reduce Exposure to Both Ionizing and Non-Ionizing Radiation

Health professionals and the public need to understand that (1) exposure to ionizing radiation can cause cancer, (2) genetic damage is cumulative over a lifetime and (3) the younger one is at the time of exposure, the greater the risk of cancer development. Medical procedures involving radiation exposure involve both risks and benefits, and patients are entitled to know both in order to provide informed consent.³⁷³ Physicians and others referring patients for a radiological procedure should tell the patient what radiation dose is involved, just as they currently tell the patient the dosage of a medication.

In addition, scientists must develop a non-radiological replacement for mammography. The public needs a method for accurate and early detection of breast cancer that will be effective for women of all ages without exposing them to a known carcinogen.

Public education also is needed about the risks of non-ionizing radiation (EMF) exposure, how people can measure EMF levels in their environment and how they can mitigate them if necessary. This educational effort should identify prudent avoidance measures for consumers, particularly women and their families, as well as for certain labor and professional groups, such as teachers, nurses and flight attendants. An informed public

can help shape public policy to reduce EMF exposure at the local, state and national level.

3. Monitor Chemical Body Burden and Health Outcomes

The documented contamination of our bodies demands that we establish a comprehensive program of biomonitoring, using breast milk and other biospecimens such as fat, urine and blood as markers of community health. Such a program would reflect the principles of community-based participatory research, involving the community from the outset and providing support and practical information to those who agree to be tested. Identifying the chemical constituents of a community's body burden and linking this information to data on health outcomes creates health tracking that can and should underpin a plan to eliminate these contaminants.

The 2003 CDC report clearly demonstrates that public policy changes based on biomonitoring make a difference. Body burdens of PCBs, DDT and cotinine (the metabolite of nicotine) have all declined since PCBs and DDT were banned in the United States and smoking controls were implemented. Precautionary public health measures, based on information that exists about the dangers of chemical pollutants, can and do make a difference.

Body burdens of PCBs, DDT and cotinine (the metabolite of nicotine) have all declined since PCBs and DDT were banned in the United States and smoking controls were implemented.

4. Hold Corporations Accountable for Hazardous Practices and Offer Incentives for Clean, Green Practices

Companies should not only be held accountable for releasing cancer-causing chemicals into our environment and into our bodies but should also be rewarded for instituting new policies and processes that are healthier for our environment when alternatives to these chemicals exist. Many companies are already learning that being “green” builds consumer loyalty and increases profitability. Offering additional incentives to corporations that encourage them to eliminate harmful chemicals in their products and processes will help them initiate new policies.

Such incentives might include: non-monetary public awards; a labeling system to highlight companies that use pollutant-reducing technology; prioritizing “green” companies when awarding government contracts; investigating new tax credits for companies that reduce their use of natural resources; providing grants to small businesses for one-time purchase of equipment or materials that would help them reduce their use of cancer-causing chemicals.

5. Enact “Sunshine” Laws and Enforce Existing Environmental Protection Laws

Federal and state governments should follow the example of Massachusetts by passing a Toxics Use Reduction Act, which requires corporations to disclose the names and quantities of chemicals they use. Since passing the Toxics Use Reduction Act in 1990, the amount of toxic chemicals released into the environment in Massachusetts has plummeted by 73 percent, from 20.6 million pounds to 5.5 million pounds.³⁷⁴

Existing environmental protection laws need to be enforced and, in some cases, toughened. Environmental protection laws such as the Clean Air Act and the Federal Insecticide, Fungicide and Rodenticide Act must be strengthened, not weakened. Sufficient funding must be appropriated for regulatory agencies and commissions, such as the EPA and the Consumer Products Safety Commission, to increase environmental surveillance and enforcement of existing regulations.

“I think that women who are willing to get involved just aren’t going to accept that we have to die in the numbers that we are, and that there are not answers. We’re not going to let them give up on us.” ■ Elenore G. Pred, Founder, Breast Cancer Action

6. Practice “Healthy Purchasing”

Businesses, government, consumers and hospitals should purchase products that are free from chemicals linked to breast cancer, such as chlorine-free paper or plastic products made without polyvinyl chloride. Such subtle changes in purchasing practices would mean that fewer cancer-causing chemicals would enter our homes, be dumped in our landfills and pollute our air and water. Further, these actions will encourage industry to provide non-hazardous products that consumers want.

Local, state and federal governments should lead the way by adopting environmentally-preferable purchasing practices, thereby creating an example for individuals, businesses and hospitals to follow. Two San Francisco Bay Area municipalities are leading the way. In August, 2003, San Francisco adopted a precautionary principle ordinance as a policy framework for decision-making. In October 2003, the city of Berkeley, Calif. adopted a precautionary principle resolution. A “healthy purchasing” ordinance is being readied for introduction in San Francisco that would require the city to choose the safest alternatives when purchasing city vehicles, janitorial products and other commodities that make up the city’s \$600 million in annual purchasing power. In 2002, the Los Angeles Unified School District, the second largest in the United States, adopted an Integrated Pest Management Policy based on the precautionary principle. The California General Services Division of State Architect (DSA) has launched a list of environmentally-preferable building products to be used in school construction. See www.eppbuildingproducts.org for more information.

Local, state and international governments offer many useful examples and models for policy changes to protect public health. We ignore at our peril evidence that chemicals are contributing to the rising incidence of breast cancer. Stemming that tide requires that we take action based on existing evidence to protect the health of people and the planet. Waiting for absolute proof only means more needless loss of lives. It is in our power to change the course we are on. Now is the time to act on the evidence.

Stemming the rising tide of breast cancer requires that we take action based on existing evidence to protect the health of people and the planet. Waiting for absolute proof only means more needless loss of lives.

Appendix

Chemicals Shown To Induce Mammary Tumors In Animals

(National Toxicology Program, 2003)

<http://ntp-server.niehs.nih.gov/htdocs/Sites/MAMM.html>

- Acronycine
- Benzene
- 2,2-BIS(Bromomethyl)-1,3-Propanediol
- 1,3-Butadiene
- 2-Chloroacetophenone (CN)
- Chloroprene
- C.I. Acid Red 114
- C.I. Basic Red 9 Monohydrochloride
- Clonitralid
- Cytembena
- 2,4-Diaminotoluene (2,4-Toluene Diamine)
- 1,2-Dibromo-3-Chloropropane
- 1,2-Dibromomethane
- 2,3-Dibromo-1-Propanol
- 1,1-Dichlorethane
- 1,2-Dichlorethane
- 1,2-Dichloropropane (Propylene Dichloride)
- Dichlorvos
- 3,3'-Dimethoxybenzidine Dihydrochloride
- 3,3'-Dimethylbenzidine Dihydrochloride
- 2,4-Dinitrotoluene
- Ethylene Oxide
- Furosemide (Lasix)
- Glycidol
- Hydrazobenzene
- Indium Phosphide
- Isophosphamide
- Isoprene
- Methylene Chloride
- Methyleugenol
- Nithiazide
- 5-Nitroacenaphthene
- Nitrofurazone
- Nitromethane
- O-Nitrotoluene
- Ochratoxin A
- Phenesterin
- Procarbazine Hydrochloride
- Reserpine (Serpasil)
- Sulfallate
- 2,4- & 2,6-Toluene Diisocyanate
- O-Toluidine Hydrochloride
- 1,2,3-Trichloropropane
- Urethane
- Urethane and Ethanol Combination

Substances listed in the U.S. National Toxicology Program's 10th Report on Carcinogens

Part A. Known to be a Human Carcinogen

Aflatoxins
Alcoholic Beverage Consumption
4-Aminobiphenyl
Analgesic Mixtures Containing Phenacetin
Arsenic Compounds, Inorganic
Asbestos
Azathioprine
Benzene
Benzidine
Beryllium and Beryllium Compounds
1,3-Butadiene
1,4-Butanediol Dimethylsulfonate (Myleran®)
Cadmium and Cadmium Compounds
Chlorambucil
1-(2-Chloroethyl)-3-(4-methylcyclohexyl)-1-nitrosourea (MeCCNU)
bis (Chloromethyl) Ether and Technical-Grade Chloromethyl Methyl Ether
Chromium Hexavalent Compounds
Coal Tar Pitches
Coal Tars
Coke Oven Emissions
Cyclophosphamide
Cyclosporin A (Ciclosporin)
Diethylstilbestrol
Dyes Metabolized to Benzidine)
Environmental Tobacco Smoke
Erionite
Estrogens, Steroidal
Ethylene Oxide
Melphalan
Methoxsalen with Ultraviolet A Therapy (PUVA)
Mineral Oils (Untreated and Mildly Treated)
Mustard Gas
2-Naphthylamine
Nickel Compounds

Radon
Silica, Crystalline (Respirable Size)
Smokeless Tobacco
Solar Radiation
Soots
Strong Inorganic Acid Mists Containing Sulfuric Acid 218
Sunlamps or Sunbeds, Exposure to
Tamoxifen
2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD); "Dioxin"
Thiotepa
Thorium Dioxide
Tobacco Smoking
Vinyl Chloride
Ultraviolet Radiation, Broad Spectrum UV Radiation
Wood Dust

Part B. Reasonably Anticipated to be a Human Carcinogen.

Acetaldehyde
2-Acetylaminofluorene
Acrylamide
Acrylonitrile
Adriamycin® (Doxorubicin Hydrochloride)
2-Aminoanthraquinone
o-Aminoazotoluene
1-Amino-2-methylantraquinone
2-Amino-3-methylimidazo [4,5-f]quinoline (IQ)
Amitrole
o-Anisidine Hydrochloride
Azacitidine (5-Azacitidine®, 5-AzaC)
Benz[a]anthracene
Benzo[b]fluoranthene
Benzo[j]fluoranthene
Benzo[k]fluoranthene
Benzo[a]pyrene
Benzotrichloride
Bromodichloromethane
2,2-bis-(Bromoethyl)-1,3-propanediol (Technical Grade)

Butylated Hydroxyanisole (BHA)
Carbon Tetrachloride
Ceramic Fibers (Respirable Size)
Chloramphenicol
Chlorendic Acid
Chlorinated Paraffins (C12, 60% Chlorine)
1-(2-Chloroethyl)-3-cyclohexyl-1-nitrosourea
bis(Chloroethyl) nitrosourea
Chloroform
3-Chloro-2-methylpropene
4-Chloro-o-phenylenediamine
Chloroprene
p-Chloro-o-toluidine and p-Chloro-o-toluidine Hydrochloride
Chlorozotocin
C.I. Basic Red 9 Monohydrochloride
Cisplatin
p-Cresidine
Cupferron
Dacarbazine
Danthron
(1,8-Dihydroxyanthraquinone)
2,4-Diaminoanisole Sulfate
2,4-Diaminotoluene
Dibenz[a,h]acridine
Dibenz[a,j]acridine
Dibenz[a,h]anthracene
7H-Dibenzo[c,g]carbazole
Dibenzo[a,e]pyrene
Dibenzo[a,h]pyrene
Dibenzo[a,i]pyrene
Dibenzo[a,l]pyrene
1,2-Dibromo-3-chloropropane
1,2-Dibromoethane (Ethylene Dibromide)
2,3-Dibromo-1-propanol
tris(2,3-Dibromopropyl) Phosphate
1,4-Dichlorobenzene
3,3'-Dichlorobenzidine and 3,3'-Dichlorobenzidine Dihydrochloride
Dichlorodiphenyltrichloroethane (DDT)

1,2-Dichloroethane (Ethylene Dichloride)	Lindane and Other Hexachlorocyclohexane Isomers	Phenacetin
Dichloromethane (Methylene Chloride)	2-Methylaziridine (Propylenimine)	Phenazopyridine Hydrochloride
1,3-Dichloropropene (Technical Grade)	5-Methylchrysene	Phenolphthalein
Diepoxybutane	4,4'-Methylenebis(2-chloroaniline)	Phenoxybenzamine Hydrochloride
Diesel Exhaust Particulates	4-4'-Methylenebis(<i>N,N</i> -dimethyl benzenamine	Phenytoin
Diethyl Sulfate	4,4'-Methylenedianiline and 4,4'- Methylenedianiline Dihydrochloride	Polybrominated Biphenyls (PBBs)
Diglycidyl Resorcinol Ether	Methyleugenol	Polychlorinated Biphenyls (PCBs)
3,3'-Dimethoxybenzidine	Methyl Methanesulfonate	Polycyclic Aromatic Hydrocarbons (PAHs)
4-Dimethylaminoazobenzene	<i>N</i> -Methyl- <i>N'</i> -nitro- <i>N</i> - nitrosoguanidine	Procarbazine Hydrochloride
3,3'-Dimethylbenzidine	Metronidazole	Progesterone
Dimethylcarbamoyl Chloride	Michler's Ketone	1,3-Propane Sultone
1,1-Dimethylhydrazine	[4,4'-(Dimethylamino)benzophenone]	γ-Propiolactone
Dimethyl Sulfate	Mirex	Propylene Oxide
Dimethylvinyl Chloride	Nickel (Metallic)	Propylthiouracil
1,6-Dinitropyrene	Nitilotriacetic Acid	Reserpine
1,8-Dinitropyrene	<i>o</i> -Nitroanisole	Safrole
1,4-Dioxane	6-Nitrochrysene	Selenium Sulfide
Disperse Blue 1	Nitrofen (2,4-Dichlorophenyl- <i>p</i> - nitrophenyl ether)	Streptozotocin
Dyes Metabolized to 3,3'- Dimethoxybenzidine	Nitrogen Mustard Hydrochloride	Styrene-7,8-oxide
Dyes Metabolized to 3,3'- Dimethylbenzidine	2-Nitropropane	Sulfallate
Epichlorohydrin	1-Nitropyrene	Tetrachloroethylene (Perchloroethylene)
Ethylene Thiourea	4-Nitropyrene	Tetrafluoroethylene
di(2-Ethylhexyl) Phthalate	<i>N</i> -Nitrosodi- <i>n</i> -butylamine	Tetranitromethane
Ethyl Methanesulfonate	<i>N</i> -Nitrosodiethanolamine	Thioacetamide
Formaldehyde (Gas)	<i>N</i> -Nitrosodiethylamine	Thiourea
Furan	<i>N</i> -Nitrosodimethylamine	Toluene Diisocyanate
Glasswool (Respirable Size)	<i>N</i> -Nitrosodi- <i>n</i> -propylamine	<i>o</i> -Toluidine and <i>o</i> -Toluidine Hydrochloride
Glycidol	<i>N</i> -Nitroso- <i>N</i> -ethylurea	Toxaphene
Hexachlorobenzene	4-(<i>N</i> -Nitrosomethylamino)-1- (3-pyridyl)-1-butanone	Trichloroethylene
Hexachlorocyclohexane Isoomers	<i>N</i> -Nitroso- <i>N</i> -methylurea	2,4,6-Trichlorophenol
Hexachloroethane	<i>N</i> -Nitrosomethylvinylamine	1,2,3-Trichloropropane
Hexamethylphosphoramide	<i>N</i> -Nitrosomorpholine	Ultraviolet A Radiation
Hydrazine and Hydrazine Sulfate	<i>N</i> -Nitrosornicotine	Ultraviolet B Radiation
Hydrazobenzene	<i>N</i> -Nitrosopiperidine	Ultraviolet C Radiation
Indeno[1,2,3- <i>cd</i>]pyrene	<i>N</i> -Nitrosopyrrolidine	Urethane
Iron Dextran Complex	<i>N</i> -Nitrososarcosine	Vinyl Bromide
Isoprene	Norethisterone	4-Vinyl-1-cyclohexene Diepoxide
Kepone® (Chlordecone)	Ochratoxin A	Vinyl Fluoride
Lead Acetate	4,4'-Oxydianiline	
Lead Phosphate	Oxymetholone	

**Bold entries indicate new or changed
listing in *The Report on Carcinogens*,
Tenth Edition**

Glossary

AROMATIC AMINE—A pollutant from the chemical and plastics industries, and a by-product of high temperature cooking of meat and fish. Many aromatic amines are known to cause mammary tumors in animals.

CARCINOGEN—Any substance or process known to cause cancer.

DIOXIN—The name given to a group of highly toxic chemicals created by industrial processes that use chlorine, such as the manufacture of paper or the incineration of polyvinyl chloride plastics. Dioxin is an endocrine (hormone) disrupting chemical linked to several types of cancer, birth defects, learning disabilities, infertility, endometriosis and suppression of the immune system. Dioxin persists in the environment and accumulates in the food chain. It is found everywhere: in Arctic snow, in the bloodstream of newborn babies, in breast milk and in the body fat of every human being.

ENDOCRINE DISRUPTING CHEMICALS (EDCs)—Chemicals such as dioxin that disturb the body's finely tuned hormonal (endocrine) balance. Any disruption in hormonal activity can interfere with an organism's ability to grow, develop and function normally. Some EDCs act like the hormone estrogen and may be referred to as xenoestrogens. Prenatal exposure to these chemicals may interfere with development of the breast, predisposing it to cancer in adult life. These chemicals also may be linked to increased rates of testicular cancer in young men and birth defects such as cryptorchidism (undescended testicles) and hypospadias (misplaced urinary opening on the penis). The incidence of hypospadias doubled between 1970 and 1993.

ELECTROMAGNETIC FIELDS (EMFs)—Non-ionizing radiation that includes electrical fields, magnetic fields, radio frequency transmissions and microwaves. A growing body of research evidence suggests an association between EMF exposure and many cancers, including breast cancer and childhood leukemia.

IN VITRO—Derived from the Latin for “in glass,” in vitro studies are those conducted in an artificial environment, on cells in a laboratory dish, for example, rather than in a living organism.

IN VIVO—Studies conducted in a living organism such as humans or other animals.

ORGANOCHLORINES—Any chemical composed of carbon, hydrogen atoms and chlorine. Many pesticides such as DDT and chlordane are organochlorines. Organochlorines persist in body fat for years. They may also be endocrine disruptors and xenoestrogens and, just as with naturally occurring estrogens, are believed to promote growth of cancer cells.

METABOLITE—A chemical that has been converted from its original form by the body's own chemical processes. For example, the pesticide DDT is converted to DDE in the body.

PARABENS—Endocrine-disrupting compounds used as preservatives in thousands of cosmetic, food and pharmaceutical products. They are absorbed from the gastrointestinal tract, from blood and through (intact) skin. Parabens have been shown to have estrogenic activity and have been found in breast tumors.

PERSISTENT ORGANIC POLLUTANTS (POPs)—Organic chemicals that are persistent in the environment and in our bodies, usually in fatty tissues. These include polychlorinated biphenyls (PCBs) and organochlorines.

PHTHALATES—A group of chemicals used to render plastics soft and flexible and found in many household products. Phthalates have been found in women's bodies at high levels.

PHYTOESTROGENS—Plant estrogens that mimic the estrogen hormones and are commonly found in whole grains, dried beans, peas, fruits, broccoli, cauliflower and soy products.

POLYBROMINATED DIPHENYL ETHERS (PBDEs)—Flame retardants used in hundreds of consumer products including furniture, computers, televisions and automobiles. PBDE levels are accumulating in people's bodies worldwide and have been found in breast milk and in breast tumors. Some flame retardants are banned in California and in the European Union.

POLYCHLORINATED BIPHENYLS (PCBs)—A group of highly toxic, synthetic chemical compounds once used as insulation fluid in electrical transformers, lubricating oil in pipelines, as components of plastics and mixed with adhesives, paper, inks, paints and dyes. When PCBs are burned, as in transformer explosions and fires, dioxin is released. Sale of PCBs was banned in the United States in 1976. However, as many as two-thirds of all PCBs ever produced are still in use. The remaining one-third persists in the environment; all living animals, including humans, contain PCBs in their fat. PCBs are implicated in breast cancer, brain cancer, melanoma, lymphoma and soft tissue sarcomas.

POLYCYCLIC AROMATIC HYDROCARBONS (PAHs)—Byproducts of combustion, including high-temperature cooking of meats and fish, the combustion of fuels such as diesel, gasoline and heating oil, and the burning of cigarettes and other tobacco products.

POLYVINYL CHLORIDE (PVC)—A type of plastic also referred to as vinyl, used in construction, packaging, medical products, appliances, cars, toys, credit cards and rainwear. The life cycle of PVC is toxic from beginning to end. PVC is linked to liver and breast cancer among workers who manufacture it. It contains heavy metals such as lead and cadmium as well as phthalates, all of which can be ingested by children when vinyl toys are sucked or chewed. When PVC is incinerated in medical waste, for example, it releases dioxin as well as heavy metals into the environment.

RADIATION—Energy transmitted in the form of rays, waves or particles. There are two types of radiation: ionizing and non-ionizing. Ionizing radiation can strike our genetic material and break off electrons, thereby changing the way new cells are formed. Exposure to ionizing radiation occurs during medical procedures such as X-rays and other radiological diagnostic tests, during mining and processing of uranium or other radioactive ores, from nuclear weapons manufacture and testing, from nuclear accidents such as those at Chernobyl and Three Mile Island, and from hazardous waste produced by nuclear power plants. Non-ionizing radiation includes electromagnetic fields (EMF) and radio frequency (RF) transmission (explained earlier). How non-ionizing radiation affects our health is not clearly understood but is thought to affect hormone function.

SYNERGY—The interaction of two or more elements or forces that creates an effect greater than the sum of the individual effects. This is a key concept in understanding why current regulation of hazardous chemicals does not take account of real world exposures. Chemicals are often regulated as if people were exposed to them one at a time when, in fact, we have multiple chemical exposures every day in air, water, food, at home and in the workplace. Research has shown that chemicals can act in synergy with each other as well as with radiation, either ionizing or non-ionizing.

XENOESTROGENS—Chemicals that mimic the action of the hormone estrogen but come from outside the body (xeno means foreign), such as organochlorine pesticides.

Endnotes

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Raging Light

by Susan Gray

Inspired by the Tibetan prayer flags used on the Breast Cancer Fund's Climb Against the Odds expedition, this quilt contains over 7,000 signatures and memorial names squares.

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