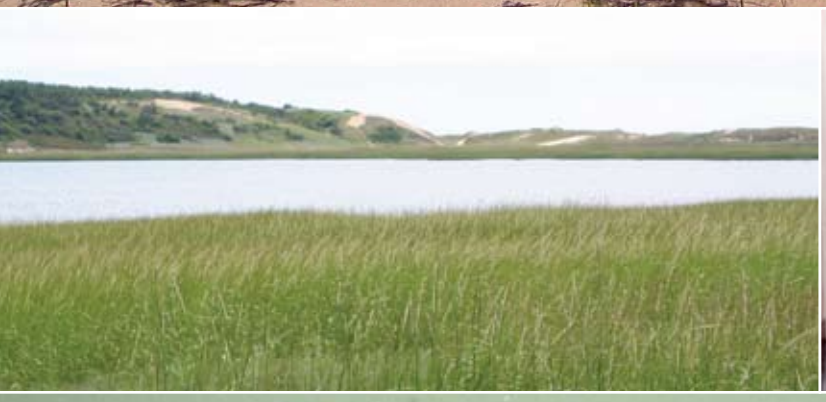
SILENT SPRING INSTITUTE

FINDINGS OF THE CAPE COD BREAST CANCER AND ENVIRONMENT STUDY



Clockwise from top, Cape Cod, Massachusetts sand dunes; a Silent Spring Institute scientist uses a specially modified vacuum cleaner to collect dust samples from a Cape Cod home; a staff scientist labels and stores dust samples prior to analysis; researchers conduct hour-long telephone interviews with 2,171 Cape women for the Cape Cod Breast Cancer and Environment Study; sandy soils and a shallow aquifer on Cape Cod make the water supply vulnerable to contamination.

WE TOLERATE CANCER-CAUSING AGENTS IN OUR ENVIRONMENT AT OUR PERIL...FOR THOSE IN WHOM CANCER IS ALREADY A HIDDEN OR A VISIBLE PRESENCE, EFFORTS TO FIND CURES MUST OF COURSE CONTINUE. BUT FOR THOSE NOT YET TOUCHED BY THE DISEASE AND CERTAINLY FOR THE GENERATIONS AS YET UNBORN, PREVENTION IS THE IMPERATIVE NEED.

RACHEL CARSON, SILENT SPRING

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When we started the Cape Study, we naively thought the hard part was done. We expected to know at the end of the study what was causing elevated breast cancer on Cape Cod. Once we started work, though, I was appalled to learn how little was known about environmental links to breast cancer. We even had to create tools to collect and analyze environmental samples. Although I've revised my expectations for a quick answer, I'm proud of our accomplishments, especially the role of the Cape Study as a model for partnerships between researchers and communities.

Ellen Parker, Chair, Board of Directors, Silent Spring Institute

In the early 1990s, statewide data from the Massachusetts Cancer Registry showed breast cancer incidence rates were significantly higher on Cape Cod than in the rest of Massachusetts. The Massachusetts Department of Public Health reported that seven of the state's ten highest incidence cities and towns were located on Cape Cod. Concerned and motivated to find out why, the Massachusetts Breast Cancer Coalition (MBCC) successfully advocated for state funding for an environmental study. Following a competitive bidding process, the Massachusetts Department of Public Health (MDPH) selected Silent Spring Institute's proposal.

By pledging to study why breast cancer was elevated on the Cape, Massachusetts assumed a leadership role in uncovering links between the environment and breast cancer. The goal of this work is to identify preventable causes of the disease.

Breast cancer is the most common invasive cancer in women and the leading cause of death among women from their late thirties to mid fifties. Only five to 10 percent of breast cancers are due to high risk genes (BRCA1/BRCA2). Further, increased incidence among migrants to higher risk regions — for example, immigrants from Asia to the US — suggests that preventable factors are contributing to rising incidence.

We know that breast cancer risk increases as women get older. Risk is higher for women who were younger when they reached puberty or older at menopause, have never given birth, were older at their first full-term pregnancy, never breastfed, or have gained weight after menopause. Alcohol consumption and lack of physical activity increase risk. Taken together, these established breast cancer risk factors don't adequately explain why a particular woman gets breast cancer or why incidence is higher in some regions.

Research has begun to pinpoint some modifiable, environmental factors. For example, recent epidemiological studies have found substantial evidence that polychlorinated biphenyls (PCBs) increase breast cancer risk in some women. PCBs were widely used in electrical equipment until 1978 when they were banned in the US; however, they can still be found in older buildings and electrical appliances; and they persist as pollutants. Evidence of links to polycyclic aromatic hydrocarbons (PAHs), which are in air pollution, second-hand smoke, and foods cooked at high temperature, is growing. Laboratory research points to hundreds of other suspects.

Because breast cancer is so common and environmental chemical exposures are so widespread, identifying even small effects of environmental factors on breast cancer could spare thousands.

ACTIVISTS AND SCIENTISTS COLLABORATE ON STUDY DESIGN: AN OVERVIEW

The Cape Cod Breast Cancer and Environment Study has gained national recognition not only for its focus on understanding causes of breast cancer and how to prevent it, but also as a model for research that encourages community participation.

MBCC has been our partner throughout the study. Our multi-disciplinary scientific staff collaborates with researchers at Boston, Brown, Tufts, and Harvard Universities. In addition, we created two key committees, the Science Advisory Committee (SAC) and Public Advisory Committee (PAC). The PAC, which was jointly chaired by Silent Spring Institute and MDPH, included over 20 community representatives, physicians, and public officials who met quarterly with our study team to review and assist with the research. The Center for Environmental Health Assessment at MDPH provided the state's oversight of the study.

During the initial research phase, the study team sought public input about priorities. We reviewed scientific literature, analyzed Cape environmental and epidemiologic data, conducted pilot environmental and biological sampling studies, designed and built a geographic information system (GIS) that could integrate a wide-variety of environmental data, tested new statistical methods to identify small pockets of high incidence, and developed other new methodologies suited to addressing the research questions.

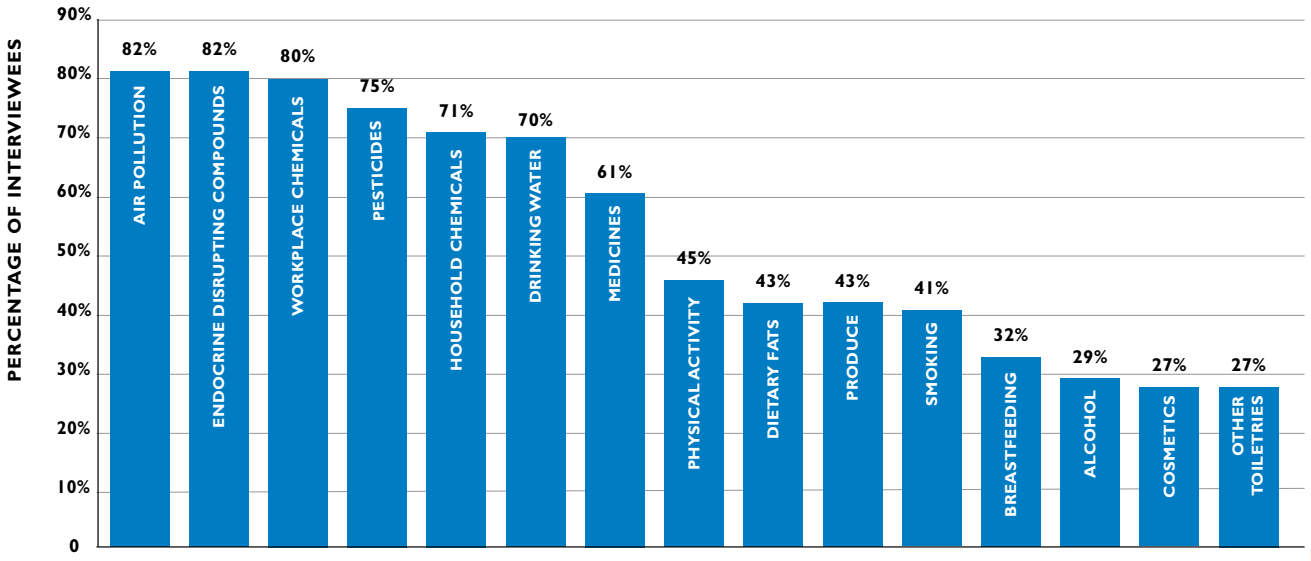
Based on this comprehensive assessment, the study team recommended further investigation of endocrine disrupting compounds (EDCs), including exposures that are distinctive on Cape Cod. Endocrine disrupting compounds are chemicals that mimic or otherwise interfere with natural hormones, including estrogen, a known breast cancer risk factor. They are present in everyday products including plastics, pesticides, and personal care items.

Epidemiologic study of 2,171 women. In phase 2 of the study, we conducted a case-control epidemiologic study that included a 50-minute interview with 2,171 Cape Cod women. Interview questions covered established and suspected risk factors for breast cancer.

Historical reconstruction of pesticide exposure. In the Cape Study GIS we integrated information from the women who participated in the study with extensive environmental data on Cape Cod. Using new methods developed for the study, we assessed each woman's historical exposure to wide-area pesticide use dating back to 1948, the first year DDT was used on the Cape. This marks the start of exposure to synthetic organic compounds, many of which are now identified as endocrine disruptors or mammary carcinogens.

Members of the Massachusetts Breast Cancer Coalition rally in Boston, Massachusetts to raise awareness of the steady increase in breast cancer incidence.

GRASSROOTS BREAST CANCER LEADERS PRIORITIZE ENVIRONMENTAL RESEARCH NEEDS



In a 2004 Silent Spring Institute survey of 56 leaders of grassroots breast cancer organizations in the US and Canada, we asked about organizational priorities and the relationship between environmental issues and breast cancer advocacy. The above figure shows the research areas these leaders identified as most pressing.
The full report is available at www.silentspring.org/newweb/activists/grassroots_rpt.html

Historical reconstruction of drinking water exposure. We also assessed historical drinking water quality and examined whether tap water might be a possible route of exposure. This is especially relevant on Cape Cod, where wastewater is disposed in septic systems; and the aquifer is covered by highly permeable, sandy soils, making it vulnerable to contamination.

Groundwater and drinking water study. We tested wastewater, groundwater, and private well water to evaluate the potential of drinking water as a source of EDC exposure. Working with Dr. Ana Soto at Tufts University, we applied the E-SREEEN bioassay to assess total estrogenic activity in water samples, and we tested for about 20 individual EDCs.

Household exposure study of 120 homes. To identify chemical exposures in the home, an area where women spend a significant portion of time, we collected samples of air and dust from 120 homes, as well as urine samples from the women who lived there. We developed new methods to test for low levels of exposure to 89 EDCs.

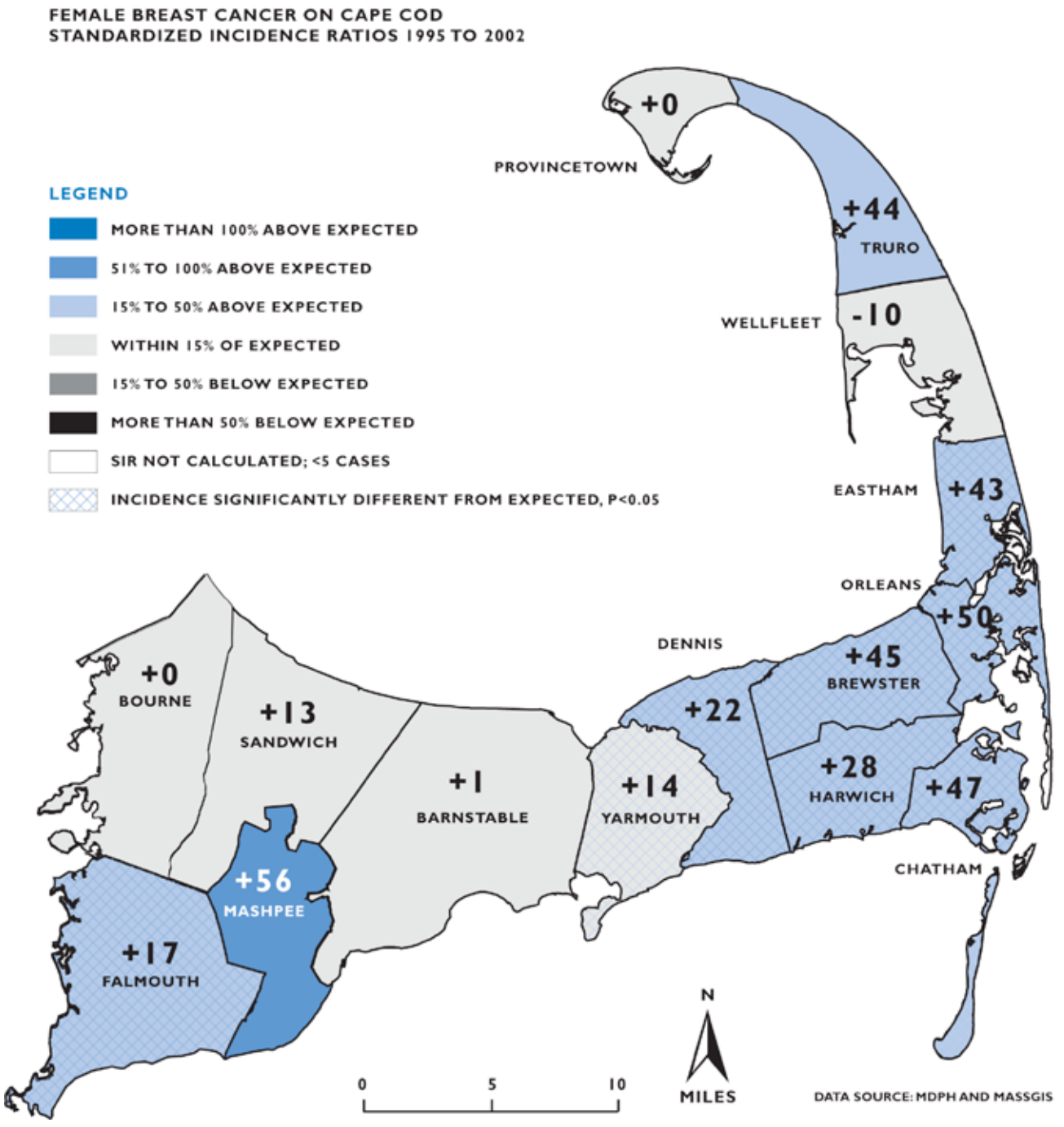
Breast cancer surveillance. As more years of breast cancer data become available, we continue to track changes in the high rates of breast cancer on Cape Cod. From 1995 through 2002, the most recent data available, breast cancer was elevated in nine of the 15 Cape towns.

While the Cape Study and other studies tease out the complex relationship between chemicals and health, we hope that by sharing our research as it unfolds, we enable individuals to take common sense, precautionary steps to reduce exposures to suspect chemicals. This proactive approach to protecting health is formalized in the Precautionary Principle.

BREAST CANCER INCIDENCE REMAINS HIGH ACROSS THE CAPE

Breast cancer incidence remains at least 15 percent higher than the rest of Massachusetts in nine of the 15 towns on the Cape. In eight of these towns, the elevation is statistically significant.

Between 1998 and 2002, Cape Cod had the third highest rate of death from breast cancer in Massachusetts, only behind Dukes and Franklin Counties.



This map shows eight years of breast cancer data, including the most current data available from the Massachusetts Cancer Registry.

NEW METHODS DETECT POCKETS OF ELEVATED BREAST CANCER INCIDENCE

Boston University School of Public Health researchers used a new analytic technique to detect pockets of elevated breast cancer incidence on upper Cape Cod. The study, published in 2005 by Vieira et al. in Environmental Health: A Global Access Science Source, shows three significant hot spots of breast cancer in areas with groundwater contamination plumes, some from the MMR. The study cannot make a causal link, but the authors recommend further investigation of the potential association between breast cancer and pollution plumes. The work was funded by the Superfund Basic Research Program with some additional support from the Cape Cod Breast Cancer and Environment Study. For the full text, please visit http://www.pubmedcentral.gov/articlerender.fcgi?tool=pubmed&pubmedid=15955253.

KNOWN RISK FACTORS FAIL TO EXPLAIN CAPE COD'S HIGHER RISK

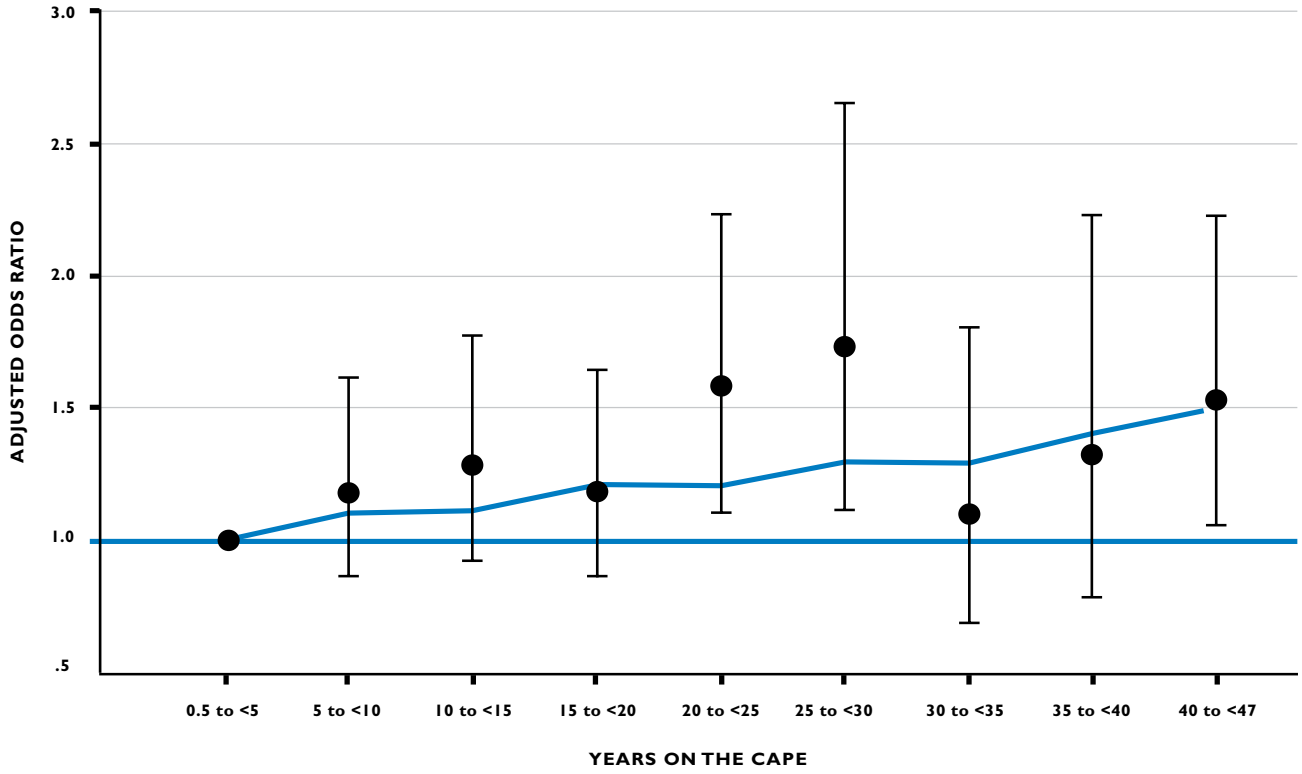
Three different data sources provide evidence that higher breast cancer risk on Cape Cod, compared with the rest of Massachusetts, is not due to an older population, in-migration, mammography use, or established breast cancer risk factors. These results strengthen the case that one or more regional — perhaps environmental — risk factors remain to be discovered, but do not guide us where to look.

Residency on Cape Cod.
The Cape Study found that women who have lived longer on Cape Cod are at higher risk for breast cancer than new arrivals. Women who lived on Cape Cod for 25-29 years were at highest risk: 72 percent higher risk than women who lived there fewer than five years. This finding is independent of established risk factors, including the women's age, family history of breast cancer, childbearing experience, education, and weight.

Risk Factors.
The Harvard-based Collaborative Breast Cancer Study showed 21 percent higher risk for Cape Cod women 50–74 years of age compared with other Massachusetts women after controlling for a comprehensive list of established and suggested risk factors, including family history, reproductive history, use of pharmaceutical hormones and alcohol, and aspects of diet. The study includes women diagnosed between 1989 and 1993.

Mammography.
Higher incidence on the Cape does not seem to be explained by better access to screening, such as mammography. According to a Massachusetts state survey from the mid-1990s, Cape Cod women are no different from women in the rest of the state in their access to mammography—88 percent of Cape Cod women reported ever having had a mammogram compared with 89 percent in the rest of Massachusetts. In addition, if women on the Cape were more likely to be screened than others in the state, we would expect to see both a higher incidence of breast cancer and more cancers caught at an earlier stage. In fact, the proportion of cases diagnosed at earlier stages was lower on Cape Cod than in the rest of the state.

WOMEN WHO LIVED LONGER ON CAPE COD SINCE 1948 HAVE HIGHER BREAST CANCER RISK (P TREND = .02)



This graph shows that there is a higher risk of breast cancer with longer years of residency on Cape Cod, after controlling for established risk factors. The trend to higher risk with longer residence on the Cape is statistically significant.

Whatever is causing the elevated incidence of breast cancer on Cape Cod has not gone away. The most recent Cancer Registry data confirm that breast cancer incidence remains higher than the state average. These data point out the continuing problem; it is now up to us to keep searching for the cause or causes until we have a fuller explanation. I believe the environment is where we need to keep looking.

Richard Clapp, DSc, Professor of Environmental Health,
Boston University School of Public Health and Founding Director,
Massachusetts Cancer Registry

2,171 CAPE COD WOMEN PARTICIPATED IN THE CAPE COD BREAST CANCER AND ENVIRONMENT STUDY

Researchers conducted detailed telephone interviews with 2,171 Cape Cod women. Combining information from these interviews with historical data on the Cape environment, we were able to assess each woman's environmental exposures as well as evaluate her established and suspected risk factors for breast cancer.

The Cape Cod Breast Cancer and Environment Study included 50-minute telephone interviews with 1,165 Cape Cod women diagnosed with breast cancer between 1988 and 1995 and 1,006 comparison women who were similar in age and vital status. For women who were deceased, a close relative, usually a spouse, was interviewed as a proxy.

Interview questions covered established and suspected risk factors for breast cancer, including family history of breast cancer, menstrual and reproductive history, height and weight, and education, an indicator of socioeconomic status. To understand chemical exposures, we asked about use of products, such as pesticides that contain endocrine disrupting compounds (EDCs); and we recorded each Cape Cod address where the woman lived since 1948, the first year of wide-area spraying with DDT. Use of DDT on Cape Cod represents the beginning of widespread exposure to synthetic organic compounds, many of which are now identified as endocrine disruptors or mammary carcinogens.

We then geocoded the study participants' 3,631 Cape addresses in the geographic information system (GIS) and linked GIS data with the interview responses. We analyzed this rich data set to assess each individual's environmental exposures.

Among women who were eligible for the study, 74 percent of women living with breast cancer participated — we were unable to locate 14 percent and 12 percent decided not to participate. Participation of proxies of deceased women with breast cancer was 77 percent. The response rate for the comparison women was 68 percent.

Many of the established risk factors for breast cancer are related to a woman's exposure to her natural hormones, including estrogen, through her reproductive history (for example, her age at onset of menses, at first full-term pregnancy, and at menopause, and her history of breast feeding). Environmental exposures that mimic estrogen or disrupt other hormones come from everyday products including plastics, detergents, pharmaceuticals and pesticides, as well as from drinking water and air pollutants. We know that pharmaceutical hormones affect breast cancer risk; it makes sense to ask if these other environmental exposures might also affect it.

CHEMICAL SUSPECTS IDENTIFIED IN LABORATORY STUDIES

Laboratory studies suggest two types of compounds as priorities for breast cancer research:

- Endocrine disrupting compounds (EDCs) that mimic or otherwise interfere with natural hormones, and
- Compounds that cause mammary tumors in animals.

TIMING OF EXPOSURE MAY MATTER

In addition, the effects of an exposure may depend on when it occurs in the life cycle, such as in utero or during pre-pubertal or postmenopausal time periods. Animal studies show, for example, changes in mammary gland development that could increase the offspring's sensitivity to carcinogens following in utero exposure to the pesticide atrazine or to bisphenol A, which is found in polycarbonate plastics and polyester, among many other sources.

FEW CHEMICALS TESTED FOR HORMONAL ACTIVITY

Of the 80,000 chemicals in commerce in the US, few have been evaluated to see if they affect hormone systems or cause cancer. Among chemicals that have been evaluated, researchers have identified

- 500 EDCs, and
- More than 100 mammary carcinogens.

LIMITING ENVIRONMENTAL EXPOSURES COULD LOWER BREAST CANCER RISK

These compounds are in common commercial products and are ubiquitous pollutants to which women in industrial societies are widely exposed. Because breast cancer is so common and environmental exposures are so widespread, identifying even small effects on breast cancer has the potential for important advances in prevention.

In the early 1990s, knowing that some natural hormones increased cancer in animals, a number of colleagues and I began to wonder if some environmental chemicals might also boost levels of bad estrogen. The renowned biochemist, H. Leon Bradlow, agreed to test a few pesticides for their interaction with estrogens. He and I were astonished to discover that some of these organochlorine chemicals were able to mimic natural estrogen. We termed these chemicals "xenoestrogens" because these were foreign compounds that mimicked estrogen. The theory that we devised has fueled research at Silent Spring Institute and other organizations exploring possible environmental links to disease.

Devra Davis, PhD
Director of the Center for Environmental Oncology, University of Pittsburgh Cancer Institute and Professor of Epidemiology, University of Pittsburgh Graduate School of Public Health

HOUSEHOLD EXPOSURE STUDY: HOUSEHOLD AIR AND DUST ARE IMPORTANT SOURCES OF TOXIC EXPOSURES

Silent Spring Institute researchers collected air and dust samples from 120 Cape Cod homes. For dust samples, top photograph, we used a vacuum cleaner with a specially modified crevice tool to collect approximately 4 grams of dust from rugs, upholstery, wood floors, windowsills, ceiling fans, and furniture. Our analysis of these samples found 66 different endocrine disrupting compounds, ranging from 6 to 42 compounds per home. For air samples, bottom photograph, we collected 24-hour samples of particulate and vapor phase materials from a frequently used room of the home, such as the living room or family room. Our analysis of these samples found 52 different endocrine disrupting compounds, ranging from 13 to 28 compounds per home.

A variety of chemicals enter our homes in cleaning and personal care products as well as through the materials we use in building and renovating. As we have built tighter, more energy efficient homes, these chemicals increasingly linger in our air and dust.

Indoor air specifically has been described as one of the most serious environmental threats to human health. Yet data are lacking on the sources of many of these toxic exposures and how to minimize risk.

To address these issues, we collected urine and household air and dust samples from 120 women who had participated in the interview portion of the Cape Cod Breast Cancer and Environment Study. The urine samples identify chemicals in women's bodies and the air and dust samples help track whether the exposure likely occurs at home.

We analyzed urine samples for 21 endocrine disrupting compounds (EDCs) and air and dust samples for 89 EDCs. EDCs are compounds that have been shown to affect hormone systems. They are being studied in relation to breast cancer and other hormonally-mediated diseases.

INDOOR CONTAMINATION IS WIDESPREAD

Overall, we found

- 52 compounds in air, ranging from 13 to 28 compounds per home,
- 66 compounds in dust, ranging from 6 to 42 compounds per home, and
- 20 compounds in urine.

There were 23 pesticides in air and 27 in dust. Our measurements are the first reported in indoor environments for over 30 of the compounds.

COMPOUNDS ARE PERSISTENT INDOORS

Compounds from plastics, detergents, disinfectants, and personal care products were the most abundant, with most homes exceeding US Environmental Protection Agency (EPA) health-based guidance values for

- Polyaromatic hydrocarbons (PAHs), which are ubiquitous products of combustion, and
- Di (2-ethyl hexyl) phthalate (DEHP), a phthalate used to make plastics, such as vinyl, flexible.

We found evidence that persistent chemicals used legally in the past break down slowly indoors and contribute to ongoing health risks.

- Ten percent of the homes had levels of a degradation product of the carcinogenic flame retardant tris (2,3-dibromopropyl)phosphate that was used in children's sleepwear. US production of tris was banned in 1978.
- The banned industrial chemical polychlorinated biphenyls (PCBs) and the banned pesticides DDT, chlordane, dieldrin, heptachlor, and lindane were all detected at levels that exceeded US EPA health-based guidelines. The Massachusetts Department of Public Health banned chlordane use in Massachusetts in 1983, five years before EPA's ban.

EVERYDAY PRODUCTS INCREASE EXPOSURE TO SUSPECT CHEMICALS

CHEMICAL CLASSES, POTENTIAL SOURCES AND EXAMPLE CHEMICALS FOR COMPOUNDS MEASURED IN THE STUDY

CHEMICAL CLASS	POTENTIAL SOURCES	EXAMPLE CHEMICAL
Phthalates	Plastic, nail polish and other cosmetics	dibutyl phthalate
Alkylphenols	Detergents, plastic, pesticide formulations	nonylphenol
Flame retardants	Furniture foam or stuffing, carpets and drapes, electronic equipment (TVs, computers)	polybrominated diphenyl ether (PBDE 47)
Polycyclic aromatic hydrocarbons (PAHs)	Combustion sources such as fireplaces; stoves and heaters, cigarette smoke, outdoor air pollution and auto exhaust	benzo(a)pyrene
Polychlorinated biphenyls (PCBs)	Older electrical equipment	PCB 52
Banned pesticides	Historical pesticide use in/near the home	DDT, dieldrin, chlordane
Current-use pesticides	Recent pesticide use in/near the home	Chlorpyrifos, permethrin
Other phenols and miscellaneous	Disinfectants, polycarbonate plastics, cosmetics	o-phenyl phenol, bisphenol A, parabens

Indoor air is one of the most serious environmental risks to human health. We were surprised to find residues of chemicals like pesticides and flame retardants that have been banned for decades in the dust and air of Cape Cod homes. Some of these compounds do not break down easily indoors, so we should be concerned about what gets into our homes in the first place.

John D. Spengler, PhD
Akira Yamaguchi Professor of Environmental Health and Human Habitation,
Department of Environmental Health,
Harvard School of Public Health

HIGH LEVELS PROMPTED RETESTING IN 11 HOMES

Of the 120 homes, we retested 11 where we had detected high levels of a contaminant that exceeded a federal health guideline or where we found higher-than-expected levels of a contaminant for which the federal government has not set a health guideline.

Seven of the homes were selected because we detected residues of the carcinogenic flame retardant tris. During retesting we again found tris in five of these seven homes. The homes with the highest levels during the initial testing remained the highest during the retest. None of the women in these homes had detectable levels in their urine, though we did detect a metabolite related to tris in urine from other women in the study. We have asked the US Centers for Disease Control and Prevention (CDC), where the urine samples were analyzed, to investigate further.

We retested two homes for high levels of PCBs and two homes for high levels of chlordane. Over the four to five years between samplings, the levels of these chemicals were still as high as, or higher than, the original test results.

RESULTS REPORTED TO STUDY PARTICIPANTS

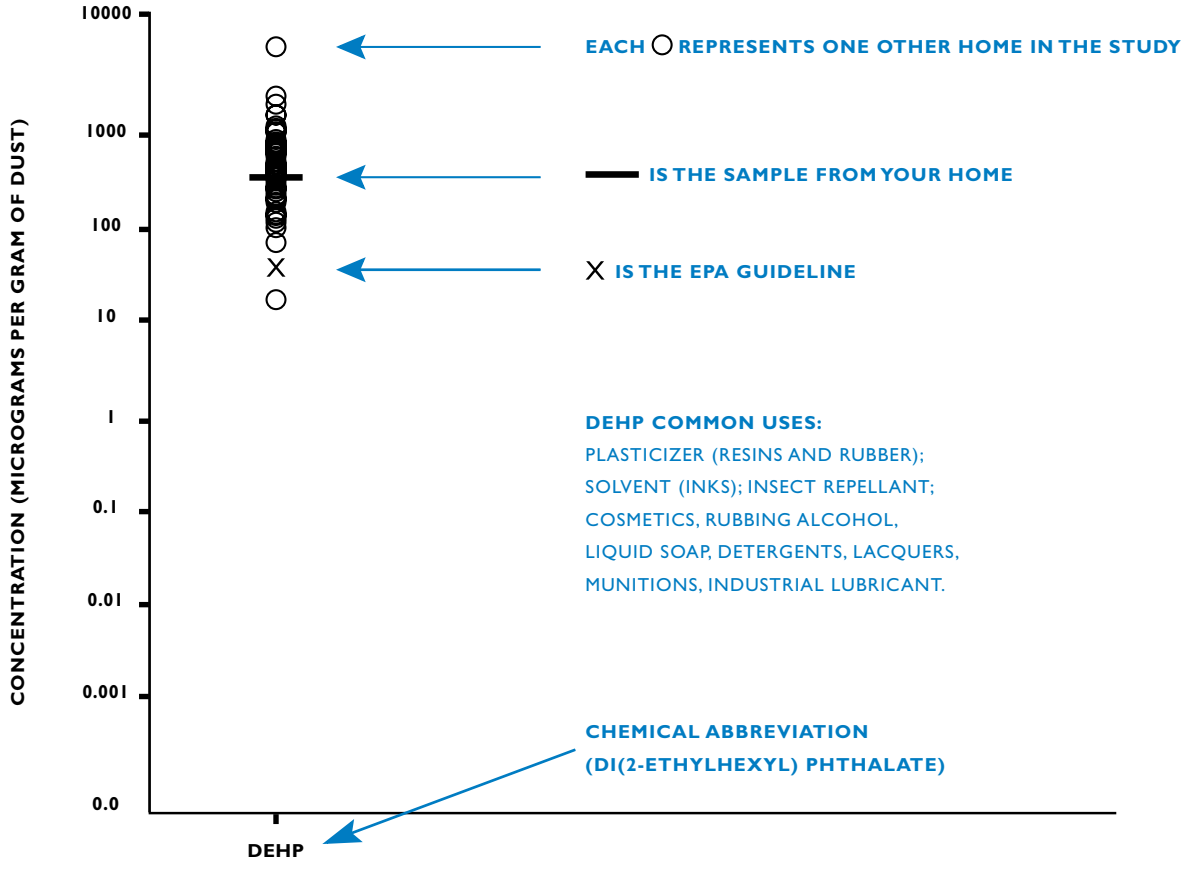
We reported the overall results of the study in public forums on Cape Cod and mailed them to each woman who participated in the study. In addition, the women in the study received the results from their own home. To help participants evaluate their results, we included graphs showing results from other homes in the study and information on the federal health guidelines for the 39 compounds for which guidelines exist. We also provided information about the types of products that may be sources of the specific EDCs detected in the home. This information helps individuals consider ways to reduce exposure to chemicals currently in use.

Public information materials included summary information for all the homes and reported on individual homes without identifying them. Confidential information that could be linked to an individual was only provided to the individuals themselves.

There are exposures to many toxic chemicals that occur in our own home and those may be more dangerous than occur in our air and water.

Nancy Crumpacker, MD
Secretary-Treasurer of the Board,
Rachel's Friends Breast Cancer Coalition
and retired Oncologist

REPORT OF INDIVIDUAL RESULTS



Above is a report showing the level of DEHP detected in one of the 120 homes in which we collected air, dust, and urine samples. The report shows the level of DEHP in this home, and most of the other homes in the study, was higher than the EPA guideline. A sample packet of materials sent to study participants is available on the Silent Spring Institute website at www.silentspring.org/newweb/research/report-back_sample.pdf. Included in the packet is a table listing the sources of the 95 chemicals in the study.

This study shows that the home environment may be a source of exposure to hormonally active chemicals which potentially can affect human health. The products we use in our homes for cleaning and personal care as well as the materials used to build and furnish our homes all contribute to the chemical mix in which we currently live.

Mary Wolff, PhD
Professor of Community and Preventive Medicine and Oncological Sciences, Mount Sinai School of Medicine

IS CAPE COD DIFFERENT?

Some comparison data from other locations are available for some pesticides, PAHs, PCBs, polybrominated diphenyl ethers (PBDEs), and phthalates. Comparisons must be interpreted with caution because of differences in methods of sample collection and characteristics of the study populations, such as the typically older age of women in the Cape Cod Study.

- PBDEs (flame retardants) were five to ten times higher in Cape Cod samples than in two studies in Europe.
- Phthalate levels in urine were generally similar to levels in a representative sample of US women tested by the CDC.
- Pesticide levels in urine were similar overall to US older women tested by CDC, but a small number of Cape Cod women had very high levels.

Compared with study results for Detroit, Iowa, Long Island, Los Angeles, and Yuma (Arizona), Cape Cod levels of pesticides in house dust were higher for

- DDT (currently banned),
- Methoxychlor (currently banned),
- Carbaryl,
- Ortho-Phenylphenol, and
- Propoxyr.

Cape Cod levels of pesticides in house dust were second highest for:

- Chlordane (currently banned),
- Permethrin, and
- PAHs.

Cape Cod levels in house dust were neither highest nor lowest for the pesticides chlorpyrifos and diazinon, and for PCBs (currently banned).

WIDE-AREA PESTICIDE USE: NO CONSISTENT LINK FOUND BETWEEN BREAST CANCER AND WIDE-AREA PESTICIDE APPLICATIONS

Environmental breast cancer studies frequently examine pesticide exposures because many pesticides mimic estrogen, a known breast cancer risk factor, or cause mammary tumors in animals. Most previous studies have been limited to only a few banned pesticides, and most have used one-time measurements taken near the time of diagnosis. To more fully assess exposures to real-world mixtures of many pesticides over time, we used geographic information system (GIS) technology.

We developed new methods to estimate pesticide exposure for the 2,171 study participants at each of their 3,631 Cape addresses for every year between 1948 and 1995.

We collected data starting in 1948 because that was when DDT began to be widely used on the Cape. DDT is one of the first of the synthetic chemicals that mimic estrogen. Pesticide exposures may occur at the time of spraying and thereafter from residues in soil, food crops, or drinking water. The Cape Study is the first breast cancer study to extensively reconstruct historical exposure using GIS techniques, and represents an innovative approach that complements other studies.

All of Cape Cod was sprayed with DDT in 1948-1950 and again in 1955 with the intent to eradicate the gypsy moth.

WEAK EVIDENCE SUGGESTS LINK BETWEEN SOME PESTICIDES AND BREAST CANCER

We found no consistently clear association between breast cancer and more than two dozen chemicals, including DDT, dieldrin, and Sevin®, which were applied as insecticides, herbicides, and fungicides on Cape Cod. However, we found weak evidence of a possible link — independent of established risk factors — between some pesticides and breast cancer during certain time periods.

Specifically breast cancer risk was approximately 20 to 80 percent higher for women who lived

- In or near areas treated for tree pests in 1948-1995,
- Near cranberry bogs in 1948 to the mid 1970s, and
- Near agricultural land since the mid 1970s.

Although these findings are intriguing, most failed to reach traditionally accepted levels of statistical significance. Variations in breast cancer risk following exposure to different categories of pesticides may be related to the mode and frequency of application, the mixtures of chemicals used, or due to chance alone.

Other studies of pesticides have also yielded mixed results. A 1996 study by Aschengrau et al. in the American Journal of Public Health found an elevated risk for breast cancer among women living near cranberry bogs on Cape Cod. Yet, numerous studies have failed to show an association between blood pesticide levels measured near the time of diagnosis and breast cancer. However, it is unclear how well such blood levels correlate with exposure, because individual differences in metabolism and factors like weight gain and loss, lactation, and recent dietary pesticide exposures result in measurements that may not represent original exposure levels, particularly for exposures that occurred long ago.

MISSING INFORMATION HAMPERS STUDY

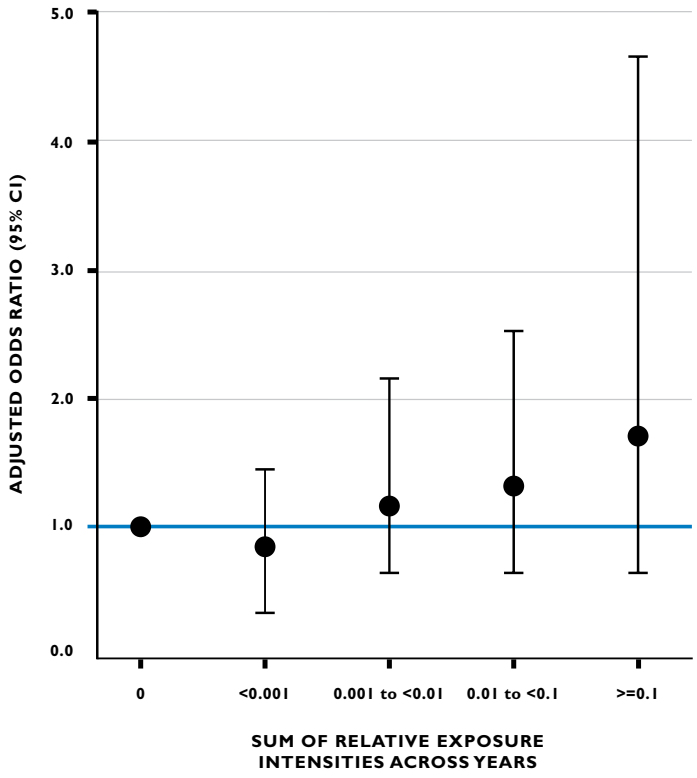
The full potential of exposure assessment using GIS was not realized because of limitations in the data. A particularly significant problem was missing information about historical town and private pesticide use on the Cape, exposures during years when women lived off Cape Cod, and address locations before universal use of street numbers. Unmapped pesticide use is known to have occurred, so exposure is generally underestimated.

The Cape Cod study probably represents the most comprehensive evaluation of historical agricultural pesticide applications and breast cancer risk conducted to date, and it illustrates the complexity of constructing these kinds of risk indicators. Through GIS, the Cape Cod study was able to estimate the relative intensity of pesticide exposure associated with residences of a > 40-year time span.

Peggy Reynolds et al. in Environmental Health Perspectives, August 2005

Reynolds P, Hurley SE, Gunier RB, Yerabati S, Quach T, Hertz A. 2005. Residential proximity to agricultural pesticide use and incidence of breast cancer in California, 1988-1997. Environ Health Perspect 113(8):993-1000.

LIVING NEAR CRANBERRY BOGS MAY BE WEAKLY ASSOCIATED WITH HIGHER BREAST CANCER RISK (1948 TO THE MID 1970s)



This graph shows a possible increased breast cancer risk associated with living near cranberry bogs from 1948 to the mid 1970s, though the association is not statistically significant.

SPATIAL PROXIMITY TOOL
NEW TOOLS RECONSTRUCT HISTORICAL PESTICIDE EXPOSURES FOR EACH WOMAN

Winner of the New Technology Award of the Environmental Business Council of New England, the Spatial Proximity Tool assesses a woman's cumulative historical exposures to pesticides at each address for each year of the study. The tool incorporates factors such as distance to spray areas, wind direction, and environmental features, such as forest vegetation, that reduce pesticide drift. In addition to assessing exposures that occur at the time of the pesticide application, we were able to account for ongoing exposures from chemicals that breakdown slowly in the in the environment.

Wastewater and run-off from developed land carry pollutants that are important targets for breast cancer studies. Cape Cod water is especially susceptible to this type of contamination because 85 percent of Cape residents use septic systems and the Cape's sandy soil allows wastewater and run-off to leach into the aquifer, making drinking water a potential source of exposure.

Using new methods to assess contamination, we tested wastewater, groundwater, and private well water for endocrine disrupting compounds (EDCs) and total estrogenic activity. We worked with researchers at Tufts University School of Medicine to apply the E-SCREEN bioassay to these water samples to determine if they, like estrogen, make breast cancer cells grow.

In addition, to investigate whether contaminated drinking water is linked to breast cancer, we needed indicators to assess exposure over many years. Because EDCs are not routinely measured in drinking water, we used nitrate levels in public supply wells (an indicator of wastewater impact) and the extent of developed land in drinking water recharge zones.

In a previous study of women who lived in towns where homes were accidentally exposed to perchloroethylene (PCE) from water distribution pipes, Dr. Ann Aschengrau and her colleagues at Boston University reported a small to moderate increased risk of breast cancer in women with the highest PCE exposure levels (Aschengrau et al., 2002; Vieira et al., 2005).

DRINKING WATER IS A PATHWAY OF EXPOSURE TO ENDOCRINE DISRUPTING COMPOUNDS

In 1998, Cape Cod Study research first confirmed that drinking water is a pathway of exposure to EDCs. We found EDCs in Cape Cod septage at the highest levels that have been reported in wastewater and substantial concentrations in groundwater contaminated by wastewater. We found low levels in six of 28 private drinking water wells. Our tests in public supply wells did not detect these chemicals, but the results were hampered by higher detection limits for these samples. We are the first team to measure estrogenic activity in groundwater.

We have since found that EDCs are discharged from septic systems to groundwater at substantial concentrations and are relatively persistent and mobile in the aquifer. We have detected estrogen (excreted in urine), alkylphenols (estrogenic, from detergents), fluorescent whitening agents (also from detergents), caffeine, and a variety of other chemicals in sewage-impacted groundwater. Groundwater is the source of nearly all of Cape Cod's drinking water and most supplies show some wastewater impact. Septic systems were designed to prevent bacterial contamination of neighboring water supplies and do not appear to be effective at removing these types of contaminants from wastewater.

NITRATE LEVELS IN DRINKING WATER ARE INCREASING, BUT FEDERAL STANDARDS MET

Although we found evidence of increasing impacts of wastewater on drinking water, we found no association between breast cancer and average annual nitrate levels.

We found average levels of nitrate in public drinking water were

- More than 15 times higher than the natural background level (0.05 mg/l), and
- More than double the impact in 1972 when routine nitrate monitoring began.

The study's painstaking well-by-well analysis revealed that some districts are supplied by wells with little or no nitrate impact. Although nitrate levels in the other Cape Cod districts comply with federal drinking water standards, they indicate increasing wastewater impacts on the water supply.

RESIDENTIAL DEVELOPMENT SPREADS ON LAND BUFFERING WELLS

Using geographic information system technology, we found the greatest change in land use feeding recharge into wells was from residential development, which impacts groundwater and drinking water via wastewater from septic systems.

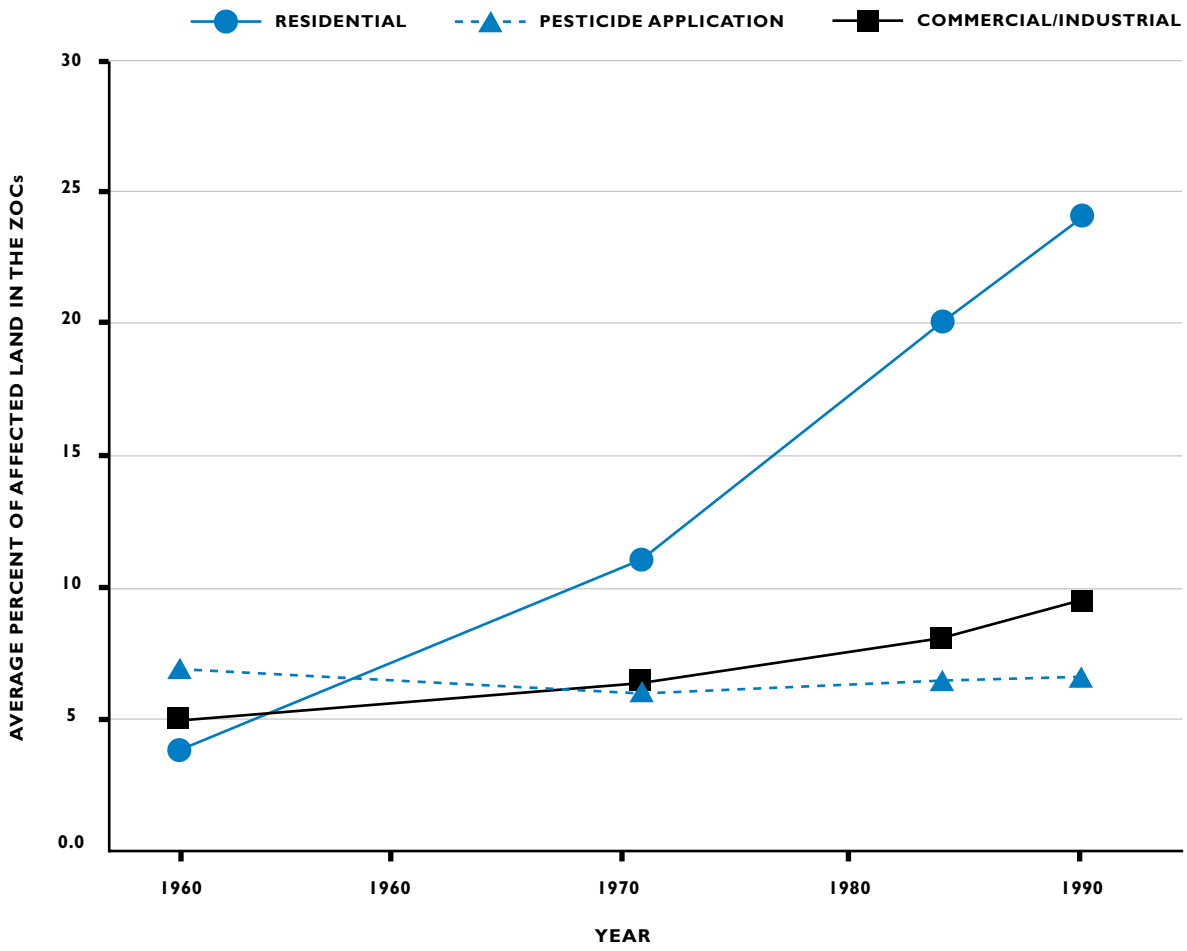
- The median percentage of residential land increased more than 10-fold from two percent in 1950 to 23 percent in 1990, with a maximum of 80 percent residential land in one recharge zone.
- Commercial development also increased with a maximum 69 percent in 1951 to 82 percent in 1984 and 1990.

These findings may encourage communities to consider more restrictive land use policies to protect their public and private drinking water supply wells. They may also consider replacing onsite septic wastewater treatment systems with improved onsite technologies or centralized wastewater treatment plants, at least in densely populated areas that rely on shallow groundwater as a drinking water source.

The Cape Study shows that pollutants, especially endocrine disrupting compounds, can contaminate our drinking water. We are increasingly finding pollutants in our bodies and the bodies of our unborn children. We need to protect this vulnerable resource and ensure our water remains safe to drink.

Lee Ketelsen,
New England Director,
Clean Water Action and Alliance for a Healthy Tomorrow

LAND USES IN ZONES OF CONTRIBUTION (ZOCS) TO PUBLIC SUPPLY WELLS



Using data in the GIS, we conducted a well-by-well analysis of land use in the recharge zones for the approximately 145 groundwater wells and one surface water source serving Cape Cod residents. We measured land use falling into three broad categories: residential development; routine pesticide applications; and, industrial, commercial, waste disposal, military activities, cemeteries, and transportation features.

STUDY LIMITATIONS MAY OBSCURE LINKS

This study allowed us to take into account known and suspected breast cancer risk factors and improved on previous breast cancer and drinking water studies. However, a number of factors limit our confidence in the results. The lack of association with breast cancer may mean that drinking water contamination at the level found on Cape Cod is not associated with breast cancer risk, or it may mean that our data were inadequate to evaluate this question the right way. For example, although nitrate is an established marker for wastewater contamination on the Cape, we do not know how close a proxy it is for EDCs specifically. In addition, we were unable to assess effects of early life exposure, exposure of longer duration, exposure at higher concentrations, and exposures in individual homes versus the water district average.

The Cape Cod Breast Cancer and Environment Study delved deeply into the role the environment may play in elevated breast cancer in a specific geographic region, Cape Cod, Massachusetts. The research included an epidemiologic study of 2,171 women, creation of a geographic information system to analyze historical environmental data for locations where the women lived, and an environmental and biological sampling program that included testing air, dust, and women's urine from 120 households and groundwater and drinking water for endocrine disrupting compounds (EDCs) and estrogenic activity.

Although we found no smoking gun that could explain the elevated incidence of breast cancer on Cape Cod, the study contributed important "firsts" that have significantly advanced our understanding of the complex relationship between cancer and environmental exposures. It also identified precautionary steps the Cape can take now to protect its future.

CAPE STUDY CHARTS NEW TERRITORY

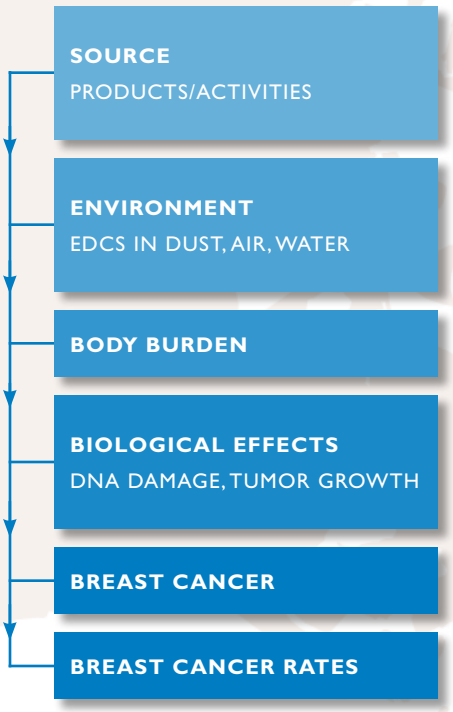
The Cape Study was the first to

- Develop tools to measure estrogenic activity in groundwater, in collaboration with Tufts University researchers,
- Test groundwater for a range of EDCs from consumer products,
- Build a sophisticated GIS for use in a breast cancer study, and
- Measure EDCs in homes more comprehensively than ever before. This is especially important since women spend a large percentage of time indoors.

STUDY FINDINGS UNDERSCORE NEED FOR LONG-TERM PROTECTION OF THE AQUIFER

The study also highlighted areas of vulnerability in the Cape's environment, specifically the aquifer, to residential and commercial development. This information on the effect of residential and commercial development on water quality can be used to help preserve the Cape's natural resources and protect the health of its residents. Additional steps to preserve the aquifer might entail developing new septic system technologies, curtailing development in the recharge areas for drinking water wells, installing sewer systems and water treatment facilities in some areas, and changing product use since waste is disposed of in septic systems.

LINKS BETWEEN ENVIRONMENT AND HEALTH



Considerable resources are spent each year to encourage women to make changes in their personal lives that might reduce the risk of breast cancer, but many factors that contribute to the disease lie far beyond a woman's personal control and can only be addressed by a revolution in thinking on the parts of government and the private sector.

Jeanne Rizzo
Executive Director,
Breast Cancer Fund

KEY FINDINGS FROM THE CAPE STUDY

Epidemiologic Study of 2,171 Women
Results strengthen the case that one or more regional—perhaps environmental—factors may play a role in higher breast cancer incidence on Cape Cod, given that established risk factors are not the explanation. Three different data sources provide evidence that the elevated incidence of breast cancer on the Cape is not explained by an older population, in-migration, mammography use, or established breast cancer risk factors. The study revealed a statistically significant trend toward higher breast cancer risk for women who lived longer on Cape Cod compared to new arrivals.

Sampling Program: Household Environmental Study
In sampling air, dust, and women's urine from 120 households, we found that chemicals are surprisingly persistent indoors. The most abundant chemicals we detected were from plastics, detergents, and personal care products. These are the first reported measurements in indoor environments for over 30 of the compounds. We also detected many pesticides. Among the persistent chemicals we detected were chemicals long since banned that were used legally in the past. These multi-year, ongoing exposures have created health risks that are hard to identify and harder still to eliminate. Our work identifying the types of chemicals to which women are exposed at home was an essential step. Our future focus includes identifying the sources of these chemicals, collecting comparison data in other geographic areas, and testing steps that can be taken to reduce exposures. Our results sound a caution about putting chemicals into use before their health and environmental effects have been evaluated.

Geographic Information System: To Assess Relationships between Wide-area Pesticide Use and Disease
Using the GIS to assess Cape Cod pesticide exposures for the women in the study, we found no consistent or clear association between breast cancer and wide-area pesticide applications for tree pests, mosquito control on wetlands, cranberry bogs, other agriculture, golf courses, and rights-of-way. We found weak evidence of a possible link between some pesticides and breast cancer during certain time periods. Breast cancer risk was approximately 20 to 80 percent higher for women who lived in or near areas treated for tree pests in 1948-1995, near cranberry bogs in 1948 to the mid 1970s, and near agricultural land since the mid 1970s. Although these findings are intriguing, most failed to reach traditionally accepted levels of statistical stability. A previous study by Dr. Ann Aschengrau and her colleagues at Boston University also found an elevated risk for breast cancer among women living near cranberry bogs on Cape Cod.

Sampling Program: Drinking Water

We measured low levels of EDCs in drinking water, providing evidence that drinking water is a pathway of exposure to these compounds. However, it is still unknown how widespread the contamination is, what the most prevalent contaminants are, or what typical levels of exposure are.

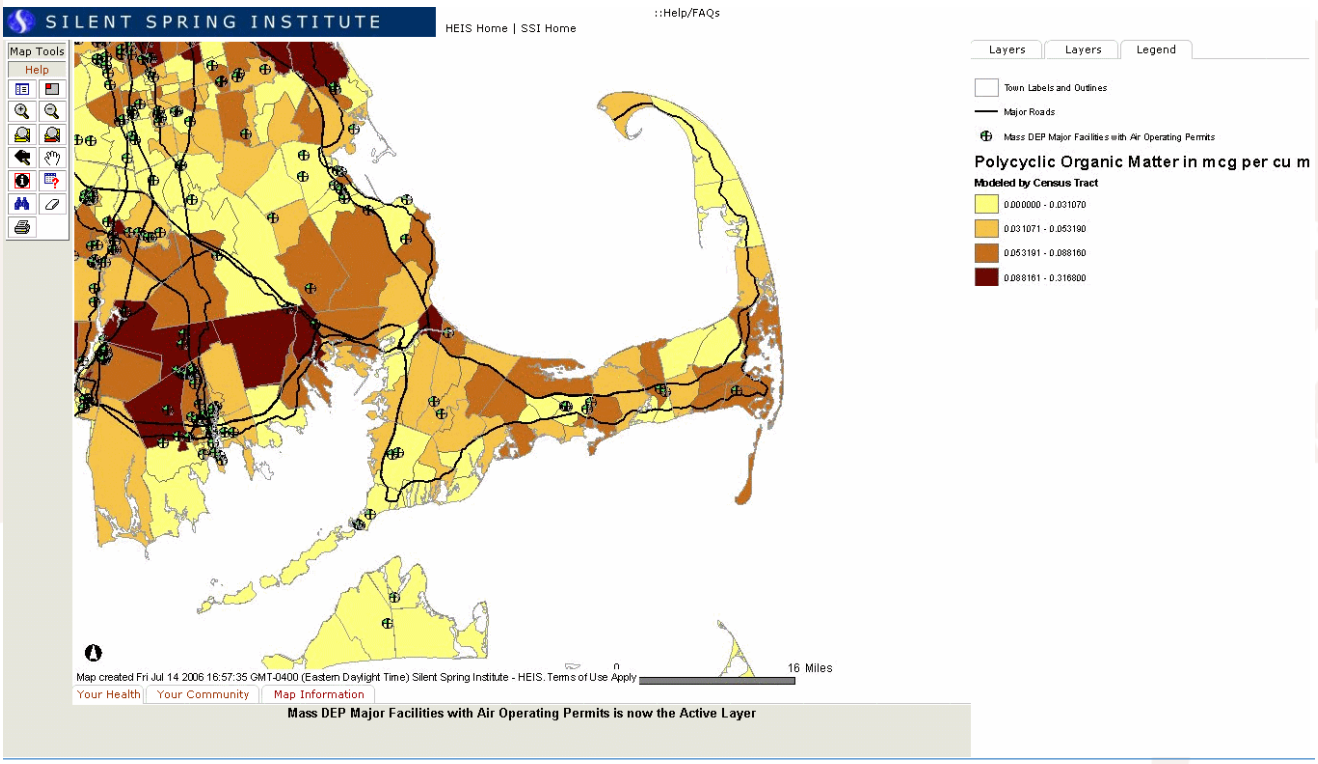
Historical Drinking Water Quality

We found evidence of increasing impacts of wastewater on public drinking water in many Cape Cod supplies since 1972. However, we found no association between breast cancer and measurements of nitrate, a wastewater indicator, in public drinking water supplies. These negative results are difficult to interpret. They may mean that drinking water contamination at the level found on Cape Cod is not associated with breast cancer risk. However, they may also mean that nitrates, an established marker for wastewater contamination on the Cape, may not be appropriate for tracking EDCs specifically.

I think the fact that breast cancer incidence is on the rise and most cases are not genetic indicates it has to be something else. We believe there are environmental causes to breast cancer — and we want to find the link.

Joan Sheehan, Co-President, Capital Region Action Against Breast Cancer! (CRAAB!)

MASSACHUSETTS HEALTH AND ENVIRONMENT INFORMATION SYSTEM



The Massachusetts Health and Environment Information System (MassHEIS) is an interactive web mapping service that brings together health, environmental, and demographic data. This mapping tool gives greater access to available data and empowers individuals to investigate links between the environment and health. Silent Spring Institute's work to create and maintain the MassHEIS is supported through a grant by the National Library of Medicine.

To use this mapping tool go to http://library.silentspring.org/heis/quickstart.asp. The above map, created using data in the MassHEIS, shows the spatial relationship between facilities with air operating permits and modeled polycyclic organic matter levels in air.

Silent Spring Institute Researcher Allan Just is shown training researchers from Citizen's for a Better Environment (CBE) on the use of air sampling equipment.

We will compare the data CBE collects from homes in Richmond, CA, with data from Cape Cod homes. Using the methods we developed to measure endocrine disrupting compounds in air, we have found that these compounds, including many that were banned years ago, appear to break down surprisingly slowly indoors.

Over the past decade, we have seen substantial growth in research into the links between the environment and women's health. With results from the Cape and other studies now available, we have expanded our knowledge and identified the most productive directions for continuing analysis. We believe future work should focus on

- Human studies of many more of the chemicals identified as mammary carcinogens and endocrine disruptors in laboratory research,
- Women with high exposures,
- Exposures at different times in the life course,
- Health effects that signal nascent biological damage from environmental exposures,
- How genes affect the way our body processes pollutants, and
- Risks from exposures to pollutants in the home.

NEW RESEARCH BUILDS ON CAPE STUDY FINDINGS

To design successful studies, we need to know what to look for and how to measure it. Our State of the Science Review is identifying additional chemicals to target.

State of the Science Review

In collaboration with researchers at Harvard University, Roswell Park Cancer Institute, and the University of Southern California, we are reviewing the scientific literature on possible environmental factors in breast cancer. The factors we are reviewing include diet, physical activity, body size, environmental pollutants, gene-environment interactions, medicines, workplace chemicals, smoking, stress, light at night, radiation, and early life exposure. As part of this initiative, we have developed the most comprehensive assessment to date of studies of mammary carcinogens. A database of results will be available to researchers and the public to target the most important compounds for future study. This project is supported by the Susan G. Komen Breast Cancer Foundation.

In three new exposure studies we are analyzing environmental samples, including air, dust, and groundwater, for endocrine disrupting compounds (EDCs) and mammary carcinogens. In addition, we will be exploring potential sources and pathways of exposure to these compounds.

Linking Breast Cancer Advocacy and Environmental Justice

In collaboration with Communities for a Better Environment, in Oakland, CA, and Brown University we will be comparing household samples from Cape Cod homes with samples from homes in Richmond, California. We will also be investigating how outdoor pollution from an oil refinery and transportation corridor affects indoor exposures in nearby homes. In both Massachusetts and California, we are investigating the best ways to report environmental monitoring data to individuals and communities. This project is funded by the National Institute of Environmental Health Sciences.

Household Exposure: Identifying Exposure Pathways for Phthalates, Pesticides, and Other EDCs
We will be analyzing indoor air and dust concentrations as predictors of urinary levels of phthalates and pesticides in order to better understand sources and pathways of exposure. This work is supported by Hurricane Voices Breast Cancer Foundation, the National Cancer Institute, and the US Centers for Disease Control and Prevention.

Septic System Impacts to Groundwater Quality on Cape Cod
We will be continuing to measure degradation of groundwater quality from wastewater leaching from septic systems into the aquifer. We are quantifying the levels of hormonally active compounds introduced into groundwater from septic systems and studying how these compounds behave as they travel through the aquifer. Babylon Breast Cancer Coalition and the Massachusetts Environmental Trust are supporting this initiative.

Since we don't have the luxury of waiting for all of the data to inform how to lead our lives on a daily basis, we are undertaking studies to evaluate precautionary steps we can take now to reduce exposures. In conjunction with this, we are developing methods for communicating study results in a way that helps individuals and communities take action to protect health.

Green Homes: Assessing Whether Product Changes Can Reduce Household Exposures
We are recruiting women both on and off the Cape to test exposure reduction strategies. The women in the study will adopt new cleaning products, eliminate products with fragrance, and take other steps to minimize potential sources of exposure in their homes. We will sample air and dust before and after the intervention to evaluate the effectiveness of these changes at lowering household exposures. This work is supported by Hurricane Voices Breast Cancer Foundation and the Susan S. Bailis Breast Cancer Research Fund of Silent Spring Institute.

The "Research Right-to-Know": Ethics and Values in Communicating Environmental Health Study Results to Individuals and Communities
In collaboration with Brown University and Communities for a Better Environment, in Oakland, CA, we will examine values and ethical issues in reporting environmental health study results to study participants, as well as to communities. This project is supported by the National Science Foundation.

These new avenues of investigation hold the promise of bringing us ever closer to our ultimate goal of finding preventable causes of breast cancer. For this work, we draw energy and inspiration from the women of Cape Cod and our daughters and granddaughters everywhere.

As long as the federal government and the cancer industry encourage women to believe that prevention of breast cancer comes in pills, we will never get to the end of this. Women have been guinea pigs for far too long.

Barbara Brenner, Executive Director, Breast Cancer Action, In "Breast Cancer Activism" by Sabrina McCormick, Ms. Magazine, summer 2002

STEPS YOU CAN TAKE TO REDUCE CHEMICAL EXPOSURES

While more studies need to be done to fully tease out the relationship between chemicals and health, we can take precautionary steps now to reduce exposure to suspect chemicals that are found in a multitude of everyday products.

10 SUGGESTIONS TO REDUCE EXPOSURE TO SUSPECT CHEMICALS

1. **Use glass containers or microwave safe ceramics in the microwave and encourage your family and friends to do the same.**
   Some plastic containers contain chemicals that mimic or disrupt hormones. These chemicals can leach into food when they are heated. When purchasing a ceramic container, check the label to confirm that use in the microwave is approved or ask a salesperson.

2. **Ask for dry cleaning services that do not use "PERC" or ask for "wet cleaning."**
   The familiar smell of dry cleaning comes from residues of perchloroethylene (PERC). Solvents, such as PERC, are under study for breast cancer and are associated with other cancers. If you use traditional dry cleaning, open the plastic bags on your clothing and air them out outdoors before putting them in a closet.

3. **Take time to read labels and avoid "phthalates" and "fragrance" in products.**
   Phthalates are endocrine disrupting compounds that have been associated with cancer, impaired fertility, and male birth defects. They are found in hundreds of products including shampoo, lotion, perfume, cosmetics, new cars, and toys and other products made from vinyl and plastics. The US Centers for Disease Control and Prevention monitors environmental pollutants, including phthalates, to better understand the relationship between exposures and health. The most common phthalates are dibutyl phthalate (DBP), diethyl phthalate (DEP), and diethylhexyl phthalate (DEHP), and phthalates are often an ingredient in "fragrance." Look for labels that say "phthalate-free" and don't hesitate to ask your favorite retailer or manufacturer if products are phthalate-free. Consumer questions help to bring about change.

4. **Look for fuel-efficient, electric, or manual vehicles and appliances.**
   Car, pleasure boat, jet ski, lawn mower, leaf blower, and snow blower exhaust releases mammary carcinogens into the air. Using less polluting or manual alternatives will lower exposures and improve air quality.

You can find additional tips to make your home safer at:

- **www.epa.gov/iaq/pubs/insidest.html**
- **www.checnet.org/healthehouse**
- **www.toxtown.nlm.nih.gov**
- **www.safecosmetics.org**

For information on name brand products and company policies on chemical use, consult The Safer Products Project at www.safer-products.org. For information about safe household products, including baby accessories and toys, visit www.healthehouse.org.

You can find information about environmental health policies and how to get involved at: Massachusetts Breast Cancer Coalition www.mbcc.org and the Collaborative on Health and the Environment's website http://www.healthandenvironment.org/.

5. **Reduce or eliminate pesticides.**
   Choose organic products for landscaping, and encourage neighbors to do the same; purchase organic foods when possible and encourage stores you patronize to expand their selection of organic foods. Many pesticides are endocrine disruptors. Pesticides are also known to affect brain development and neurological function. Using organic products reduces your exposure to pesticides and protects your family, landscapers, farmers, water supplies, and wildlife.

6. **Encourage your community to adopt policies of using natural/non-toxic solvents in public buildings, especially schools, and using organic practices in the care of green spaces.**
   Using safer cleaners and eliminating pesticides on a community-wide basis will reduce exposure to compounds that mimic estrogen or otherwise disrupt hormones.

7. **Minimize "char" on grilled foods, by reducing the heat level and/or using marinades.**
   "Char" contains PAHs — polycyclic aromatic hydrocarbons — that are known to cause mammary tumors in animals. In the Long Island Breast Cancer Study, women who had more DNA damage from PAHs had higher breast cancer risk.

8. **Choose a HEPA vacuum to reduce the chemicals in your carpets and indoor air.**
   Carpets can harbor pesticides, mold and allergens, flame retardants, and other chemicals. Vacuums with strong suction, a brush on/off switch, a multi-layered bag for dust collection, and a high efficiency particulate air (HEPA) filter are considered the best to avoid recycling dust back into the air. Consumerreports.org rates the available brands.

9. **Shop for electronics and furniture made without the flame retardant PBDEs.**
   PBDEs (polybrominated diphenyl ethers) are commercially produced flame retardants used in a multitude of products — and they are endocrine disruptors that affect thyroid hormones. PBDEs are added to polyurethane foam. When possible, choose carpet pads, bedding, cushions and upholstered furniture made from natural fibers including wool, cotton, and hemp. These are naturally flame retardant.

10. **Improve indoor air quality by opening windows and using glues, paints, solvents, fingernail polish, and, if you smoke, tobacco products, outside or in a well-ventilated area.**
    There are many sources of pollutants in our homes: cleaning products, furniture, carpets, products used for home improvement projects and hobbies, personal care products, radon, asbestos, and pesticides. Providing adequate ventilation helps dissipate these pollutant levels.

"We are just beginning to understand the role of hormonal pollutants in breast cancer and other diseases, and the Silent Spring Institute study provides crucial information that we can now use to call on government and manufacturers to regulate and reformulate products currently in everyday use. We are all unknowingly bringing estrogen mimics home from the grocery and drug store. This study shows that industry's reassurances that their products won't lead to chemical exposures just aren't true."

Janis Lippman, President, Massachusetts Breast Cancer Coalition

Aschengrau, A., P.F. Coogan, M. Quinn, L. Cashins. 1998. Occupational exposure to estrogenic chemicals and the occurrence of breast cancer: An exploratory analysis. American Journal of Industrial Medicine 34(1):6-14.

Beck, B.D., T.M. Slayton, E.J. Calabrese, L. Baldwin, R.A. Rudel. 2001. The use of toxicology in the regulatory process. In Principles and Methods of Toxicology, ed. A. Wallace Hayes. Philadelphia, PA: Taylor & Francis.

Brody, J.G., J. Tickner, R.A. Rudel. 2005. Community-initiated breast cancer and environment studies and the Precautionary Principle. Environmental Health Perspectives 113(8):920-925.

Brody, J.G., A. Aschengrau, W. McKelvey, R.A. Rudel, C.H. Swartz, T. Kennedy. 2004. Breast cancer risk and historical exposure to pesticides from wide-area applications assessed using GIS. Environmental Health Perspectives 112(8):889-897

Brody, J.G., R.A. Rudel. 2003. Environmental pollutants and breast cancer. Environmental Health Perspectives 111(8): 1007-1019.

Brody, J.G., D.J. Vorhees, S.J. Melly, S.R. Swedis, P.J. Drivas, R.A. Rudel. 2002. Using GIS and historical records to reconstruct residential exposure to large-scale pesticide application. Journal of Exposure Analysis and Environmental Epidemiology 12:64-80.

Brody, J.G. 2000. Environmental Issues. In Handbook of Community Psychology, eds. Julian Rappaport and Edward Seidman. New York: Kluwer Academic/Plenum.

Brody, J.G., R.A. Rudel, S.J. Melly, N.I. Maxwell. 1998. Endocrine disruptors and breast cancer. Forum for Applied Research and Public Policy 13(3):24-31.

Brody, J.G., R.A. Rudel, N.I. Maxwell, S.R. Swedis. 1996. Mapping out a search for environmental causes of breast cancer. Public Health Reports 3(6):495-507.

Coogan, P.F., A. Aschengrau. 1999. Occupational physical activity and breast cancer risk in the Upper Cape Cod Cancer Incidence Study. American Journal of Industrial Medicine 36(2):279-285.

Coogan, P.F., A. Aschengrau. 1998. Exposure to power frequency magnetic fields and risk of breast cancer in the Upper Cape Cod Cancer Incidence Study. Archives of Environmental Health 53(5):359-367.

Gray, SM. 2003. Looking for Information: A Survey of Research on Information Seeking, Needs, and Behavior [Book Review]. Journal of the Medical Library Association 91(2): 259-260.

Kennedy, T., J.G. Brody. 2003. Mapping the environment and breast cancer on Cape Cod, MA. The Ribbon, Newsletter of the Cornell University Program on Breast Cancer and Environmental Risk Factors in the New York State (BCERF) 8(1): 4-7.

Kriebel, D., J. Tickner, P. Epstein, J. Lemons, R. Levins, E.L. Loechler, M. Quinn, R.A. Rudel, T. Schettler, M. Stoto. 2001. The Precautionary Principle in environmental science. Environmental Health Perspectives 109(9):871-875.

McCormick, S., J.G. Brody, P. Brown, R. Polk. 2004. Public involvement in breast cancer research: An analysis and model for future research. International Journal of Health Services 34(4): 625-646.

McKelvey, W., J.G. Brody, A. Aschengrau, C.H. Swartz. 2004. Association between residence on Cape Cod, Massachusetts, and breast cancer. Annals of Epidemiology 14(2):89-94.

Ozonoff, D.A., T. Webster. 1997. The Lattice Diagram and 2 x 2 Tables. Toxicology and Industrial Health 13(2-3):339-355.

Paulu, C., A. Aschengrau, D. Ozonoff. 2002. Exploring associations between residential location and breast cancer incidence in a case-control study. Environmental Health Perspectives 110(5):471-478.

Rudel, R.A., E. Newton. 2004. Letter to the Editor: Exposure assessment for decabromodiphenyl ether (decaBDE) is likely to underestimate general US population exposure. Journal of Children's Health 2(2): 171-173.

Rudel, R.A., D.E. Camann, J.D. Spengler, L.R. Korn, J.G. Brody. 2003. Phthalates, alkylphenols, pesticides, polybrominated diphenyl ethers, and other endocrine-disrupting compounds in indoor air and dust. Environmental Science & Technology 37(20): 4543-4553.

Rudel, R.A., P. Geno, G. Sun, A. Yau, J. Spengler, J. Vallarino, J.G. Brody. 2001. Identification of selected hormonally active agents and animal mammary carcinogens in commercial and residential air and dust samples. Journal of Air and Waste Management Association 51:499-513.

Rudel, R.A., J.G. Brody, J.D. Spengler. 2001. Identification of selected hormonally active agents and animal mammary carcinogens in commercial and residential air and dust samples [response]. Journal of Air and Waste Management Association 51:1388-1390.

Rudel, R.A. 2000. Polycyclic aromatic hydrocarbons, phthalates, and phenols. In Indoor Air Quality Handbook, eds. J. Spengler, J. Samet, and J. McCarthy. New York: McGraw-Hill.

Rudel, R.A., P. Geno, S.J. Melly, G. Sun, and J.G. Brody. 1998. Identification of alkylphenols and other estrogenic phenolic compounds in wastewater, septage, and groundwater on Cape Cod, Massachusetts. Environmental Science & Technology 32(7):861-869.

Rudel R.A. 1997. Predicting health effects of exposures to compounds with estrogenic activity: Methodological issues. Environmental Health Perspectives 105(suppl 3):655-663.

Swartz, C.H., R.A. Rudel, J.R. Kachajian, J.G. Brody. 2003. Historical reconstruction of wastewater and land use impacts to groundwater used for public drinking water: Exposure assessment using chemical data and GIS. Journal of Exposure Analysis and Environmental Epidemiology 13(5): 403-416.

Swartz C.H., S. Reddy, M.J. Benotti, H. Yin, L.B. Barber, B.J. Brownawell, and R.A. Rudel. 2006. Steroid estrogens, nonylphenol ethoxylate metabolites, and other wastewater contaminants in groundwater affected by a residential septic system on Cape Cod, MA. Environmental Science and Technology 40(16):4894-4902.

Aschengrau, A., P.F. Coogan, M. Quinn, L.J. Cashins. 1998. Occupational exposure to estrogenic chemicals and the occurrence of breast cancer: An exploratory analysis. American Journal of Industrial Medicine 34(1):6-14.

We conducted a population-based case-control study to describe the relationship between occupational exposure to estrogenic chemicals and the occurrence of breast cancer in Cape Cod, Massachusetts.

METHODS Incident cases of breast cancer (n =261) diagnosed from 1983 through 1986 and controls (n =753) were interviewed to gather information on breast cancer risk factors and all full-time jobs held since age 18. Blinded exposure assessments were employed using the data from the National Institute for Occupational Safety and Health (NIOSH) National Occupational Exposure Survey, chemical production and usage information, and the expert judgment of a certified industrial hygienist.

RESULTS Overall, 29.5% of cases and 32.5% of controls had probable occupational exposure to one or more xenoestrogens. Probable exposure to nonylphenol (21.5% of cases, 21.4% of controls), butyl benzyl phthalate (10.0% of cases, 13.2% of controls), BHA (7.3% of cases, 9.6 of controls), bisphenol A (9.6% of cases, 11.6% of controls), and 4-tert-butylphenol (2.7% of cases and 5.3% of controls) were relatively common, while probable exposure to the other xenoestrogens was rare. Only PCBs and 4-octylphenol were associated with moderate increases in the odds of breast cancer (PCBs: 5 exposed cases and 6 exposed controls, adjusted odds ratio: 3.2, 95% CI = 0.8-12.2, and 4-octylphenol: 6 exposed cases and 5 exposed controls, adjusted odds ratio: 2.9, 95% Cl = 0.8-10.8).

CONCLUSIONS Additional research is needed to corroborate these findings.

Brody, J.G., J. Tickner, R.A. Rudel. 2005 Community-initiated breast cancer and environment studies and the Precautionary Principle. Environmental Health Perspectives, 113(8): 920-925.

The precautionary principle implies the need for research paradigms that contribute to "strength of the evidence" assessments of the plausibility of health effects when scientific uncertainty is likely to persist and prevention is the underlying goal. Previous discussions of science that inform precautionary decision making are augmented by examining three activist-initiated breast cancer and environment studies--the Long Island, New York, and Cape Cod, Massachusetts, studies and the National Institute of Environmental Health Sciences breast cancer and environment centers. These studies show how the choice of research questions affects the potential of results to inform action. They illustrate a spectrum of public involvement, population- and individual-level epidemiologic study designs, and the crucial importance of developing and applying new exposure assessment methods. The exposure studies are key because they are critical in assessing plausibility (without exposure to a causal agent, there is no health effect), are prerequisite to health studies, and identify preventable exposures that could be reduced by precautionary policies, even in the absence of strong evidence of harm. The breast cancer studies have contributed to environmental and biological sampling programs for endocrine-disrupting compounds in drinking water and household air and dust and the application of geographic information systems for surveillance and historical exposure assessment. They leave unanswered questions about when to invest in large epidemiologic studies, when negative results are sufficient, and how to pursue ambiguous positive results in further research and policy.

Brody, J.G., A. Aschengrau, W. McKelvey, R.A. Rudel, C.H. Swartz, T. Kennedy. 2004. Breast cancer risk and historical exposure to pesticides from wide-area applications assessed using GIS. Environmental Health Perspectives 112(8):889-897.

Pesticides are of interest in etiologic studies of breast cancer because many mimic estrogen, a known breast cancer risk factor, or cause mammary tumors in animals, but most previous studies have been limited by using one-time tissue measurements of residues of only a few pesticides long banned in the United States. As an alternative method to assess historical exposures to banned and current-use pesticides, we used geographic information system (GIS) technology in a population-based case-control study of 1,165 women residing in Cape Cod, Massachusetts, who were diagnosed with breast cancer in 1988-1995 and 1,006 controls. We assessed exposures dating back to 1948 (when DDT was first used there) from pesticides applied for tree pests (e.g., gypsy moths), cranberry bogs, other agriculture, and mosquito control on wetlands. We found no overall pattern of association between pesticide use and breast cancer. We found modest increases in risk associated with aerial application of persistent pesticides on cranberry bogs and less persistent pesticides applied for tree pests or agriculture. Adjusted odds ratios for these exposures were 1.8 or lower, and, with a few exceptions, confidence intervals did not exclude the null. The study is limited by uncertainty about locations of home addresses (particularly before 1980) and unrecorded tree pest and mosquito control events as well as lack of information about exposures during years when women in the study lived off Cape Cod and about women with potentially important early life exposures on Cape Cod who were not included because they moved away.

Brody, J.G., R.A. Rudel. 2003. Environmental pollutants and breast cancer. Environmental Health Perspectives 111(8): 1007-1019.

Breast cancer is the most common cancer in women and the leading cause of cancer death among women 35-54 years of age. Rising incidence, increased risk among migrants to higher risk regions, and poor prediction of individual risk have prompted a search for additional modifiable factors. Risk factors for breast cancer include reproductive characteristics associated with estrogen and other hormones, pharmaceutical hormones, and activities such as alcohol use and lack of exercise that affect hormone levels. As a result, investigation of hormonally active compounds in commercial products and pollution is a priority. Compounds that cause mammary tumors in animals are additional priorities. Animal models provide insight into possible mechanisms for effects of environmental pollutants on breast cancer and identify chemical exposures to target in epidemiologic studies. Although few epidemiologic studies have been conducted for chemical exposures, occupational studies show associations between breast cancer and exposure to certain organic solvents and polycyclic aromatic hydrocarbons (PAHs). Population-based studies have been limited to a few organochlorine compounds and PAHs and have been mostly negative. A variety of challenges in studies of breast cancer and the environment may have contrib-

uted to negative findings. Lack of exposure assessment tools and few hypothesis-generating toxicologic studies limit the scope of epidemiologic studies. Issues of timing with respect to latency and periods of breast vulnerability, and individual differences in susceptibility pose other challenges. Substantial work is needed in exposure assessment, toxicology, and susceptibility before we can expect a pay-off from large epidemiologic studies of breast cancer and environment.

Brody, J.G., D.J. Vorhees, S.J. Melly, S.R. Swedis, P.J. Drivas, R.A. Rudel. 2002. Using GIS and historical records to reconstruct residential exposure to large-scale pesticide application. Journal of Exposure Analysis and Environmental Epidemiology 12(1):64-80.

Investigation of pesticide impacts on human health depends on good measures of exposure. Historical exposure data are needed to study health outcomes, such as cancer, that involve long latency periods, and other outcomes that are a function of the timing of exposure. Environmental or biological samples collected at the time of epidemiologic study may not represent historical exposure levels. To study the relationship between residential exposure to pesticides and breast cancer on Cape Cod, Massachusetts, historical records of pesticide use were integrated into a geographic information system (GIS) to estimate exposures from large-scale pesticide applications between 1948 and 1995. Information on pesticide use for gypsy moth and other tree/vegetative pest control, cranberry bog cultivation, other agriculture, mosquito control, recreational turf management, and rights-of-way maintenance is included in the database. Residents living within or near pesticide use areas may be exposed through inhalation due to drift and volatilization and through dermal contact and ingestion at the time of application or in later years from pesticides that deposit on soil, accumulate in crops, or migrate to groundwater. Procedures were developed to use the GIS to estimate the relative intensity of past exposures at each study subject's Cape Cod addresses over the past 40 years, taking into account local meteorological data, distance and direction from a residence to a pesticide use source area, size of the source area, application by ground-based or aerial methods, and persistent or nonpersistent character of the pesticide applied. The resulting individual-level estimates of relative exposure intensity can be used in conjunction with interview data to obtain more complete exposure assessment in an epidemiologic study. While the database can improve environmental epidemiological studies involving pesticides, it simultaneously illustrates important data gaps that cannot be filled. Studies such as this one have the potential to identify preventable causes of disease and guide public policies.

Brody, J.G., R.A. Rudel, S.J. Melly, N.I. Maxwell. 1998. Endocrine disruptors and breast cancer. Forum for Applied Research and Public Policy 13(3):24-31.

The hypothesis that endocrine disrupting chemicals affect breast cancer is a short, logical step away from what we already know about the disease. Since the eighteenth century when the Italian physician Bernardino Ramazzini observed a higher incidence among nuns, researchers have known that women's natural reproductive hormones affect risk. More recently, Devra Davis with the World Resources Institute and her colleagues published the troubling hypothesis that other estrogenic compounds — including synthetic estrogens found in commercial products and the environment, as well as natural phytoestrogens in food — might also affect breast cancer risk. This hypothesis poses a critical challenge concerning the possible human health effects of endocrine disruptors, and, at the same time, it opens the doors for new research such as the Silent Spring Institute's study of breast cancer on Cape Cod. This research offers the hope of identifying preventable causes of the disease. Each year, 180,000 women are diagnosed with breast cancer in the United States. Preventable environmental factors — even if they represent relatively small, incremental risks — translate into many saved lives.

Brody, J.G., R.A. Rudel, N.I. Maxwell, S.R. Swedis. 1996. Mapping out a search for environmental causes of breast cancer. Public Health Reports 111(6):494-507.

Geographic patterns and time trends for breast cancer suggest there are preventable causes that may include environmental factors. This article describes the development of new methods used in the Cape Cod Breast Cancer and Environment Study to investigate whether synthetic chemicals in the environment contribute to breast cancer risk. Our hypothesis comes from earlier research showing many of the individual risk factors for breast cancer—for example, menstrual and reproductive history—are linked to lifetime exposure to hormones, particularly estrogen. Scientists hypothesize that synthetic chemicals that mimic or otherwise interfere with hormones may also affect breast cancer. These chemicals, called endocrine disrupters, are widely distributed in the environment because of their use in some pesticides, detergents, and plastics. The Cape Cod Study uses computer mapping techniques to analyze the relationships between breast cancer incidence and geographic areas of likely exposure to endocrine disrupters through drinking water or pesticide applications. The technique incorporates historical as well as spatial data, an important strength because of cancer's latency period. It also incorporates brand-new data from chemical analyses and the E-SCREEN bioassay for estrogenic activity. Samples of drinking water and wastewater are being tested to explore possible sources of exposure to endocrine disrupters. Results of this ecologic study will point the way for future researchers to incorporate suspected environmental factors along with individual factors in assessing breast cancer risk.

Coogan, P.F., A. Aschengrau. 1999. Occupational physical activity and breast cancer risk in the Upper Cape Cod Cancer Incidence Study. American Journal of Industrial Medicine 36(2):279-285.

In several epidemiological studies, breast cancer risk has been reduced among women who reported high levels of occupational or leisure-time physical activity. We used data from a population-based case control study to evaluate the effect of occupational physical activity on breast cancer risk.
METHODS Two hundred thirty-three incident cases of breast cancer and 670 controls or their next of kin were interviewed for information on breast cancer risk factors and a complete job history. Physical activity level of jobs was classified using a Department of Labor rating scheme. We calculated adjusted odds ratios for light and medium/heavy activity jobs compared to sedentary jobs.

RESULTS Odds ratios for women who held medium/heavy jobs for less than 10 years and more than ten years were, respectively, 0.7 (95% CI = 0.4, 1.3) and 1.7 (95% CI = 0.9, 3.3).
CONCLUSIONS In these data there was no evidence that holding a job of medium/heavy activity reduced breast cancer risk. The study was limited by misclassification inherent in the occupational exposure scheme and by the lack of information on leisure time physical activity. The modest risk increase for subjects holding a medium/heavy job for at least 10 years probably represents either confounding or random variation.

Coogan, P.F., A. Aschengrau. 1998. Exposure to power frequency magnetic fields and risk of breast cancer in the Upper Cape Cod Cancer Incidence Study. Archives of Environmental Health 53(5):359-367.
Investigators used a population-based case-control study to evaluate the relationship between breast cancer risk and exposure to 60-Hz magnetic fields from various sources. There was no increase in breast cancer risk associated with (a) holding a job with high (odds ratio [OR] = 1.2; 95% confidence interval [CI] 0.4, 3.4) or medium (OR = 0.9; 95% CI = 0.5, 1.7) exposure to magnetic fields; (b) living in a home heated electrically (OR = 1.0; 95 CI = 0.7, 1.4); or (c) sleeping with an electric blanket (OR = 1.0; 95 CI = 0.7, 1.4). There was a nonsignificant 50% increase in risk for subjects who lived within 152 m (500 ft) of an electricity transmission line or substation (OR = 1.5; 95% CI = 0.6, 3.3). Although limited by small numbers and exposure misclassification, the data in this study did not support the hypothesis that exposure to 60-Hz magnetic fields increases the risk of breast cancer in women.

Kriebel, D., J. Tickner, P. Epstein, J. Lemons, R. Levins, E.L. Loechler, M. Quinn, R.A. Rudel, T. Schettler, M. Stoto. 2001. The Precautionary Principle in environmental science. Environmental Health Perspectives 109(9):871-876.
Environmental scientists play a key role in society's responses to environmental problems, and many of the studies they perform are intended ultimately to affect policy. The Precautionary Principle, proposed as a new guideline in environmental decision making, has four central components: taking preventive action in the face of uncertainty; shifting the burden of proof to the proponents of an activity; exploring a wide range of alternatives to possibly harmful actions; and increasing public participation in decision making. In this paper we examine the implications of the Precautionary Principle for environmental scientists, whose work often involves studying highly complex, poorly understood systems, while at the same time facing conflicting pressures from those who seek to balance economic growth and environmental protection. In this complicated and contested terrain, it is useful to examine the methodologies of science and to consider ways that, without compromising integrity and objectivity, research can be more or less helpful to those who would act with precaution. We argue that a shift to more precautionary policies creates opportunities and challenges for scientists to think differently about the ways they conduct studies and communicate results. There is a complicated feedback relation between the discoveries of science and the setting of policy. While maintaining their objectivity and focus on understanding the world, environmental scientists should be aware of the policy uses of their work and of their social responsibility to do science that protects human health and the environment. The Precautionary Principle highlights this tight, challenging linkage between science and policy.

McCormick, S., J.G. Brody, P. Brown, R. Polk. 2004. Public involvement in breast cancer research: An analysis and model for future research. International Journal of Health Services 34(4): 625-646.
Public involvement in health program planning has been taking place for many years and has provided a precedent for the emergence of public involvement in research conducted since the early 1990s. Such involvement is now widely seen in breast cancer research, due to the large public concern and major social movement activity. This article reviews current practices and general models of public involvement in research and constructs a prototype. The authors interviewed researchers, program officers, and laypeople in order to understand the obstacles, processes, and benefits. They conclude that public involvement has major ramifications for the democratization of science and the construction of knowledge by teaching lay people about science and sensitizing researchers to concerns of the public. There is growing support on the part of scientists and government agents for public involvement.

McKelvey, W., J.G. Brody, A. Aschengrau, C.H. Swartz. 2004. Association between residence on Cape Cod, Massachusetts, and breast cancer. Annals of Epidemiology 14(2):89-94.
Massachusetts cancer registry and case-control data suggest that breast cancer incidence is elevated on Cape Cod relative to other parts of the state. We examined the association between length of residence on Cape Cod and breast cancer, since residential history could be acting as a surrogate for unidentified environmental risk factors.
METHODS We computed odds ratios (OR) and 95% confidence limits (CL) for 1121 cases occurring between 1988 and 1995 on Cape Cod and 992 controls, according to categories of residence time on Cape Cod, after adjusting for age, family history, parity and age at first live or stillbirth, education, body mass index, and breast cancer history.
RESULTS Breast cancer risk was elevated among women living on Cape Cod 5 or more years with a peak occurring in the 25 to less than 30 year category (adjusted OR=1.72; 95% CL, 1.12, 2.64). Adjusting for confounding strengthened the associations. Odds ratios did not increase monotonically over categories of longer residence.
CONCLUSIONS Our results suggest that longer residence on Cape Cod is associated with elevated breast cancer risk, however inconsistency in the pattern of association limits conclusions that might be drawn about it. Suspected environmental exposures include pesticides and drinking water contaminated by industrial, agricultural, and residential land use.

Paulu, C., A. Aschengrau, D. Ozonoff. 2002. Exploring associations between residential location and breast cancer incidence in a case-control study. Environmental Health Perspectives 110(5):471-478.
Locating geographic hotspots of cancer may lead to new casual hypotheses and ultimately to new knowledge of cancer-causing factors. The Cape Cod region of Massachusetts has experienced elevated incidence of breast cancer compared with statewide av-

erages. The origins of the excess remain largely unexplained, even after the Upper Cape Cod Cancer Incidence Study investigated numerous potential environmental exposures. Using case-control data from this study (258 cases and 686 controls), we developed an exploratory approach for measuring associations between residential location and breast cancer incidence, adjusting for individual-level risk factors. We measured crude and adjusted odds ratios over the study region using fixed-scale grids and a smoothing algorithm of overlapping circular units. Polycircular hot spot regions, derived from the peak values of the smoothed odds ratios, delineated geographic areas wherein residence was associated with 60% [odds ration (OR), 1.6; 95% confidence interval (CI), 0.8-3.2] to 210% (OR, 3.1; 95% percent CI, 1.3-7.2) increased incidence relative to the remainder of the study population. The findings suggest several directions for further research, including the identification of potential environmental exposures that may be assessed in forthcoming case-control studies.

Rudel, R.A., D.E. Camann, J.D. Spengler, L.R. Korn, J.G. Brody. 2003. Phthalates, alkylphenols, pesticides, polybrominated diphenyl ethers, and other endocrine-disrupting compounds in indoor air and dust. Environmental Science & Technology 37(20): 4543-4553.

Chemicals identified as endocrine-disrupting compounds (EDCs) have widespread consumer uses, yet little is known about indoor exposure. We sampled indoor air and dust in 120 homes, analyzing for 89 organic chemicals identified as EDCs. Fifty-two compounds were detected in air and 66 were detected in dust. These are the first reported measures in residential environments for over 30 of the compounds, including several detected at the highest concentrations. The number of compounds detected per home ranged from 13 to 28 in air and from 6 to 42 in dust. The most abundant compounds in air included phthalates (plasticizers, emulsifiers), o-phenylphenol (disinfectant), 4-nonylphenol (detergent metabolite), and 4-tert-butylphenol (adhesive) with typical concentrations in the range of 50-1500 ng/m3. The penta- and tetrabrominated diphenyl ethers (flame retardants) were frequently detected in dust, and 2,3-dibromo-1-propanol, the carcinogenic intermediate of a flame retardant banned in 1977, was detected in air and dust. Twenty-three pesticides were detected in air and 27 were detected in dust, the most abundant being permethrins and the synergist piperonyl butoxide. The banned pesticides heptachlor, chlordane, methoxychlor, and DDT were also frequently detected, suggesting limited indoor degradation. Detected concentrations exceeded government health-based guidelines for 15 compounds, but no guidelines are available for 28 compounds, and existing guidelines do not consider endocrine effects. This study provides a basis for prioritizing toxicology and exposure research for individual EDCs and mixtures and provides new tools for exposure assessment in health studies.

Rudel, R.A., P. Geno, G. Sun, A. Yau, J. Spengler, J. Vallarino, J.G. Brody. 2001. Identification of selected hormonally active agents and animal mammary carcinogens in commercial and residential air and dust samples. Journal of Air and Waste Management Association 51:499-513.

In order to characterize typical indoor exposures to chemicals of interest for research on breast cancer and other hormonally mediated health outcomes, methods were developed to analyze air and dust for target compounds that have been identified as animal mammary carcinogens or hormonally active agents and that are used in commercial or consumer products or building materials. These methods were applied to a small number of residential and commercial environments to begin to characterize the extent of exposure to these classes of compounds. Phenolic compounds, including nonylphenol, octylphenol, bisphenol A, and the methoxychlor metabolite 2,2-bis (p-hydroxyphenyl)-1,1,1- trichloroethane (HPTE), were extracted, derivatized, and analyzed by gas chromatography/mass spectrometry (GC/MS) — selective ion monitoring (SIM). Selected phthalates, pesticides, polycyclic aromatic hydrocarbons (PAHs), and polychlorinated biphenyls (PCBs) were extracted and analyzed by GC/MS-SIM. Residential and workplace samples showed detectable levels of twelve pesticides in dust and seven in air samples. Phthalates were abundant in dust (0.3–524 µg/g) and air (0.005–2.8 µg/m^3). Nonylphenol and its mono- and di-ethoxylates were prevalent in dust (0.82–14 µg/g) along with estrogenic phenols such as bisphenol A and o-phenyl phenol. In this 7-sample pilot study, 33 of 86 target compounds were detected in dust, and 24 of 57 target compounds were detected in air. In a single sample from one home, 27 of the target compounds were detected in dust and 15 in air, providing an indication of chemical mixtures to which humans are typically exposed.

Rudel, R.A., P. Geno, S.J. Melly, G. Sun, and J.G. Brody. 1998. Identification of alkylphenols and other estrogenic phenolic compounds in wastewater, septage, and groundwater on Cape Cod, Massachusetts. Environmental Science & Technology 32(7):861-869.

As part of a larger effort to characterize impacts to Cape Cod drinking water supplies from on-site wastewater disposal, we developed two analytical methods, using HPLC and GC/MS, for a range of compounds identified as endocrine disrupting chemicals (EDCs), including the nonionic surfactants alkylphenol polyethoxylates (APEOs) and their degradation products. We analyzed samples for nonylphenol, octylphenol, and their ethoxylates up to the hexaethoxylate using an HPLC method, with detection limits ranging from 2-6 µg/L. A set of phenolic compounds including bisphenol A and nonylphenol were derivatized and analyzed by GC/MS with detection limits from 0.001 to 0.02 µg/L. Total APEOs in untreated wastewater and septage samples ranged from 1,350 to 11,000 µg/L by the HPLC method. Nonylphenol was detected in all septage samples at concentrations above 1000 µg/L. Phenylphenol and bisphenol A were detected in septage and wastewater at about 1 µg/L. In groundwater downgradient of an infiltration bed for secondary treated effluent, nonyl/octylphenol and ethoxylates were present at about 30 µg/L. Bisphenol A, nonylphenol monoethoxycarboxylate, and nonyl/octylphenol tetraethoxylate were detected in some drinking water wells at concentrations ranging from below the quantitation limit to 32.9 µg/L. Results suggest that septic systems may be a significant source of APEOs to groundwater.

Rudel R.A. 1997. Predicting health effects of exposures to compounds with estrogenic activity: Methodological issues. Environmental Health Perspectives 105(suppl 3):655-663.

Many substances are active in in vitro tests for estrogenic activity, but data from multigenerational and other toxicity studies are not

available for many of those substances. Controversy has arisen, therefore, concerning the likelihood of adverse health effects. Based on a toxic equivalence factor risk assessment approach, some researchers have concluded that exposure to environmental estrogens is not associated with estrogen receptor (ER)-mediated health effects. Their rationale cites the low potency of these compounds in in vitro assays relative to estradiol, and the widespread exposure to pharmaceutical, endogenous, and dietary estrogens. This reasoning relies on two assumptions: that the relative estrogenic potency in in vitro assays is predictive of the relative potency for the most sensitive in vivo estrogenic effect; and that all estrogens act via the same mechanism to produce the most sensitive in vivo estrogenic effect. Experimental data reviewed here suggest that these assumptions may be inappropriate because diversity in both mechanism and effect exists for estrogenic compounds. Examples include variations in ER-ligand binding to estrogen response elements, time course of nuclear ER accumulation, patterns of gene activation, and other mechanistic characteristics that are not reflected in many in vitro assays, but may have significance for ER-mediated in vivo effects. In light of these data, this report identifies emerging methodological issues in risk assessment for estrogenic compounds: the need to address differences in in vivo end points of concern and the associated mechanisms; pharmacokinetics; the crucial role of timing and duration of exposure; interactions; and non-ER-mediated activities of estrogenic compounds.

Swartz C.H., S. Reddy, M.J. Benotti, H. Yin, L.B. Barber, B.J. Brownawell, and R.A. Rudel. 2006. Steroid estrogens, nonylphenol ethoxylate metabolites, and other wastewater contaminants in groundwater affected by a residential septic system on Cape Cod, MA. Environmental Science and Technology 40(16):4894-4902.

Septic systems serve approximately 25% of US households and may be an important source of estrogenic and other organic wastewater contaminants (OWC) to groundwater. We monitored several estrogenic OWC, including nonylphenol (NP), nonylphenol mono- and diethoxycarboxylates (NP1EC and NP2EC), the steroid hormones 17β-estradiol (E2), estrone (E1), and their glucuronide and sulfate conjugates, and other OWC such as methylene blue active substances (MBAS), caffeine and its degradation product paraxanthine, and two fluorescent whitening agents in a residential septic system and in downgradient groundwater. E1 and E2 were present predominantly as free estrogens in groundwater, and near-source groundwater concentrations of all OWC were highest in the suboxic to anoxic portion of the wastewater plume, where concentrations of most OWC were similar to those observed in the septic tank on the same day. NP and NP2EC were up to 6 to 30-fold higher, and caffeine and paraxanthine were each 60-fold lower than septic tank concentrations, suggesting net production and removal, respectively, of these constituents. At the most shallow, oxic depth, concentrations of all OWC except for NP2EC were substantially lower than in the tank and in deeper wells. Yet boron, specific conductance, and the sum of nitrate-and ammonia-nitrogen were highest at this shallow depth, suggesting preferential losses of OWC along the more oxic flow lines. As far as 6.0 m downgradient, concentrations of many OWC were within a factor of 2 of near-source concentrations. The results suggest that there is the potential for migration of these OWC, which are unregulated and not routinely monitored, in groundwater.

Swartz, C.H., R.A. Rudel, J.R. Kachajian, J.G. Brody. 2003. Historical reconstruction of wastewater and land use impacts to groundwater used for public drinking water: Exposure assessment using chemical data and GIS. Journal of Exposure Analysis and Environmental Epidemiology 13(5): 403-416.

Land use in geographic areas that replenish groundwater and surface water resources is increasingly recognized as an important factor affecting drinking water quality. Efforts to understand the implications for health, particularly outcomes with long latency or critical exposure windows, have been hampered by lack of historical exposure data for unregulated pollutants. This limitation has hindered studies of the possible links between breast cancer risk and drinking water impacted by endocrine disrupting compounds and mammary carcinogens, for example. This paper describes a methodology to assess potential historical exposure to a broad range of chemicals associated with wastewater and land use impacts to 132 groundwater wells and one surface water body supplying drinking water to 18 public distribution systems on Cape Cod, MA. We calculated annual measures of impact to each distribution system and used the measures as exposure estimates for the residential addresses of control women in the Cape Cod Breast Cancer and Environment Study (Cape Cod Study). Impact was assessed using (1) historical chemical measurements of nitrate at the water supply sources (performed as required by the Safe Water Drinking Act) and (2) a geographic information system analysis of land use within the zones of contribution (ZOCs) delineated for each well in a state-mandated wellhead protection program. The period for which these impact estimates were developed (1972–1995) was constrained by the availability of chemical measurements and land use data and consideration of time required for groundwater transport of contaminants to the water supply wells. Trends in these estimates for Cape Cod suggest increasing impact to drinking water quality for land use over the study period. Sensitivity analyses were conducted to assess the effect on the distribution of controls' cumulative exposure estimates from (1) reducing the area of the ZOCs to reflect typical well operating conditions rather than extreme pumping conditions used for the regulatory ZOCs, (2) assuming residences received their drinking water entirely from the closest well or cluster of wells rather than a volume-weighted annual district-wide average, and (3) changing the travel time considered for contaminants to reach wells from land use sources. We found that the rank and distribution of controls' cumulative exposure estimates were affected most by the assumption concerning district mixing; in particular, assignment of exposure estimates based on impact values for the closest well(s) consistently produced a larger number of unexposed controls than when a district-wide average impact value was used. As expected, the results suggest that adequate characterization of water quality heterogeneity within water supplies is an important component of exposure assessment methodologies in health studies investigating impacted drinking water.

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The Silent Spring Institute Board of Directors, chaired by Ellen Parker, provided vision and strong leadership throughout the study. The Massachusetts Legislature, especially the Cape Cod delegation, understood the importance of our work and committed the substantial funds needed for an investigation that would genuinely advance the search for environmental factors that can lead to breast cancer prevention. The Massachusetts Breast Cancer Coalition and the many Silent Spring Institute volunteers were able to mobilize at a moments notice and were tireless in their efforts to support this work. Public Advisory and Science Advisory Committees provided invaluable guidance in planning, gathering data, interpreting results, and sharing their experience.

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Photos: Tanya Swann. Cover — specimen jar; Inside front cover — scientist collecting specimens and telephone interviewers; Page 10 — telephone interviewers; Page 12 — scientist.

Clockwise from top, Ellen Parker, chair Silent Spring Institute Board of Directors; far right, Karen Towne, Silent Spring Institute staffer, discusses the Institute's research at an outdoor information session; Cheryl Osimo, Silent Spring Institute cape coordinator; Silent Spring Institute staff left to right Kathleen Attfield, Karen Towne, Julia Brody, Anne Bonner, Cheryl Osimo.

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SILENT SPRING INSTITUTE

29 Crafts Street
Newton, MA 02458
tel 617.332.4288
fax 617.332.4284

info@SilentSpring.org
http://www.SilentSpring.org

Cape Coordinator
tel 508.778.1942