

## **PREFACE**

- *What role does the environment play in breast cancer?*
- *Why do some groups of women bear a greater burden of this disease than others?*

The answers to these questions have thus far eluded scientists, yet answering them could lead to great progress against breast cancer. Recognizing the need for more research into these questions, the California Breast Cancer Research Program (CBCRP) is launching our Special Research Initiatives, a five-year effort to find answers that will push breast cancer research forward.

We are setting aside 30 percent of our funds over five years for the Special Research Initiatives, approximately \$18 million. To select the research that will lead to the most progress against breast cancer, we are following a carefully-crafted, two-year, publicly-accessible strategy development process. An initial step in the process is this report reviewing previous research.

We are embarking on the Special Research Initiatives because research has been conducted for decades, and yet too many women are being diagnosed with breast cancer, living with the threat of a recurrence, and dying. There is no action women can take to assure they won't get breast cancer. Our goals are:

- To initiate research that will point to actions that can be taken to reduce the burden of breast cancer

- To conduct research that will provide recommendations to advocacy organizations and policy makers for evidence-based change.
- To stimulate more research into the environment-breast cancer connection and the reasons why some groups of women bear a greater burden of breast cancer.

We plan to identify and involve California organizations and institutions who can join forces and increase the resources available to conduct this research.

This report is not a comprehensive review of all research on the environment-breast cancer connection or the reasons why some groups of women bear more of the burden of the disease. It is instead a review of existing research—gathered from widely scattered sources—pointed toward discovering research areas that show some connection with the disease, and recommending further investigations that are likely to make the most difference toward eliminating the death and suffering caused by breast cancer.

### **The Need for This Research**

Breast cancer is a complex disease. Despite decades of intensive research, its causes and basic biology remain unclear. From the 1940s until very recently, the U.S. breast cancer rate has been rising, and this increase is not explained by better detection methods.

Scientific studies have uncovered a number of risk factors for breast cancer. Some of these risk factors can be modified by individuals to lower

their risk, and others cannot. One known risk factor is a family history of the disease, which raises a woman's risk. This can't be modified by individuals. Another known risk factor is not having children or having children later in life. Although this can be modified by individuals, it isn't a feasible strategy for most women in the U.S. economy and culture today. Other risk factors include lack of regular exercise and obesity. These can be modified by individuals and are the focus of a good deal of current research.

However, all known risk factors for breast cancer taken together can only account for some percentage of the disease. The percentage is in dispute, with estimates ranging from 50-70 percent. This means that for 30-50 percent of all cases of breast cancer, we can pinpoint nothing that may have even contributed to causing the illness. Clearly, there is a lot yet to be understood about breast cancer.

Studies of immigrant populations provide evidence that environmental causes may play a role in the 30-50 percent of unexplained breast cancer cases. For decades, researchers have noticed different patterns of breast cancer in different populations. For example, women in Asia have far lower rates of breast cancer than women in the U.S.. Soon after they move to the U.S., Asian women's rates of breast cancer begin to rise. The risk rises further for the next generation of Asian women who grow up in the U.S.. These patterns, which have remained largely unexplained for 50 years, suggest that the environment has a role in causing breast cancer. These patterns also suggest that further study into breast cancer differences among various

population groups could not only lead to a decrease in inequality among groups of women with breast cancer, but also reveal crucial information about the disease itself.

One major reason that more research has not already been done on the questions we are addressing is that they are difficult and complicated to research. There's no scientific consensus about where to begin. Previous research, as this report reveals, has been reported in widely scattered sources and conducted under a variety of paradigms and philosophies. These approaches include basic science, epidemiology, toxicology, social justice/critical theory, health services, health policy, and community-based participatory research. Each of these research paradigms has methodological challenges. Multi-disciplinary research combining some or all of the research approaches will be a complex endeavor. It will require establishing communication lines across diverse scientific subcultures.

### **California: The Unique Laboratory**

California has unique resources for investigating the environment-breast cancer connection and reasons why some groups of women bear a greater burden of the disease. This combination of resources creates an opportunity no other state or country can match. These resources include:

- **Geographic variety**, with large rural, urban, and suburban areas.
- **Diverse population**, with a wide spectrum of income, social class, and cultures; many ethnic groups; and first, second, and third

generation immigrants from low-incidence areas such as Asia.

- **Unique databases**, with high-quality data on cancer incidence and data on pesticides and pollutants mandated by state Proposition 65.
- **Excellent research institutions**, including schools of public health and a strong state Health Department, with some experience in collaborative research.
- **Strong environmentalist and breast cancer advocacy groups.**

### **What We Mean by "Environment"**

Some researchers define the influence of environment on breast cancer as everything that is not due to the influence of genes. For the purposes of our Special Research Initiatives, the CBCRP is using a narrower definition. We define "environment" as all of the non-genetic factors that might lead to breast cancer that are also largely outside an individual's control. This definition includes possible causes of breast cancer resulting from exposure to sources such as air pollution, second hand smoke, and pharmaceuticals.

Defining "environment" in this way means that under our Special Research Initiatives, the CBCRP will not pursue further studies into the well-researched connection between breast cancer and lifestyle, including diet. We believe studies of this type are valuable and should be continued. However, the focus of our Special Research Initiatives will be on how the environment directly

affects breast cancer or affects lifestyle in a way that can lead to breast cancer. For example, we might pursue an investigation of how the environment shapes American women's diets, by investigating how different neighborhood characteristics affect women's food choices.

"Environment," by this definition, includes the human-created, built environment. We may include investigations of how features of the built environment might impact breast cancer, for example, whether racial segregation makes survival less likely. We may also include ways the built environment has an impact on lifestyle. For example, we would not investigate further the question of whether regular exercise may help prevent breast cancer, but we might study the ways that features of the built environment, such as neighborhood design, create opportunities or barriers to women getting exercise.

### **Challenges of Investigating the Environment-Breast Cancer Connection**

One logical place to look for causes of breast cancer in the environment is to investigate the role of toxic chemicals, pollutants, and other similar agents. This type of research already has led to controversy, with some experts claiming that research has demonstrated that there is no connection, and others saying researchers have barely scratched the surface of these questions.

Researching the connection between toxic exposures and breast cancer presents methodological challenges. These include:

#### **Lack of basic biological knowledge.**

Researchers do not know exactly what biological

changes a cell goes through as it transforms from normal to cancerous. Therefore, it is hard to determine whether exposure to a particular substance or a particular combination of exposures stimulates the development of breast cancer.

**Many subtypes of the disease.** DNA analysis shows that breast cancer is not one disease, but many. A particular toxic exposure could be related to just one subtype.

**Timing of exposure.** A toxic exposure may lead to breast cancer years, or even decades, after the substance has been eliminated from the body. Toxic exposures as early as when a baby girl is still in the womb could predispose her to breast cancer as an adult. Uncovering the connection between the exposure and the disease is difficult.

**Dose.** Researchers don't know how much the amounts of exposure matter. For example, it is unclear whether one massive dose of a toxic chemical is more or less likely to cause breast cancer than exposures to small amounts of the same substance over a long period of time.

**Combinations of exposures.** Testing for the role of one toxic substance ignores the fact that most people have experienced a variety of toxic exposures in combination.

**Gene-environment interactions.** Some toxic exposures may only increase the risk for breast cancer in women who carry certain genes.

**Privacy Concerns.** Federal privacy regulations make it difficult to conduct studies on large populations of women who may have experienced

toxic exposures, because each individual must consent to the use of her medical record.

**Lack of tests for exposures.** The single biggest challenge to researching the breast cancer-environment connection is that scientists have developed few reliable tests to determine whether a given woman has been exposed to chemicals, pollutants, or other agents that could lead to cancer in breast tissue. Especially needed are tests that can detect biomarkers that provide a trace of past exposure to toxics that the body eliminates quickly.

All of these challenges complicate research into the breast cancer-environment connection.

### **The Unequal Burden of Breast Cancer**

Different groups of women in the U.S. are impacted differently by breast cancer. African American women, for example, get the disease at younger ages. They are less likely than white women to get breast cancer, but once they have it, they are more likely to die from the disease. Some of the disparities between various groups of women can be explained by unequal access to care, but not all of them.

Much of the previous research into why some groups of women bear more of the burden of breast cancer has been descriptive and has not addressed how to decrease or eliminate the inequality.<sup>1</sup>

## **Challenges of Investigating Why Some Women Bear More of the Burden of Breast Cancer**

Investigating why different groups of women are impacted differently by breast cancer presents its own set of challenges. These include:

**Problems with definitions.** "Race" is more of a social construct than a biologic category. The commonly-used racial groupings in the U.S.—African American, white, Hispanic, Asian, Pacific Islander—do not have consistent genetic profiles within the groups or consistent genetic differences between groups. However, this is an area of scientific controversy, with some geneticists arguing that some genes are commonly distributed among some racial groups. In any case, differences in breast cancer among various groups are probably due to a combination of genetics and differences in the environments in which these groups live and work. This underscores how intertwined are the two questions being investigated under the CBCRP's Special Research Initiatives.

**Variations within groups.** There are great variations within racial/ethnic groups. "African American" includes people whose ancestors were brought to this country as slaves eight generations ago, and people who immigrated from Kenya last month. Their genetic profiles, environmental exposures and experiences of the human-made environment are likely to be very different. Similarly, "Asian/Pacific Islander" combines people of Japanese ancestry with people from India, who aren't similar. However, if each subgroup in the "Asian/Pacific Islander"

population of California is studied separately, the numbers of women are often too small for statistically meaningful research.

**Socioeconomic status adds complexity.** Higher socioeconomic status is a risk factor for breast cancer. Comparisons of breast cancer incidence and death rates for various ethnic groups often fail to address differences in socioeconomic status. Taking socioeconomic status into account adds another level of complexity.

**Confusion between the biological and the environmental.** Differences in breast cancer related to race may be biological, environmental, or a combination. For example, African American women being more likely to die from the disease could be due to a genetic predisposition toward more lethal types of tumors. It could also be due to the stress of racism, to lack of access to treatment, to living in neighborhoods that make survival less likely, or to a combination of any of these factors and other unknown factors. Untangling multiple, related causes complicates research.

## **The Framework for Each Chapter of this Report**

Researchers JudyAnn Bigby and Michelle D. Holmes have provided a framework for studying how breast cancer differently impacts various groups of women. Each chapter of this report follows a framework we have adapted from Bigby and Holmes:

**1) We begin by defining the factor related to breast cancer.**

Chapters in Section I, Exposures from the Physical Environment, define the exposure, for example, pesticides, light at night, or compounds in cosmetics and personal care products.

Chapters in Section II, Disparities in Breast Cancer: Domains of Individual-Level Social Inequality, define the characteristics of groups of women who bear unequal burdens of breast cancer. Examples include ethnicity, age, sexual orientation, and insurance status.

Section III, Disparities in Breast Cancer: Neighborhood Built and Social Environment, defines features of the human-created environment that may underlie geographic differences in breast cancer rates in California. Examples include racial segregation in housing and human-created features of the environment that alter personal behavior.

**2) We summarize the biological evidence that this factor is relevant to breast cancer.**

**3) We review research that links the exposure, characteristic of groups of women, or human-created feature of the environment to breast cancer:**

**a) incidence**

**b) etiology/prevention**

**c) screening**

**d) diagnosis**

**e) treatment**

**f) morbidity**

**g) quality of life after diagnosis**

**h) survival**

**i) mortality**

Many chapters discuss only one or a few of the topics above, because each chapter covers only those areas where some research has been conducted. The chapters in Section I, Exposures from the Physical Environment and Breast Cancer, mostly deal with etiology and tumor promotion. For example, no research has been conducted on the relationship between exposure to pesticides and quality of life after diagnosis. Therefore, quality of life after diagnosis is not discussed in Section I, Chapter B.4, Pesticides.

**4) We discuss limitations and gaps in knowledge.**

**5) We recommend the highest priority/highest payoff research for the factor being reviewed.**

We also recommend other future research and future policy interventions that could result from research.

There is considerable overlap among the chapters that follow. For example, studies of breast cancer and race (Section II, Chapter A), often overlap with studies of breast cancer and culture (Section II, Chapter D).. Some of the same chemicals discussed in Section I, Chapter B.2, Persistent Organic Pollutants, are chemicals of concern in air pollution, which is discussed in Section I, Chapter B.1. Where there is a large overlap in the research, we discuss the issue in detail in one chapter, and refer to it in other chapters.

**A General Recommendation**

One general recommendation emerges from multiple chapters of this report. It concerns possible future partners for the Special Research Initiatives. Many of the toxic exposures considered here are likely causes of other types of cancer and other diseases. This is also true of features of the built environment. Just as breast cancer impacts various population groups of women in unequal ways, some groups of women bear a greater burden of other diseases and health problems. One way to increase the financial resources for the Special Research Initiatives would be to conduct joint research with organizations investigating other diseases. For example, breast cancer researchers, childhood asthma researchers, and birth defects researchers might team up to study the role of air pollution in causing or exacerbating all three.

**References**

1. Bigby J, Holmes MD. Disparities across the breast cancer continuum. *Cancer Causes Control*. 2005, 16(1):35-44.