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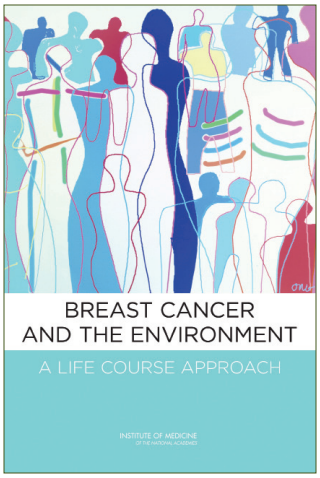
Breast Cancer and the Environment
A Life Course Approach



The prospect of developing breast cancer is a source of anxiety for many women. Breast cancer has long been the most common type of invasive cancer among U.S. women (aside from certain skin cancers), with an estimated 230,480 new cases expected to be diagnosed in 2011.

Many well-known risk factors for breast cancer—increasing age, later age at menopause, younger age at first menstruation, certain genetic traits—appear to offer little chance for intervention. Despite a substantial research effort over the past 20 years on the relationship of environmental factors to breast cancer, results have offered few opportunities for preventive actions.

Susan G. Komen for the Cure® asked the Institute of Medicine (IOM) to review the current evidence on breast cancer and the environment, consider gene–environment interactions, review the challenges in investigating environmental contributions to breast cancer, explore evidence-based actions that women might take to reduce their risk, and recommend research in all of these areas. *Breast Cancer and the Environment: A Life Course Approach* presents the IOM study committee's findings and recommendations.

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Environment, Writ Broadly

The committee interpreted "environment" broadly, to encompass all factors not directly inherited through DNA. Such factors include how a woman grows and develops during her lifetime; what she eats and drinks; the physical, chemical, and microbial agents she encounters; how much physical activity she engages in; medical treatments and interventions she undergoes; and social and cultural practices that she experiences. From this array, the committee

concentrated on a selection of factors that represent a variety of environmental agents and conditions, and that illustrate diverse challenges in evaluating the data.

The study committee sought to characterize the evidence on whether the selected environmental factors are associated with breast cancer and to identify areas of uncertainty. Evidence from epidemiologic studies on large numbers of people carried the greatest weight in identifying risk factors, but many factors have not been studied in humans. Evidence from experimental studies in animals or from other laboratory tests sometimes adds support to the results from human studies or suggests biologic plausibility when human evidence regarding breast cancer is lacking.

Review of Selected Environmental Factors

Of the environmental factors reviewed, those with the most consistent evidence of a link with increased breast cancer risk are use of hormone therapy that combines estrogen and progestin, exposure to ionizing radiation (which occurs, for example, during medical diagnostic procedures such as CT scans), excess weight among postmenopausal women, and alcohol consumption. Views on the connection between smoking and breast cancer are mixed. Some major authoritative reviews have concluded that smoking is causally related to breast cancer, while other large-scale reviews describe the evidence as limited.

In addition, sound scientific evidence links greater physical activity with decreased breast cancer risk. Also, multiple well-designed studies consistently have failed to show increased breast cancer risk for two environmental exposures—personal use of hair dyes and non-ionizing radiation (emitted by microwave ovens and other electrical devices).

For several other factors, the evidence is less persuasive but suggests a possible association with increased risk. These factors are exposure to secondhand smoke, nighttime shift work, and exposure to the chemicals benzene, ethylene oxide, or 1,3-butadiene, which can occur in some workplaces and from breathing auto exhaust, pumping gas, or inhaling tobacco smoke. Some environmental agents are at least biologically plausible hazards—that is, scientists can see a clear mechanism in animals by which the agents might cause breast cancer—but studies to assess the risk in humans are lacking or inadequate. One example is the chemical bisphenol A, or BPA, widely used in plastic containers and food packaging.

Research Challenges

Researchers face substantial challenges in trying to determine which environmental exposures may influence risk of breast cancer. The biology of breast development and the origins and progression of breast cancer are not fully understood, and much research in the past lacked tools to differentiate among types of breast cancer. Also, past studies that focused primarily on exposures during adulthood may have missed exposures during critical windows earlier in life. Women are exposed to a complex and changing mix of environmental agents over the course of their lives.

Many chemicals have never been studied in ways that could indicate whether they might be relevant to breast cancer. Experimental studies in humans—randomized controlled clinical trials—would provide the strongest evidence. But such studies are rarely an option in breast cancer research because it would not be ethical to intentionally expose women to potentially harmful substances. The contribution of genetic factors is also of interest, but because of the multitude of potential gene–environment associations, studies must be very large to detect statistically significant effects.

Experimental studies in animals and in in vitro systems are essential components of research on breast cancer. They can provide indications that a chemical or other agent may cause harm, but these

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models are approximations of human experience. Studies in laboratory animals are generally small and may expose animals to chemicals in ways and amounts that are not typical for humans.

Promising Preventive Actions

In viewing the landscape of established and suspected environmental risks, the study committee identified promising preventive actions that women can take that may reduce their breast cancer risk (see Table).

These actions include avoiding unnecessary medical radiation throughout life, avoiding use of postmenopausal hormone therapy that combines estrogen and progestin, avoiding smoking, limiting alcohol consumption, increasing physical activity, and, particularly for postmenopausal breast cancer, minimizing weight gain. Some of these actions may have additional health benefits beyond their potential contribution to reducing breast cancer risk. In many cases, women can be aided by the actions of others, including their families and health care providers.

The potential risk reductions from any of these actions for any individual woman will vary and may be modest. Because much of the evidence on breast cancer risk factors has come from studies of postmenopausal breast cancer in white women, it is hard to judge the potential benefit for younger women or women of other races. Also, few studies have investigated when exposures might best be avoided. For example, more evidence is needed on whether factors associated with increased postmenopausal risk, such as being overweight, should be avoided completely, or whether changes later in adulthood will reduce risks that might have accumulated from exposure at younger ages.

Future Research Needs

In order to identify additional opportunities to reduce breast cancer risk, further research needs to fill a host of knowledge gaps. The breast undergoes substantial changes over a woman's lifetime. Future research should emphasize a "life course" model. The committee notes a growing appreciation among researchers of the important role of the precise timing of environmental exposures in increasing or reducing later breast cancer risks. Research will need to factor in such evolving knowledge in order to yield an accurate picture of a woman's breast cancer risk status over time and how she may be affected by specific environmental risk factors at different points in her lifetime.

A broad "transdisciplinary" approach will be needed to encompass research that ranges from examining elements of the biology of breast development and carcinogenesis—the interplay between genetics, environmental exposure, and age to create conditions favorable or unfavorable to cancer development—to developing and testing potential new interventions to reduce risk. More work also needs to be done to ensure that carcinogenicity testing of chemicals can yield insights relevant to breast cancer. In addition, statistical modeling is needed to clarify how various envi-

Committee on Breast Cancer and the Environment: The Scientific Evidence, Research Methodology and Future Directions

Irva Hertz Picciotto (Chair)
Professor and Chief, Division of Environmental and Occupational Health, University of California, Davis

Lucile Adams-Campbell
Professor of Oncology, Associate Director, Minority Health and Health Disparities Research, Lombardi Comprehensive Cancer Center, Georgetown University Medical Center

Peggy Devine
Founder and President, Cancer Information and Support Network

David Eaton
Associate Vice Provost for Research, and Professor and Director, Center for Ecogenetics and Environmental Health, University of Washington

S. Katharine Hammond
Professor, Division of Environmental Health Sciences, School of Public Health, University of California, Berkeley

Kathy J. Helzlsouer
Director, The Prevention and Research Center, Mercy Medical Center

Robert A. Hiatt
Professor and Chair, Department of Epidemiology and Biostatistics, and Director, Population Sciences, Helen Diller Family Comprehensive Cancer Center, University of California, San Francisco

Chanita Hughes Halbert
Associate Professor, University of Pennsylvania, Department of Psychiatry, Director, Center for Community-Based Research and Health Disparities

David J. Hunter
Dean for Academic Affairs and Vincent L. Gregory Professor in Cancer Prevention, Harvard School of Public Health

Barnett Kramer
Editor-in-Chief, *Journal of the National Cancer Institute,* and Editor-in-Chief, National Cancer Institute Physician Data Query (PDQ) Screening and Prevention Editorial Board

Bryan M. Langholz
Professor, Division of Biostatistics, Department of Preventive Medicine, University of Southern California (resigned July 2011)

Peggy Reynolds
Senior Research Scientist, Cancer Prevention Institute of California

Joyce S. Tsuji
Principal Scientist, Center for Toxicology and Mechanistic Biology, Exponent

Cheryl Lyn Walker
Welch Professor and Director, Institute of Biosciences and Technology, Texas A&M Health Science Center

Lauren Zeise
Chief, Reproductive and Cancer Hazard Assessment Branch, Office of Environmental Health Hazard Assessment, California Environmental Protection Agency

Study Staff

Lois Joellenbeck
Study Director

Jane Durch
Senior Program Officer

Sharyl Nass
Senior Program Officer

Niharika Sathe
Research Assistant (from November 2010)

Cassandra Cacace
Research Assistant (until December 2010)

Ashley Mcwilliams
Senior Program Assistant (until December 2010)

Patrick Burke
Financial Associate

Roger Herdman
Director, Board on Health Care Services

Andrew Pope
Director, Board on Health Sciences Policy

Study Sponsor

Susan G. Komen for the Cure®

ronmental factors contribute to breast cancer risk. Finally, further research is needed to develop effective ways of communicating accurate breast cancer risk information to the public, health care providers, and policy makers.

Conclusion

Major advances have been made in understanding breast cancer and its risk factors, but more needs to be learned about its causes and how to prevent it. Familiar advice about healthy lifestyles appears relevant, but it remains difficult to discern the contribution of other environmental factors. By learning more about the significance of a woman's age and her physical maturity when she encounters environmental risk factors, as well as which preventive actions can be most be effective and when they should be taken, it may be increasingly possible to identify, develop, and implement ways to effectively prevent various forms of breast cancer.

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500 Fifth Street, NW
Washington, DC 20001
TEL 202.334.2352
FAX 202.334.1412

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