Summary Report: Early Reproductive Events and Breast Cancer Workshop

Posted: 03/04/2003 **Updated:** 03/25/2003

Page Options

Print This Page

E-Mail This Document

Quick Links

Director's Corner

Dictionary of Cancer Terms

NCI Drug Dictionary

Funding Opportunities

NCI Publications

Advisory Boards and Groups

NIH Calendar of Events

Español

NCI Highlights

NCI Offers Support for Those in Need After Katrina

NCI Announces Plan to Fight Lung Cancer

National Prostate Cancer Awareness Month

National Ovarian Cancer Awareness

NCAB Working Group Report on Biomedical Technology

The Nation's Investment in Cancer Research FY 2006

Introduction

The Early Reproductive Events and Breast Cancer Workshop convened February 24-26, 2003, and the outcomes of the meeting were reviewed and discussed at the joint meeting of the NCI Board of Scientific Advisors (BSA) and Board of Scientific Counselors (BSC) held March 3, 2003.

The Workshop was established to provide an integrated scientific assessment of the association between reproductive events and the risk of breast cancer. Participants represented a diversity of breast cancer expertise, including epidemiologists, clinicians, basic scientists and breast cancer advocates. The Workshop evaluated the current strength of evidence of the characteristics of pregnancy related to cancer (epidemiologic studies), the biologic changes resulting from pregnancy that may be involved in modifying breast cancer risk (clinical studies), and the biologic mechanisms identified (animal studies).

This report summarizes the epidemiologic, clinical and animal studies findings related to early reproductive events and breast cancer risk, and each finding is given a Strength of Evidence Rating*. Gaps in research knowledge for each scientific area are identified, and recommendations for future research directions are provided.

Epidemiologic Findings

- Early age at first term birth is related to lifetime decrease in breast cancer risk. (1)
- Increasing parity is associated with a long-term risk reduction, even when controlling for age at first birth. (1)
- The additional long-term protective effect of young age at subsequent term pregnancies is not as strong as for the first term pregnancy. (1)
- A nulliparous woman has approximately the same risk as a woman with a first term birth around age 30. (1)
- Breast cancer risk is transiently increased after a term pregnancy. (1)
- Induced abortion is not associated with an increase in breast cancer risk. (1)
- Recognized spontaneous abortion is not associated with an increase in breast cancer risk. (1)
- Long duration of lactation provides a small additional reduction in breast cancer risk after consideration of age at and number of term pregnancies. (1)
- Pregnancy-induced hypertension is associated with decreased breast cancer risk. (2)
- Maternal DES exposure is associated with an increase in breast cancer risk. (3)

Epidemiologic Gaps

- By what mechanism does pregnancy at an early age protect against breast cancer?
- Do pregnancy and age at pregnancy modify radiation-induced breast cancer risk?
- What are the effects of age at pregnancy on subgroups of women (e.g., those with BRCA-1 and BRCA-2 mutations)?
- What is the mechanism by which lactation affects breast cancer risk?
- What is the temporal pattern of breast cancer risk following lactation?

Past Highlights

- What is the effect of lactation on women with BRCA-1 and BRCA-2 mutations?
- Does gender of offspring have an effect?
- Does birth weight of offspring have an effect?
- What is the impact of multiple births in the same pregnancy, with and without assisted reproductive technology?
- What are the breast cancer risk implications of abnormal pregnancies (e.g., spina bifida, late fetal death, fertility treatment-induced pregnancy, preterm delivery, small for gestational age offspring)?
- What is the mechanism by which pre-eclampsia reduces breast cancer risk?
- Is there a distinction between hypertension and pre-eclampsia with respect to breast cancer risk?
- Is gestational diabetes associated with breast cancer risk?

Clinical Findings

- There are long-lasting decreases in mammographic density following pregnancy. (2)
- There may be changes in breast histology that can be correlated with risk in premenopausal women. (3)
- Prolactin, estradiol, and IGF-1 are decreased after pregnancy. (3)

Clinical Gaps

- What are the levels, determinants, and interactions of pregnancy-related mammotrophic factors, ligands, and receptors?
- What is the time course of pregnancy-related hormonal changes?
- Are pregnancy-related hormonal changes influenced by genetic polymorphisms?
- What is the precise nature of pregnancy-related changes in breast histology?
- How is the epithelial/stromal relationship altered in pregnancy?
- Can pregnancy-related changes in breast histology be correlated with ductal lavage findings?
- Can noninvasive procedures for assessing breast composition (e.g., MRI and other imaging techniques, particularly functional imaging) substitute for histology?
- What are the molecular changes in the breast during and after pregnancy?
- What are the histologic and molecular characteristics of breast tumors during and after pregnancy?
- Are there immune system changes that may be relevant to breast cancer risk following pregnancy?
- Are there pregnancy-related, non-hormonal metabolic changes relevant to breast cancer risk?

Animal Model Findings

- Pregnancy protects against subsequent chemical carcinogen-induced breast cancer in rats and mice. (1)
- Estrogen and progesterone combinations and hCG protect against carcinogen-induced cancer in rodents by mimicking pregnancy. (1)
- Short-term estrogen exposure, at levels of estrogen mimicking pregnancy, is protective for carcinogen-induced cancer in rats. (1)

Animal Model Gaps

- What are the mechanisms of hormone action when they are given before or after chemical carcinogen exposure?
- What is the relationship between pregnancy and risk of preneoplastic lesions?
- What are the levels, determinants, and interactions of pregnancy-related mammotrophic factors, ligands, and receptors?

Future Research Directions

- Develop additional animal and treatment models, including further examination of existing models.

- Examine the molecular mechanisms of hormone-induced protection, including epithelial/stromal interactions.
- Integrate the methodology of genomics and proteomics into the study of pregnancy in relation to risk of breast cancer.
- Pursue descriptive studies about human breast development in order to formulate new hypotheses.
- Pursue international studies to develop hypotheses for observed international differences in breast cancer risk.
- Develop surrogate markers to identify risk of breast cancer following pregnancy.
- Translate knowledge about protective effects of pregnancy into intervention trials with human populations.
- Promote interactions among epidemiologists, clinicians, and basic scientists.
- Consider a funding mechanism aimed at interdisciplinary research concerning pregnancy and breast cancer.
- Develop high-throughput technology for hormone measurement.
- Support the collecting, archiving, and sharing of relevant biospecimens.

Boards' Response

The NCI Board of Scientific Advisors and Board of Scientific Counselors reviewed and discussed the results of the Early Reproductive Events and Breast Cancer Workshop, and unanimously approved the Workshop findings. One additional gap in our clinical understanding of breast cancer was identified: Do breast cancers diagnosed during pregnancy have different morphologic or molecular characteristics than those diagnosed at other times? It is hoped that the outcomes of this Workshop will help guide the Institute's future research agenda and public communication materials.

*Strength of Evidence Ratings Key

Strength of Evidence Ratings: Epidemiology

1
= Well established
2
= Weight of evidence favors
3
= Suggested from human population studies, but speculative
4
= Suggested from laboratory or theoretical considerations but essentially unevaluated in human populations

Strength of Evidence Ratings: Biologic Changes

1
= Well established
2
= Weight of evidence favors
3
= Suggested by human evidence, but speculative
4
= Suggested from laboratory findings or theoretical considerations but essentially unevaluated in humans

Strength of Evidence Ratings: Biological Mechanisms from Laboratory Studies

1
= Well established
2
= Weight of evidence favors
3
= Suggested by experimental evidence, but speculative
4

= Not supported by experimental evidence

Minority Dissenting Comment

Participant comment regarding the outcome of the workshop.

Back to Top