



# JALBCA

JUDGES AND LAWYERS BREAST CANCER ALERT

Vol. 10 No. 5

Editor: Martha L. Golar, Esq.

September 2006

## ELEVENTH ANNUAL ELLEN P. HERMANSON MEMORIAL SYMPOSIUM

**Topic:** From the Lab to the Bedside: The Uncertain Path to New Treatments

**Date:** October 23, 2006

**Time:** 6:00 - 8:30 p.m.

**Place:** Association of the Bar of the City of New York, 42 W. 44th St., NY, NY

### Panel of Experts

Larry Norton, MD, Head, Div., Solid Tumor Oncology, Memorial Sloan-Kettering Cancer Center  
Minna Elias, Esq., NY Chief of Staff & Counsel to Congresswoman Carolyn B. Maloney

### **Panel in formation**

#### Panel of Judges

Chief Judge Judith S. Kaye, Chief Judge, NYS Court of Appeals  
Hon. Helen Freedman, Supreme Court, NY County  
Hon. Shirley W. Kornreich, Supreme Court, Acting, NY County  
Hon. E. Leo Milonas, formerly NYS Appellate Div, 1st Dept.  
Hon. Charles E. Ramos, Supreme Court, NY County

The Symposium will cover two topics: (1) the widening gap between bench research and application at the bedside, addressing the issue of market-driven research versus government-driven research and what impact the trend has and will have on cancer treatment; and (2) the current trend to bring civil, *qui tam* lawsuits against pharmaceutical companies for their marketing and promotion practices involving off-label use of drugs under the False Claims Act, the role of Federal law enforcement agencies with regard to such suits, and what impact the court opinions and civil settlement agreements may have on oncologists and cancer patients.

### Supporting Organizations

Co-Chairs: Mikki Golar, Esq., Hon. Shirley W. Kornreich, Barbara A. Ryan, Esq.  
2 CLE Credits – approval pending

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## **RACE FOR THE CURE**

As always, JALBCA was a strong presence at the 2006 Komen Race for the Cure. Sixty JALBCA runners joined over 20,000 others on Sunday, September 10, in celebrating the lives of breast cancer survivors, remembering those we have lost to the disease and lending our voices to breast cancer awareness. We thank our co-captains Shirley Werner Kornreich and Emily Ascher for their hard work, our t-shirt supplier Howard Simon of The Corporate Edge for our beautiful, red t-shirts and Sharon Hewitt, Ayanna Ross and Joan Levenson for helping us distribute the shirts in Brooklyn and the Bronx. Finally, our heartfelt thanks to all the members of our team for helping make the race a success!

## **OBESITY AND BREAST CANCER RISK**

(This article was prepared specifically for JALBCA by the authors identified below and JALBCA wants to extend a special thanks to them for their time and effort.)

### ***Summary***

Obesity is well established as a risk factor for breast cancer. It is one of the few breast cancer risk factors which women can modify. Studies of body mass index (BMI), a relative measure of obesity, and breast cancer risk have found that postmenopausal women whose BMI falls in the obese category have about twice the breast cancer risk of women with normal weight category BMI values. The relationship of obesity to postmenopausal breast cancer risk may be modified by several other breast cancer risk factors such as menopausal status, use of postmenopausal hormones, drinking alcohol, age, genetics, and physical activity.

Other measures of obesity also have been linked to breast cancer risk. Increased body weight after menopause, abdominal body fat distribution, and adult weight gain have all been linked to increased risk of breast cancer. However, while adult weight gain has been consistently associated with increased risk, less consistency has been reported for body weight and fat distribution.

Obesity makes a substantial contribution to the incidence of breast cancer because it is a common condition and is

associated with a moderate level of breast cancer risk.

### ***Introduction***

Obesity is defined as a condition of having too much body fat and its health effects are largely determined by body fat. As such, obesity research is concerned with the levels of fat, not body weight. Obesity is typically determined by the size of a person's BMI which is the acronym for Body Mass Index. BMI takes into account differences in individual height and weight. It is calculated by dividing weight (in kilograms) by the square of height (in meters) or kg/m<sup>2</sup>. While BMI is an accurate measure of obesity, it is not a direct measure of body fat. Because of this, BMI values must be adjusted for use in some groups of people, such as the elderly and some racial groups. A BMI calculator is available at the National Heart, Lung and Blood Institute's web site located at: <http://www.nhlbisupport.com/bmi/bmicalc.htm>.

### ***Studies of Obesity and the Risk of Breast Cancer***

Epidemiological studies have examined the association of breast cancer risk to a number of measures and aspects of obesity. The major goals of these studies are to find characteristics, called risk factors, that are predictive of disease incidence and to use these characteristics to understand the formation of and potential prevention of the disease. In the section below I will discuss the four major breast cancer risk factors associated with obesity - body weight, body mass index, weight gain/loss and body fat distribution.

***Body Weight.*** Early studies of obesity and breast cancer looked at body weight. Many of these studies found that greater body weight is associated with a decrease in breast cancer risk before menopause (premenopause) and an increase in breast cancer risk after menopause (postmenopause). This effect was also reported in a study produced within the Pooling Project of Diet and Cancer. This important series of studies were joint collaborations of investigators from major cohort studies. Collaborators provided their primary data which was pooled and analyzed. This resulted in very large sample sizes and statistical robustness that could not be found in individual studies. In addition, the pooled studies used a cohort design which is considered the most reliable type of epi-

demiological study. For the examination of body characteristics, including obesity, this approach resulted in the study of 337,819 women and 4,385 cases of breast cancer. The risk values reported by this study were: 1) in agreement with most earlier studies, for premenopausal women there was a moderate decrease in breast cancer risk (relative risk = 0.58, statistically significant) for women weighing more than 176 pounds compared to women weighing less than 132 pounds; and 2) for postmenopausal women there was a weak increase in breast cancer risk (relative risk = 1.25, statistically significant) for women of the same weight ranges noted above. This value was in the broad range of most of the earlier studies of postmenopausal women.

***BMI.*** More recent studies have focused on BMI as it is considered a more accurate measure of obesity than body weight. The relationship between BMI and breast cancer risk was broadly similar to that seen for body weight; high BMI was associated with decreased breast cancer risk premenopausally and increased breast cancer risk postmenopausally. The risk associated with premenopausal breast cancer generally varied between values which can be considered weak to moderate decreases in risk. For postmenopausal breast cancer the association with BMI varied fairly widely with values regarded as weak, moderate and strong. The Pooling Project reported a moderate decrease in the relative risk of breast cancer (0.58) among premenopausal women with a BMI less than 21 (the BMI for normal weight ranges between 18.5 and 25.9) compared to women with a BMI greater than 33 (the BMI for obesity is greater than 30). The same study reported a weak increase in the relative risk values for postmenopausal breast cancer among the heavier group of women (relative risk = 1.27) using the same BMI comparison groups.

Recent examinations have taken into account how the use of postmenopausal hormonal treatment by women within their studies can affect their evaluations (detail to follow below). Because this postmenopausal hormonal treatment can have a confounding effect, these studies also examined women who had never used postmenopausal hormone treatment to more accurately measure the effects of

obesity alone. Five cohort studies used this approach. These reports found about a doubling of postmenopausal breast cancer risk associated with obese BMI values. This relative risk value is considered a moderate increase in risk. Further, all five studies reported statistically significant increases in risk. These are important results which are considered reliable. Furthermore, these studies documented a statistically significant dose response relationship for risk. This means that as BMI values increased from normal weight to overweight and on to obesity there was a progressive increase in breast cancer risk. Normal weight women had the lowest risk, overweight women had higher risk and obese women had the highest risk.

Weight Gain. Since weight gain during adulthood is largely made up of fat, a number of studies have examined the effect of weight gain on breast cancer risk. Most studies focused on adult weight change (weight change after age 18 or 20) but more recent studies have tried to determine if there is a particular life period when weight change affects breast cancer risk to the greatest extent.

The relationship of weight gain to breast cancer risk is similar to that of body weight and BMI. Weight gain is related to a decrease in breast cancer risk premenopausally and an increase in breast cancer risk postmenopausally. Among premenopausal women who gain weight in adulthood there is a moderate decrease in breast cancer risk (relative risk of about 0.7) with adult weight gain. Among postmenopausal women, there is a moderate increase in breast cancer risk associated with adult weight gain. The relationship of weight gain to postmenopausal breast cancer has been highly consistent even for studies with quite different designs. The analysis of the relationship between weight gain and breast cancer risk is also modified by postmenopausal hormone treatment. Higher risk values are reported when women who never used postmenopausal hormones are analyzed separately. These values more accurately reflect the effect of adult weight gain itself (details below).

Studies have also examined if there are critical periods of weight gain during a woman's life. Although there are biological reasons to expect that weight gain during certain life periods would be important,

almost all studies have found that weight gain during adulthood, in general, is most important.

Weight Loss. Because there is a dose-response relationship between obesity and breast cancer risk, it would be hoped that weight loss would also be linked to decreases in breast cancer risk. This may be the case for weight loss during adulthood. However, adult weight loss is much less common than weight gain and fewer studies have examined this question. All four cohort studies that have examined weight loss and postmenopausal breast cancer risk found a weak, statistically uncertain association between breast cancer and adult weight loss. Two of these studies examined the modifying effect of postmenopausal hormone treatment. One study found a weak association and the other found a moderate to strong association (relative risk = 0.43) between weight loss and breast cancer risk. More study will be required to establish the extent of the decrease in breast cancer risk associated with weight loss. Nonetheless, the results of these studies and their biological foundation make weight loss a sensible, albeit difficult, way to decrease breast cancer risk.

Abdominal Body Fat Distribution. How weight is carried on the body, called body fat distribution, may be a modifier of the relationship between obesity and breast cancer risk. Body fat distribution is usually assessed by waist measurement alone or waist measurement divided by hip measurement (known as waist to hip ratio). Individuals with a large waist to hip ratio would have what is called an apple shaped body and those with a small ratio would have a pear shaped one. Fat which is carried on the body in the abdominal or stomach areas (apple shape, high waist or waist to hip ratio) is considered metabolically more active and this type of stature has been linked to an increase in the risk of cardiovascular disease and diabetes.

The results of studies that have examined the relationship between waist or waist to hip ratio and premenopausal breast cancer risk have been inconsistent so no firm conclusions can be made about this relationship.

Studies examining waist size or waist to hip ratio and postmenopausal breast cancer have also been inconsistent. The analysis

of this relationship is also modified by the use of postmenopausal hormone treatment and studies that have analyzed groups of women who have never taken hormones have been more consistent and demonstrated an increase in breast cancer risk among women with a high waist to hip ratio. The largest of these studies reported a moderate increase in risk (relative risk value of 1.9) for women with waists 36 to 55 inches around compared to women with waists up to 28 inches around.

There may be a genetic component to this effect. One large study has also reported that a family history of breast cancer may be an important modifier of waist to hip ratio and postmenopausal breast cancer risk. When women with a first degree relative with breast cancer (mother or sister) were examined separately there was a moderate increase in breast cancer risk for those women with the highest waist to hip ratio compared to women with the lowest waist to hip ratio. But surprisingly, no association was observed between waist to hip ratio and postmenopausal breast cancer risk for women without a family history of breast cancer. More study is needed before there is a clear understanding of these relationships.

### ***Biological Explanations of the Association of Obesity and Breast Cancer Risk***

Several biological models have used a synthesis of the above risk factors, reproductive endocrinology and basic cellular biology to explain the relationship between obesity and postmenopausal breast cancer risk. Three of the major hypotheses are discussed below.

1) Obesity leads to a larger exposure to estrogen which increases breast cancer risk. It is well established that the length and magnitude of exposure to estrogen within the body are linked to postmenopausal breast cancer risk. Women who are exposed to more estrogen due to a longer period of reproductive capacity or to higher levels of estrogen within their bodies are at higher risk of getting breast cancer. Studies have reported a direct relationship between body mass index and estrogen levels after, but not before, menopause, i.e., in post- but not premenopausal women. While their ovaries are no longer producing estrogen, postmenopausal

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women with higher BMI values have elevated estrogen levels. This increase is thought to arise from the activity of a metabolic pathway present in fat cells. The key enzyme in this pathway, aromatase, is able to produce estrogen from other hormones that are produced after menopause.

There is another avenue by which obesity is thought to lead to a larger exposure to estrogen. This is through decreases in the levels of the proteins in the blood that act as carriers for estrogen, the steroid hormone binding globulins. The loss of these carrier proteins make estrogen more available and increase its activities including those that are related to breast cancer formation.

2) Fat cells, themselves, produce substances that can increase breast cancer risk. Fat can be described as an endocrine organ as there are a number of hormone-like substances that are produced by fat cells themselves. Some of these would include leptin, adiponectin, resistin and tumor necrosis factor-alpha. Several of these substances have been shown to have growth effects on breast cells in the laboratory and increases in these substances could potentially increase breast cancer risk.

3) Obesity leads to other hormonal changes that can affect breast cancer risk: Insulin Related Pathways. Obesity can also have effects on the levels of insulin and a related hormone, insulin like growth factor (IGF) levels. Both insulin and IGF can affect the growth of breast cells, and may also have effects on estrogen and its carrier proteins.

A mechanism for the decrease in breast cancer risk in premenopausal obese women. The above discussion of the effects of obesity on estrogen and other hormone levels following menopause raises the question as to how obesity can have the opposite effect on breast cancer risk before and after menopause. The most favored hypothesis for this paradox is built around levels of proliferation, or cell multiplication, in the breast. Cancer risk can, in general, be related to how rapidly cells are multiplying or proliferating within a tissue in question, including the breast. Thus, the cells that have the highest risk of becoming cancer are those that have the highest levels of proliferation. Estrogen and progesterone are considered the main hormones that affect proliferation in the breast. As

discussed above, the production of estrogen by fat cells in postmenopausal women is thought to be a likely mechanism for the association of obesity and postmenopausal breast cancer risk. Obese postmenopausal women are exposed to more estrogen and would be likely to have higher levels of breast proliferation (and breast cancer risk) than normal weight women. The opposite is the case for obese premenopausal women. Obese premenopausal women have been shown to have irregular menstrual cycles and less frequent ovulation. This disorder leads to disturbances in the production of one of the hormones linked to breast proliferation, progesterone. Thus, the breasts of obese premenopausal women undergo less proliferation, an effect which would be associated with a decrease breast cancer risk. Most women, who are obese before menopause, are also obese after menopause, but it is currently uncertain if there may or may not be some carry-over of the protective effect after menopause.

#### ***Modification of the Association of Obesity and Breast Cancer Risk***

Interactions between risk factors can have a substantial impact both clinically and for the study of a disease. Several risk factors have been reported to interact with and modify the effect of obesity on breast cancer. There are two major ways in which this can occur. First, the risk factor could modify the association itself by increasing or decreasing the actual breast cancer risk related to obesity. Second, the risk factor could modify the evaluation of the risk relationship and give the appearance that the association between obesity and breast cancer risk was less or more than it actually was.

Postmenopausal hormone treatment, commercially known as hormone replacement therapy, is the most thoroughly studied modifying factor of the relationship between obesity and breast cancer risk. A number of studies have found that postmenopausal hormone treatment must be accounted for when evaluating obesity and breast cancer risk as it may modify the risk analysis itself. Both obesity and postmenopausal hormone treatment are thought to mechanistically affect breast cancer risk by increasing levels of the hormone, estrogen, in the body. Such changes in estrogen levels would be increased to a

greater degree in women with normal weight compared to women who are obese. As a result, the breast cancer risk of women of normal weight (control subjects) who were using postmenopausal hormone treatment would be affected to a larger extent than obese women (exposed subjects) using postmenopausal hormone treatment. Early analyses of obesity and breast cancer risk analysis did not account for postmenopausal hormone treatment's effect on control subjects. This is important because the control subject's risk levels serve as the reference values for the relative risk calculations. More recent obesity and breast cancer studies have separately examined women who have never used postmenopausal hormone treatment. These, more careful, evaluations have reported a larger association of obesity and breast cancer risk than analyses which do not take postmenopausal hormone treatment into consideration. Studies of this type more accurately reflect the true association of obesity and breast cancer risk.

Less well established are risk modifications linked to the use of alcohol, age, a family history of breast cancer, and physical activity.

#### ***Obesity and Breast Cancer Risk: The Forest from the Trees***

In the end, as far as breast cancer risk reduction is concerned, what matters is how obesity compares to the other established breast cancer risk factors and contributes to the incidence of breast cancer. Obesity should be seen as one of the most important breast cancer risk factors for several reasons. First, relative to most breast cancer risk factors, obesity is associated with about a doubling of the risk of the most common form of breast cancer, postmenopausal breast cancer. Although this is considered only a moderate level of risk, most of the other established breast cancer risk factors would fall into the weak category. Second, unlike the majority of the other breast cancer risk factors, obesity can be modified by both weight loss and prevention of weight gain. Although it is not firmly established that weight loss decreases the risk of breast cancer, this is very likely to be the case. Prevention of weight gain has been described as the critical first step toward dealing with this problem. Third, obesity is common among U.S.

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women and thus obesity makes a substantial contribution to the incidence of breast cancer. Studies of what is called the attributable risk of breast cancer from obesity postulate that if obesity could be eliminated there would be a substantial 30% to 50% decrease in the number of cases of breast cancer. Finally, obesity negatively affects all aspects of breast cancer survival. Obese women are diagnosed at a more advanced stage of breast cancer. Their recurrence of breast cancer is more frequent and their survival time has been shown to be shorter.

Obesity is also linked with a number of health disturbances other than breast cancer. This includes other forms of cancer, cardiovascular disease, diabetes and arthritis.

Our program is currently conducting

research to develop a project to decrease breast cancer risk by preventing weight gain. This unique approach to breast cancer risk reduction attacks this problem at the community level and works to change eating habits and increase physical activity. Weight gain has been shown to occur gradually and our aim is to prevent weight gain by making small changes in daily lifestyle. These studies are in progress but preliminary data shows considerable promise.

**Authors:**

**Barbour S. Warren, PhD**

Dr. Barbour S. Warren is a Research Associate in the Breast Cancer and Environmental Risk Factors Program in the Sprecher Institute of Comparative Cancer Research at Cornell University. He studies

diet and lifestyle factors which affect breast cancer risk. His current research involves the development of community environmental programs to prevent weight gain and decrease breast cancer risk.

**Carol M. Devine, PhD, RD**

Dr. Carol M. Devine is Associate Professor and Extension Leader in the Division of Nutritional Sciences at Cornell University. She studies continuity and change in women's nutrition practices over the life course and how these practices are affected by work and family roles. Her current research includes: a study of work-family spillover and the food choices of working parents, a worksite obesity prevention trial, and a community environmental weight gain prevention trial.

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**RECENT NEWS ITEMS**

**Raloxifene – Results of the RUTH Study**

The New England Journal of Medicine published results in its July 13, 2006 issue of a study designed to test whether raloxifene was better than a placebo pill at reducing breast cancer and heart-related risks in women with known heart disease or at high risk for heart attack. More than 10,000 postmenopausal women in the U.S. and 25 other countries were enrolled in the study, which was paid for by the drug manufacturer, Eli Lilly and Company. The

drug, sold under the name Evista®, is FDA-approved for osteoporosis but the company is seeking approval to market it for breast cancer prevention.

Women in the Raloxifene Use for The Heart (RUTH) study had clogged arteries or multiple heart risk factors such as advanced age, diabetes, smoking, high blood pressure or high cholesterol. Approximately 40% of the participants also had elevated risk of breast cancer. After five years, while deaths and major heart problems were about equal between the two groups, the study revealed that the reduced risk of fractures (particularly ver-

tebral fractures) and reduced risk of breast cancer from raloxifene were offset by increases in strokes and blood clots in the veins. In its statement of preliminary results from the RUTH study in April 2006, the company stated that because Evista did not prevent coronary events, it wanted to reinforce for physicians that Evista should not be prescribed for cardioprotection. With the final study results now analyzed, doctors are suggesting that postmenopausal women need to take into account their unique risk factors for breast cancer, heart disease and osteoporosis if considering treatment with raloxifene.

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**SAVE THE DATE - "DAY OF HOPE"**

On Saturday, September 30, 2006, from 9 a.m. to 1 p.m., there will be a program entitled "Day of Hope: Improving Cancer Care on the East End" held at the Bay Street Theatre in Sag Harbor, L.I. The program is organized and co-sponsored by Fighting Chance: Life Skills for Cancer Patients, a Suffolk County non-profit organization set up in 2001, and Southampton Hospital. While admission is free, registration is required. To register, call (631)725.4646.

The program will feature the following speakers and subjects:

**Speakers from The Cancer Center at  
Stony Brook University Hospital**

"New Attacks on Lung Cancer", Theodore G Gabig, MD, Chief, Div. of Hematology/Oncology  
"Innovative Clinical Trials to Prevent and Treat Prostate, Bladder and Kidney Cancer", Christopher S.D. Lee, MD, Director of Urologic Oncology

"Closer To A Cure: Improving Cancer Care in Suffolk County", Martin S. Karpeh, Jr., MD, Director of The Cancer Center and Chief, Div. of Surgical Oncology (Keynote Address)

**Other Speakers from the East End**

"Ask the Experts", Q & A with Louis Avvento, MD (Panel Moderator)  
"News on Nutrition for Cancer Survivors", Donald Garrity, RD, Nutritionist at Memorial Sloan-Kettering Cancer Center, NYC  
"Coping Strategies for Chemo & Radiation", Renu Hausen, MD, Radiation-Oncologist  
"Cancer Survivors' Journey", Chan Bigalow (prostate cancer) and Susie Roden (breast cancer)

**Panel Discussion**

"Patient Empowerment & Community Support", led by Karrie Zampini Robinson, LCSW, Director of Clinical Programs at Fighting Chance

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## **CALENDAR**

### **SHARE** (*Self-Help for Women with Breast or Ovarian Cancer*)

1501 Broadway, Ste. 704A  
New York, NY

Also: QueensSHARE, HarlemSHARE,  
and BrooklynSHARE

[www.sharecancersupport.org](http://www.sharecancersupport.org)  
212.719.0364

SHARE Breast Cancer Hotline  
212.382.2111

SHARE Ovarian Cancer Hotline  
212.719.1204

### MEMORIAL SLOAN KETTERING CANCER CENTER

*Post-Treatment Resource Program  
Educational Forums*

1275 York Avenue- Room-M107  
New York, NY 10021

[www.ptp@mskcc.org](http://www.ptp@mskcc.org)  
212.717.3527

#### *Clinical Genetics Service*

222 East 70th Street (betw. 2nd & 3rd  
Aves.)

New York, NY 10021  
212.434.5149

Offers hereditary cancer risk assessment,  
genetic counseling, and genetic testing by  
genetic counselors and physicians

### **ADELPHI NY STATEWIDE BREAST CANCER**

*Hotline & Support Program*

Adelphi University School of Social Work  
Garden City, NY 11530

[www.breastcancerhotline@adelphi.edu](mailto:www.breastcancerhotline@adelphi.edu)

### **CANCERCARE**

1.800.813.HOPE (4673)

[info@cancercare.org](mailto:info@cancercare.org)

## **JALBCA**

c/o Jennifer Fiorentino  
Executive Director  
1324 Lexington Avenue, PMB 324  
New York, New York 10128  
[www.jalbca.org](http://www.jalbca.org)

