New For You:
Updates in Testing and Treatment Options for Hereditary Breast and Ovarian Cancer

Tuesday, November 17, 2015

To listen to the presentation by phone,
Dial: 800-862-9098
Code: SHARSHERET
WELCOME

Shera Dubitsky, MEd, MA
Director of Navigation and Support Services
Sharsheret

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THANK YOU

And the Cooperative Agreement DP14-1408 from the Centers for Disease Control and Prevention

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Sharsheret is a national not-for-profit organization supporting young Jewish women and their families facing breast cancer. Our mission is to offer a community of support to women, of all Jewish backgrounds, diagnosed with breast cancer or at increased genetic risk, by fostering culturally-relevant individualized connections with networks of peers, health professionals, and related resources.

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• 1 in 40 Ashkenazi Jews carries a BRCA gene mutation

• 80% risk of breast cancer

• 40% risk ovarian cancer
UPDATES IN TESTING AND TREATMENT OPTIONS

Sheila Solomon, MS, LGC
Genetics Program Coordinator
Sharsheret

Inherited Cancer Genetic Counselor
GeneDx

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AGENDA FOR THIS EVENING

• Welcome!
• Review and Updates in Inherited Breast Cancer and Ovarian Cancer
• Next Steps for You and Your Families

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WHAT IS GENETIC ABOUT BREAST CANCER AND OVARIAN CANCER?

• Cancer is a common disease
• Cancer can occur in family members even when there is no hereditary cause
• For some families, there is a hereditary pattern to cancer...

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RISK FACTORS FOR BREAST CANCER

• Aging
• Family History
• Personal History of Cancer
• Hormonal Factors:
  – Beginning periods before age 12
  – Later menopause (change of life)
  – Not having biological children or having them later in life
• Lifestyle Exposure
RISK FACTORS FOR OVARIAN CANCER

• Aging
• Family History
• Personal History of Cancer
• Hormonal Factors:
  – Not having biological children
• Lifestyle Exposure

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HEREDITARY VS. SPORADIC CANCER

All cancer is genetic, but not all cancer is hereditary

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• 5-10% of all breast cancers are hereditary
• 25% of all ovarian cancers are hereditary
• What does this mean for ME?
OUR GENES, LIKE BOOKS...

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An estimated 1 in 40 Ashkenazi Jews carries a BRCA1 or BRCA2 mutation.
COMING TO AMERICA

1 in 40 Ashkenazi Jews with a BRCA1 or BRCA2 mutation

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CANCER RISKS IN BRCA1 AND BRCA2 MUTATION CARRIERS

• BRCA1
  – Breast 40-85%
  – Second Breast 40-60%
  – Ovarian 24-54%

• BRCA2
  – Breast 40-85%
  – Second Breast 40-60%
  – Ovarian 11-27%

Other cancer risks include: Prostate, Pancreatic, Male Breast Cancer and in some families Gastric and Melanoma

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MALE BREAST CANCER

• Accounts for ~1% of all breast cancer (rare)
• BRCA1 Mutation Carriers
  – Male breast cancer risk elevated over the general population
• BRCA2 Mutation Carriers
  – Up to 7% male breast cancer risk

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• BRCA1 and BRCA2 are not the only players in the game – Panels are here to stay
• Lifestyle Changes
• Population Screening
• Treatment Updates
• Online Research Databases and Studies
IT’S MORE THAN JUST BRCA1 AND BRCA2

<table>
<thead>
<tr>
<th>Gene</th>
<th>Cancers Linked with Gene Mutations</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATM</td>
<td>Breast, Pancreatic, Colon</td>
</tr>
<tr>
<td>CDH1</td>
<td>Breast, Diffuse Gastric</td>
</tr>
<tr>
<td>CHEK2</td>
<td>Female and Male Breast, Ovarian, Endometrial, Colon, Others</td>
</tr>
<tr>
<td>PALB2</td>
<td>Female and Male Breast, Ovarian, Pancreatic</td>
</tr>
<tr>
<td>PTEN</td>
<td>Breast, Thyroid, Endometrial, Colon</td>
</tr>
<tr>
<td>STK11</td>
<td>Breast, Pancreatic, Small Intestine, Others</td>
</tr>
<tr>
<td>TP53</td>
<td>Breast, Brain, Leukemia, Lymphoma, Lung, Others</td>
</tr>
</tbody>
</table>

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INHERITED CANCER PANEL TESTING FOR MULTIPLE GENES

• Many laboratories offering Next Generation Sequencing
  – Analysis of many genes at the same time
  – Fraction of the price from years’ past
• Panels provide more information in a single test
• Important to discuss options with a certified genetic counselor or genetics healthcare provider prior to ordering testing

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• Rinsky et al (2015)
  – Studied 3,532 patients with Ashkenazi Jewish heritage undergoing Panel Testing
  – AJ Panel Testing:
    • BRCA1 and BRCA2 non-founder mutations: 20%
    • CHEK2 mutations: 16.9% (majority were founder mutation)
    • ATM mutations: 12.3%
    • Many other genes with mutations

• What does this mean to ME?
CANCER RISKS IN CHEK2

• Leedom et al (2015)
  – Studied the family histories of cancer in over 500 individuals with CHEK2 mutations
  – No significant difference between the type of mutation in CHEK2
  – Cancer risks observed in patients with CHEK2 founder mutations can be generalized to all CHEK2 mutations
  – What does this mean for ME?

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NEWER GENES LINKED WITH BREAST CANCER IN YOUNG WOMEN

• Andolina et al (2015) studied 848 young women with breast cancer diagnosed at age 45 or younger
  – Inherited cancer panel testing
  – 1 in 10 women had a BRCA1 or BRCA2 mutation
  – 61% of the mutations were not in BRCA1 or BRCA2
  – In fact, half of mutations in newer described genes
  – What does this mean for ME?
LIFESTYLE MODIFICATIONS

• Breast self awareness
  – Normal breast look/feel
  – Personal and family history risk factors
  – Mammograms

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Recent public media and press

Population-based screening for breast and ovarian cancer risk due to BRCA1 and BRCA2

Efrat Gabai-Kapara, Amnon Lahad, Bella Kaufman, Eitan Friedman, Shlomo Segev, Paul Renberg, Rachel Beeri, Moran Gal, Julia Grinshpun-Cohen, Karen Raphael, Catane, Mary-Claire King, and Ephrat Levy-Lahad

Medical Genetics Institute, Sheba Zedek Medical Center, Jerusalem 91031, Israel; Department of Family Medicine, Ophir Health Services, Jerusalem, Israel; Susanne Levy Gertner Oncogenetics Unit, Sheba Medical Center, Tel-Aviv 69978, Israel; Institute of Medical Screening, Sheba Medical Center, Tel-Aviv, Israel; Departments of Medicine and Genomic Sciences, University of Washington, Seattle, Washington, US

Contribution by Mary-Claire King, August 19, 2015 (sent for review July 17)

In the Ashkenazim Jewish (AJ) population of Israel, 11% of breast cancer and 40% of ovarian cancer are due to two inherited founder mutations in the predisposition genes BRCA1 and BRCA2. Carriers of these mutations, risk-reducing salpingectomy significantly reduces morbidity and mortality. Population screening for these mutations among AJ women may be justifiable if accurate estimates of cancer risk for mutation carriers can be obtained. We therefore undertook to determine risks of breast and ovarian cancer for BRCA1 and BRCA2 mutation carriers ascertained irrespective of personal or family history of cancer. Families harboring mutations in BRCA1 or BRCA2 were ascertained by identifying mutation carriers among healthy AJ males recruited from health screening centers and outpatient clinics. Female relatives of the carriers were then enrolled and genotyped. Among the female relatives with BRCA1 or BRCA2 mutations, cumulative risk of developing breast or ovarian cancer by age 60 was 80%, respectively, were 0.60 (± 0.07) and 0.83 (± 0.07) for BRCA carriers and 0.33 (± 0.09) and 0.76 (± 0.13) for BRCA2 carriers. Risk

The Breast Cancer Gene and Me

By ELIZABETH WURTZEL SEPT. 25, 2015

I DID not know I have the BRCA mutation. I did not know I would likely develop cancer. I was still young, when the disease is a wild animal. I caught it. I acted fast. I must have looked away: By the time of my double mastectomy, cancer had spread to five lymph nodes.

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PARP inhibitors

– What are they?

– Who can they help?
WHAT’S NEXT?

• Stay in touch!
• Research and Public Databases
• Find a local genetic counselor:
  – National Society of Genetic Counselors

www.nsgc.org

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Lara, a Sharsheret Link, shares her personal story about her genetic history and experience with genetic testing.

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QUESTION & ANSWER SESSION

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info@sharsheret.org
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