BRCA in Men

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BRCA in Men

- Inheritance patterns of BRCA1/2
- Cancer Risks for men with BRCA1/2 mutations
- Risk management recommendations for men with BRCA1/2 mutations
- Involvement of men in the risk communication process
BRCA1

- BRCA1 was cloned in 1994
- BRCA1 is located on chromosome 17q21
- Autosomal dominant transmission
- ~1000 different mutations (mutations, polymorphisms, and variants) reported

Nonsense  Missense  Splice-site
BRCA2

- BRCA2 was cloned in 1995
- BRCA2 is located on chromosome 13q12-13
- Autosomal dominant transmission
- ~1000 different mutations (mutations, polymorphisms, and variants) reported

[Diagram with categories: Nonsense, Missense, Splice-site]
Pedigree: Hereditary Breast/Ovarian Cancer

- BREAST, 62
- OVARY, 49

- BREAST, 44
- OVARY, 52

- PROSTATE, 52

- BREAST, 47

- BREAST, 30

- OVARY, 32

- BILATERAL BREAST, 40
### Cancer Risks for Male Carriers Of BRCA Mutations

<table>
<thead>
<tr>
<th>Organ</th>
<th>U.S. White Male</th>
<th>BRCA1 (%)</th>
<th>BRCA2 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>0.11</td>
<td>↑</td>
<td>7.0</td>
</tr>
<tr>
<td>Prostate</td>
<td>16.2</td>
<td>33</td>
<td>↑</td>
</tr>
<tr>
<td>Pancreas</td>
<td>1.2</td>
<td>3.0 – 4.0</td>
<td>2.0 – 8.0</td>
</tr>
</tbody>
</table>

Liede et al, 2005
Risks for Women vs Men in BRCA Families

- **Breast**: 85% (Women) vs 10% (Men)
- **Ovary**: 60% (Women) vs 8% (Men)
- **Prostate**: 33% (Men)
- **Pancreas**: 10% (Men)

**Lifetime Risk For Cancer**
Factors Affecting Penetrance

- Modifier genes
- Response to DNA damage
- Hormonal factors
- Carcinogens

Not everyone with an altered gene develops cancer.
Hereditary Breast and/or Ovarian Cancer

**MEN**
- Breast self-exam training and education and regular monthly BSE.
- Clinical breast exam, semiannually.
- Consider baseline mammogram; annual mammogram if gynecomastia or parenchymal/glandular breast density on baseline study.
- Adhere to screening guidelines for prostate cancer (See NCCN Prostate Cancer Early Detection Guidelines).

**MEN and WOMEN**
- Education regarding signs and symptoms of cancer(s), especially those associated with BRCA gene mutations.
- Refer to appropriate NCCN guidelines for other cancer screening. (See NCCN Guidelines for Detection, Prevention, & Risk Reduction of Cancer).
Hereditary Breast and/or Ovarian Cancer

RISK TO RELATIVES
• Advise about possible inherited cancer risk to relatives, options for risk assessment, and management.
• Recommend genetic counseling and consideration of genetic testing for at-risk relatives.

REPRODUCTIVE OPTIONS
• For couples expressing the desire that their offspring not carry a familial BRCA mutation, advise about options for prenatal diagnosis and assisted reproduction, including pre-implantation genetic diagnosis. Discussion should include known risks, limitations, and benefits of these technologies.
• For reproductive-age BRCA2 mutations carriers, discussion of risk of a rare (recessive) Fanconi anemia/brain tumor phenotype in offspring of populations with an increased population frequency of founder mutations.
What Do We Know about the Communication of Genetic Risk in a Family?

Men are:

- Less likely to be informed about hereditary pattern of cancer in their family
- Less likely to be included in family conversations about genetic risk
- Less likely to be fully informed about genetic test results
- Less likely to be tested themselves
- Less likely to be tested for their own benefit
Why are Men Underrepresented in Conversations about \textit{BRCA1/2}?

1. Predominant cancers are female
   - Confusion about inheritance of female cancers through paternal side of the family
   - Lack of awareness of male breast cancer
   - Lack of awareness of other cancers in the syndrome
   - Fewer management strategies available
Why are Men Underrepresented in Conversations about $BRCA1/2$?

2. Gender Differences in Health Roles
   - Women usually the caregivers in the family and are often responsible for the communication of health information
   - Women more likely to experience vulnerability to health threats
   - Men more likely to minimize health threats, perceive illness as a weakness, or use avoidance techniques
3. Gender Differences in Family Relationships
   - Women more likely to turn to each other for emotional support
   - Perceived discomfort with discussing genetic information with male members of the family
   - Biologic vs. social ties

Why are Men Underrepresented in Conversations about BRCA1/2?
Why are Men Underrepresented in Conversations about *BRCA*1/2? 

4. Psychologic Reaction to Genetic Risk
   - Guilt
   - Worry
   - Isolation
   - Loss of control
Some General Barriers to Information Exchange

- Lack of perceived usefulness
- Serious nature of the message
- Difficult or distant family relationships
- Reluctance to share upsetting or alarming information
- Fear of rejection
Familial Dynamics Effect

- Family organization
- Family beliefs
- Family communication process
- Patterns of coping
- Life cycle challenges
Why is this Important?

- Genetic information has implications for other family members
- The proband is expected to be the first conduit of genetic information
- Yet interpretation of genetic information is complex and often uncertain