IDENTIFICATION AND MANAGEMENT OF HEREDITARY CANCER SYNDROMES

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Objectives

- Review of clinical features and diagnostic criteria of hereditary cancer syndromes
- Update on national recommendations and/or consensus guidelines for surveillance, chemoprevention, and surgical options
- Present psychosocial, ethical, and legal implications associated with genetic testing
Disease-Associated Mutations Alter Protein Function

- Functional protein
- Nonfunctional or missing protein
THE DEVELOPMENT OF HEREDITARY CANCER

2 normal genes → 1 damaged gene → 2 damaged genes → Tumor develops

In hereditary cancer, one damaged gene is inherited.

1 damaged gene → 1 normal gene → 2 damaged genes → Tumor develops
SOCIETAL STANDARDS AND GUIDELINES

- ACCC – Association of Community Cancer Centers
- ACOG – American Congress of Obstetricians and Gynecologists
- AMA – American Medical Association
- ASBS – American Society of Breast Surgeons
- ASCO – American Society of Clinical Oncologists
- NCCN – National Comprehensive Cancer Network
- NSGC – National Society of Genetic Counselors
- ONS – Oncology Nursing Society
- SGO – Society of Gynecologic Oncologists
- SSO – Society of Surgical Oncology
- USPSTF – U.S. Preventive Services Task Force
Genetic testing for high risk individuals

- Societal Standards and Guidelines
  - ACOG – America Congress of Obstetricians and Gynecologists
  - AMA – American Medical Association
  - ASCO – American Society of Clinical Oncologists
  - NCCN – National Comprehensive Cancer Network
  - SGO – Society of Gynecologic Oncologists
  - SSO – Society of Surgical Oncology
  - USPSTF – US Preventive Services Task Force
  - ACCC - Association of Community Cancer Centers
  - NSGC – National Society of Genetic Counselors
  - ASBS – American Society of Breast Surgeons
Genetic Predisposition Testing Is a Multistep Process

Identify at-risk patients
Provide pretest counseling
Provide informed consent
Select and offer test
Disclose results
Provide posttest counseling and follow-up


Cancer Genetics Professionals Can Assist With

- Pedigree interpretation and cancer risk assessment
- Complex psychosocial issues
- In-depth counseling and education
- Ordering and interpreting genetic tests
- Facilitating entry into clinical studies

International Society of Nurses in Genetics. Available at:


When to Suspect Hereditary Cancer Syndrome

- Cancer in two or more close relatives (on same side of family)
- Early age at diagnosis
- Multiple primary tumors in the same individual
- Bilateral or multiple rare cancers
- Constellation of tumors consistent with specific cancer syndrome (e.g., breast and ovary)
- Evidence of autosomal dominant transmission, including:
  - Multiple affected generations
  - Presence of congenital anomalies or syndromes associated benign lesions

Hereditary Breast Cancer

- Hereditary Breast Ovarian Cancer Syndrome
- Li Fraumeni Syndrome
- Cowden Syndrome
- Peutz Jegher (reviewed as GI syndrome)
- Hereditary Diffuse Gastric Cancer (reviewed as GI syndrome)
Hereditary Breast Ovarian Cancer Syndrome (HBOC)

- **Gene:** BRCA1 and BRCA2
- **Carrier frequency:** 1/500 to 1/1,000
  - Ashkenazi Jewish: 1/40

<table>
<thead>
<tr>
<th>Cancer site</th>
<th>BRCA1 Lifetime risk %</th>
<th>BRCA2 Lifetime risk %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>55-85%</td>
<td>55-85%</td>
</tr>
<tr>
<td>Contralateral Breast</td>
<td>40-60%</td>
<td>40-60%</td>
</tr>
<tr>
<td>Ovary</td>
<td>20-45%</td>
<td>10-20%</td>
</tr>
<tr>
<td>Male Breast</td>
<td>1-2%</td>
<td>6-8%</td>
</tr>
<tr>
<td>Pancreatic</td>
<td>Variable depending on study</td>
<td>7%</td>
</tr>
<tr>
<td>Prostate, Melanoma, Gastric</td>
<td>Variable depending on study</td>
<td>Variable depending on study</td>
</tr>
</tbody>
</table>
Diagnosis

- BRCA 1 and BRCA 2 germline genetic testing
  - Patented gene
  - BRCA sequencing
  - Deletions/duplications/rearrangements (BART)
    - More prevalent in African American and Latinos
    - Most recent revision to NCCN guidelines recommend including BART on all patients

- Personal and Family History
  - Multiple generations of early onset breast cancer + ovarian cancer
  - Negative BRCA results
  - Follow HBOC surveillance and surgery recommendations
## Surveillance and Risk Reduction

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<td>Breast (55-85%)</td>
<td>• Annual mammogram and breast MRI</td>
<td>25y</td>
</tr>
<tr>
<td></td>
<td>• Clinical Breast exam every 6 months</td>
<td>25y</td>
</tr>
<tr>
<td></td>
<td>• Discussion of prophylactic mastectomy</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Chemoprevention (i.e. tamoxifen) for women electing breast conservation</td>
<td></td>
</tr>
<tr>
<td>Ovarian (20-45%)</td>
<td>• Transvaginal ultrasound and CA-125 levels every 6 months</td>
<td>30y</td>
</tr>
<tr>
<td></td>
<td>• Recommend BSO</td>
<td>35-40y</td>
</tr>
<tr>
<td></td>
<td>• Chemoprevention (i.e. OCP)</td>
<td></td>
</tr>
<tr>
<td>Male Breast (6%)</td>
<td>• Clinical Breast exam every 6-12 months</td>
<td>35y</td>
</tr>
<tr>
<td></td>
<td>• Consider baseline mammogram</td>
<td>40y</td>
</tr>
<tr>
<td>Pancreatic (7%)</td>
<td>• No recommendations</td>
<td></td>
</tr>
</tbody>
</table>
Clinical Considerations

- Surgical decision making
  - BRCA status can be valuable information for patients considering lumpectomy vs mastectomy
  - Beneficial to offer genetic counseling/testing before surgery

- Chemotherapy/Clinical Trials
  - PARP Inhibitors
Li Fraumeni syndrome

- p53 gene (also CHEK2)
- Autosomal dominant with up to 20% de novo
- Core cancers
  - Sarcomas (soft tissue and osteosarcomas)
  - Breast cancer
  - Hematologic malignancies
  - Malignant brain tumors
  - Adrenocortical carcinoma
- Widely variable expressivity with regards to cancer type – predominant feature is age of onset
- 50% of patients have first cancer before age 30, 90% by age 50
- Nearly 100% lifetime risk for cancer in females, slightly lower for males
Diagnosis

- Personal and Family History
  - Classic criteria
  - Chompret criteria
  - Birch criteria
  - Eeles criteria

- p53 germline sequencing and del/dup/rearrangements

- Strongly suggest involvement of pre-test genetic counseling
Clinical Description

- **Classic LFS**
  - Proband diagnosed with sarcoma before 45 years of age, and
  - A first-degree relative with cancer before 45 years of age, and
  - Another first- or second-degree relative with any cancer diagnosed under 45 years of age or with sarcoma at any age

- **Chompret (Li Fraumeni-Like)**
  - Proband with tumor belonging to LFS tumor spectrum (e.g., soft tissue sarcoma, osteosarcoma, brain tumor, premenopausal breast cancer, adrenocortical carcinoma, leukemia, lung bronchoalveolar cancer) before age 46 years
  - AND at least one first- or second-degree relative with LFS tumor (except breast cancer if proband has breast cancer) before age 56 years or with multiple tumors; OR
  - Proband with multiple tumors (except multiple breast tumors), two of which belong to LFS tumor spectrum and first of which occurred before age 46 years; OR
  - Patient with adrenocortical carcinoma or choroid plexus carcinoma
Surveillance and Risk Reduction

- High risk breast surveillance protocol vs mastectomy
- Colonoscopy every 2-5 years starting no later than 25y
- Otherwise, efficacy of surveillance is limited
  - Annual physical with special attention to derm and neurologic findings
  - Emerging data on annual rapid whole-body MRI
    - NIH study for Li Fraumeni families to evaluate novel screening approaches involving age-specific biochemical markers and imaging techniques
Clinical Considerations

- Susceptibility to radiation-induced sarcoma
  - Pt with breast ca and p53 mutation - favor mastectomy over lumpectomy and radiation

- Consider as a differential for breast ca <30y with BRCA negative testing
Cowden syndrome

- PTEN gene
- PTEN Hamartoma Tumor Syndrome
  - Major
    - Macrocephaly
    - Oral papillomas, trichilemmomas
    - Breast cancer
    - Non-medullary thyroid cancer
    - Uterine ca
    - Hamartomatous polyps
  - Minor
    - Papillary renal ca
    - Thyroid goiter/nodules
    - Benign breast disease
    - Mental Retardation/Learning Disabilities
    - AVMs
Diagnosis

- Personal and Family History
  - Features that warrant further testing:
    - Two major criteria
    - One major and two minor criteria
    - Three minor criteria involving different organ systems

- PTEN germline sequencing and del/dup/rearrangements
  - Research testing at Cleveland Clinic
  - Clinical testing
## Cancer Risks and Management

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<tr>
<th>Cancer Site (lifetime risk)</th>
<th>Management</th>
<th>Age of Initiation</th>
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<tr>
<td>Breast (25-50%)</td>
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</tr>
<tr>
<td></td>
<td>• Clinical Breast exam every 6 months</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Discussion of prophylactic mastectomy</td>
<td></td>
</tr>
<tr>
<td>Uterus (10%)</td>
<td>• Annual pelvic exam and Pap</td>
<td>18y</td>
</tr>
<tr>
<td></td>
<td>• Review signs and symptoms of cancer</td>
<td>18y</td>
</tr>
<tr>
<td></td>
<td>• Discussion of prophylactic hysterectomy</td>
<td></td>
</tr>
<tr>
<td>Thyroid (10%)</td>
<td>• Baseline thyroid ultrasound</td>
<td>18y</td>
</tr>
<tr>
<td></td>
<td>• Consider annual thyroid ultrasound vs physical exam</td>
<td>18+y</td>
</tr>
<tr>
<td>Mucocutaneous –benign</td>
<td>• Annual dermatologic exam</td>
<td>10y</td>
</tr>
<tr>
<td>(99%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colon (9%)</td>
<td>• Consider colonoscopy every 5-10 years</td>
<td>35y</td>
</tr>
</tbody>
</table>
Breast Referral Guidelines – Affected Individual

- **Patient with:**
  - Breast ca dx <50y
  - Triple negative dx <60y
  - Epithelial ovarian ca dx any age
  - Male breast ca dx any age
  - Bilateral breast ca
  - Breast cancer and Ashkenazi Jewish ancestry
  - Breast PLUS sarcoma, thyroid, endometrial, diffuse gastric, pancreatic, adrenocortical carcinoma, and/or early onset leukemia

  *No additional family history required**

- **Patient with breast ca dx >50y and**
  - 1 family member ovarian any age or breast dx <50y
  - 2 family members with breast dx >50y
  - Sarcoma, thyroid, endometrial, diffuse gastric, pancreatic, adrenocortical carcinoma, and/or early onset leukemia on same side of family
Referral Guidelines – Unaffected Individual

- Ideal candidate for testing are affected individuals
  - Results are more informative
- Family history of 1st or 2nd degree relative with any of the criteria above
Hereditary GI Cancer Syndromes

- Lynch syndrome (HNPCC)
- Familial Adenomatous Polyposis
- MYH Associated Polyposis
- Overlap with breast cancer syndromes
  - Peutz Jeghers
  - Hereditary Diffuse Gastric Cancer
Lynch Syndrome

- Hereditary NonPolyposis Colon Cancer (HNPCC)
  - 2-3% of all colorectal and endometrial cancer diagnoses
  - Caused by mutations in one of multiple genes in the mismatch repair family
    - MLH1
    - MSH2
    - MSH6
    - PMS2
    - EpCAM (upstream of MSH2)
<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>General Population</th>
<th>Lynch Syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colon</td>
<td>5-6%</td>
<td>80%</td>
</tr>
<tr>
<td>2nd colon within 10 years</td>
<td></td>
<td>30%</td>
</tr>
<tr>
<td>Endometrial</td>
<td>2-3%</td>
<td>20-60% (gene specific)</td>
</tr>
<tr>
<td>Stomach</td>
<td>1%</td>
<td>6-13%</td>
</tr>
<tr>
<td>Ovarian</td>
<td>1-2%</td>
<td>9-12%</td>
</tr>
<tr>
<td>Hepatobiliary</td>
<td>1%</td>
<td>2-7%</td>
</tr>
<tr>
<td>Urinary tract</td>
<td>&lt;1%</td>
<td>4-5%</td>
</tr>
<tr>
<td>Small Bowel</td>
<td>&lt;1%</td>
<td>&lt;4%</td>
</tr>
<tr>
<td>CNS</td>
<td>&lt;1%</td>
<td>&lt;3%</td>
</tr>
</tbody>
</table>
Diagnosis

- Amsterdam criteria
- Bethesda criteria
- MSI/IHC tumor testing
- Germline molecular genetic testing
Amsterdam Criteria II

- Three or more relatives with verified HNPCC-associated cancer (CRC, cancer of the endometrium, small bowel, ureter, or renal pelvis) in family
  - any combination of histologies in three different relatives
  - One case a first-degree relative of the other two
- At least two successive generations affected
- One or more cancer cases by age 50 years
- FAP excluded

Failure to meet these criteria does not exclude HNPCC

Bethesda Guidelines

- Patients who meet Amsterdam Criteria
- Colorectal or uterine cancer diagnosed in a patient who is less than 50 years of age
- Presence of synchronous, metachronous colorectal, or other HNPCC-associated tumors, regardless of age.
- Colorectal cancer with the MSI-H histology diagnosed in a patient who is less than 60 years of age.
- Colorectal cancer diagnosed in one or more first-degree relatives with an HNPCC-related tumor, with one of the cancers being diagnosed under age 50 years.
- Colorectal cancer diagnosed in two or more first- or second-degree relatives with HNPCC-related tumors, regardless of age.

Designed to determine who is a good candidate for MSI/IHC tumor screening
MMR Failure Leads to Microsatellite Instability (MSI)
Tumor Testing

- Microsatellite Instability (MSI)
  - 15% of all colorectal tumors show MSI by PCR
  - The majority are NOT Lynch syndrome related

- Immunohistochemistry (IHC)
  - Staining of MLH1, MSH2, MSH6, and PMS2 proteins
  - MLH1/PMS2 dimerize – absent together
    - 80% of MLH1 absense is due to methylation, most often because of somatic mutation in BRAF
  - MSH2/MSH6 dimerize – absent together
Tumor testing pros and cons

- Compared to direct germline sequencing

- Pros:
  - Cost effective
    - Eliminates unnecessary testing for low risk individuals
    - Allows for targeted germline testing
  - Universal screening increases pick up
  - Consistent with NCCN guidelines

- Cons:
  - Slower TAT for results
  - Logistically more to arrange
  - Possibility of false negative (especially in lesions other than colon ca and endometrial ca)
Colorectal or Endometrial Tumor

IHC (hMLH1, hMSH2, hMSH6, hPMS2)

Normal IHC
- No further testing

Absent MLH1 +/- PMS2
- Reflex to BRAF Mutation testing
  - Mutation detected
    - No further testing
  - No mutation detected

Absent MSH2, MSH6, or PMS2

Equivocal IHC

Consider referral for genetic counseling

Targeted germline testing of defective MMR gene
Call your friendly neighborhood genetic counselor

- MLH/West Clinic genetic counselors
  - Carrie Horton: 901-683-0055 x1322
  - Morgan Depas 901-683-0055 x8029
- Baptist/Boston Baskin genetic counselors
  - Regina Nuccio 901-226-4064
  - Lorrell White 901-226-4038
- Genetic counselors available on call at many genetic testing laboratories
  - Ambry Genetics and Myriad Genetics
## Management

<table>
<thead>
<tr>
<th>Cancer Site (lifetime risk)</th>
<th>Management</th>
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</tr>
</thead>
</table>
| Colon (80%)                 | • Colonoscopy every 1-2 years  
                             • Consideration of colectomy with IRA based on polyp burden | 20-25 years  
                             Possibly later for MSH6 and PMS2? |
| Uterus (20-60%) and Ovarian (12%) | • Annual pelvic exam and Pap  
                             • TAH/BSO  
                             • TVUS, Endometrial sampling, CA125 | • 18y  
                             • 35y or after childbearing |
| Gastric (20%) and Small Bowel (4%) | • Extended EGD every 2-3 years  
                             • Consider capsule | 30-35y  
                             30-35y |
| Urothelial (5%)             | • Consider annual urinalysis | 25-30y |
| CNS (3%)                    | • Annual physical exam | 25-30y |
| Pancreatic (7%)             | • No current recommendations |
Clinical Considerations

- Endometrial cancer can be the first diagnosis in Lynch pts
  - 50% of women present with endometrial first and then develop a potentially avoidable colon ca
- When available, tumor screening is a cost effective and informative method of identifying pts
Familial Adenomatous Polyposis

- APC gene
- Clinical Description
  - Classic FAP
    - >100 to 1000s of polyps
    - Onset in adolescence
    - Near 100% lifetime risk for colon cancer
    - Average age of colon cancer dx 39y
  - Attenuated FAP
    - <100 polyps
    - Later onset of polyps
    - 70% lifetime risk for colon cancer
    - Average age of colon cancer dx 55y
  - Gardner syndrome = FAP + Desmoids and Osteomas
  - Turcot Syndrome = FAP + Brain Tumor (Glioblastoma)
Genotype Phenotype Correlation

- Location of gene mutation can predict phenotype
- Number of adenomas, average age of colon cancer, extracolonic features
# Management

<table>
<thead>
<tr>
<th>Management option</th>
<th>Classic FAP</th>
<th>Attenuated FAP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colon Surveillance</td>
<td>Every year beginning age 10-12y</td>
<td>Every year beginning age 18-20y</td>
</tr>
<tr>
<td>Surgery</td>
<td>Proctocolectomy with IPAA at onset of polyps  •Evaluate pouch for polyps</td>
<td>Consider colectomy with IRA  •Evaluate rectum for polyps</td>
</tr>
<tr>
<td>Gastric/Duodenum</td>
<td>Baseline extended EGD with side-viewing exam by age 20-25, interval frequency determined by polyp burden</td>
<td>*same as classic</td>
</tr>
<tr>
<td>Thyroid, CNS Desmoids</td>
<td>Annual physical exam beginning late teens</td>
<td>*same as classic</td>
</tr>
<tr>
<td>Hepatoblastoma</td>
<td>Abdominal ultrasound and AFP every 3-6 months until age 5y</td>
<td>*same as classic</td>
</tr>
</tbody>
</table>
MYH Associated Polyposis

- **MutYH**
  - Adenomatous polyposis
- **Autosomal recessive**
  - Family history absent or confined to sibship
  - Questionable haploinsufficiency – breakthrough phenotype for “carriers”
- Follow Attenuated FAP recommendations for colon and duodenum, low risk for non-GI findings
Clinical Considerations

- In practice, clinical diagnosis of FAP is often not confirmed with genetic testing
  - Genetic test results can influence surgical options
  - Informative for the family
    - Duty to warn lawsuits
    - Identify low risk individuals
  - A de novo case of FAP is clinically indistinguishable from MYH polyposis but has different implications for surveillance and inheritance
- Even in apparently de novo cases, test siblings
Peutz Jeghers syndrome

- STK11 gene
- Typically presents as small bowel polyposis
  - Hamartomas
- Breast Cancer
- Colon, small bowel, pancreatic cancer
- GYN, testicular and sex cord tumors
- Mucocutaneous freckling
# Cancer Risks and Management

<table>
<thead>
<tr>
<th>Cancer Site (lifetime risk)</th>
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| Breast (40-50%)             | •Annual mammogram and breast MRI  
•Clinical Breast exam every 6 months  
•Discussion of prophylactic mastectomy | 25y  
18y |
| Colon (40%)                 | •Colonoscopy every 2-3 years | 18y |
| Stomach (30%)               | •Upper endoscopy every 2-3 years | 18y |
| Pancreas (11-35%)           | •MR cholangiopancreatography and/or endoscopic ultrasound every 1-2 years  
•CA 19-9 every 1-2 years | 25-30y |
| Small bowel (13%)           | •CT enterography/small bowel enteroclysis baseline  
•CT enterography/small bowel enteroclysis every 2-3 years | 8-10y  
18y |
| Ovary (20%), cervix (10%), uterus (9%) | •Annual Pelvic exam and Pap  
•Consider TV US | 18y |
| Testes                      | •Annual testicular exam and observation for feminization | 10y |
| Lung (15%)                  | •Smoking cessation counseling |
Hereditary Diffuse Gastric Cancer Syndrome (HDGC)

- CDH1 gene (e-cadherin)
- Genetic pathway directly informs the phenotype
  - Gastric Cancer – diffuse (signet ring cell) type
  - Breast Cancer – lobular only
Clinical Considerations

- Detection of diffuse gastric cancer is challenging
  - 74% of HDGC pts who undergo “prophylactic” gastrectomy have an occult gastric cancer
  - Number of endoscopic biopsies necessary to have 90% sensitivity?

- Gastrectomy is strongly favored
  - 1% mortality in young healthy individuals
  - 100% morbidity
## Cancer Risks and Management

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<tr>
<td>Gastric (60-80%)</td>
<td>• Annual endoscopy with minimum of 30 biopsies</td>
<td>• 16-18y</td>
</tr>
<tr>
<td></td>
<td>• Total gastrectomy</td>
<td>• 20y</td>
</tr>
<tr>
<td>Breast (40-50%)</td>
<td>• Annual mammogram and breast MRI</td>
<td>• 35y</td>
</tr>
<tr>
<td>Colon (?)</td>
<td>• Colonoscopy every 3-5 years</td>
<td>• 40y</td>
</tr>
</tbody>
</table>
GI Referral Guidelines

- Colon cancer diagnosed under 60y
  - NCCN endorses universal tumor screening with IHC/MSI tumor screening regardless of age or family hx
- Endometrial cancer <50y
- Colon or Endometrial cancer at any age with a family history of 2 or more family members with Lynch related cancer
- Pancreatic adenocarcinoma <50y
- All epithelial ovarian cancers
- >10 adenomatous polyps
- >2 “Peutz Jegher” type hamartomas
- >3 Juvenile type polyps
- Diffuse gastric ca <50y
- Diffuse gastric ca >50y + additional relatives with gastric ca
Other syndromes

- Multiple Endocrine Neoplasia Type 1
- Multiple Endocrine Neoplasia Type 2
- Hereditary Kidney Cancer
  - Von Hippel Lindau
  - Hereditary Leiomyomatosis and Renal Cell Carcinoma
  - Hereditary Papillary Carcinoma
- Familial Paraganglioma/Pheo syndrome
- Hereditary Melanoma and Pancreatic Cancer
- Childhood cancer syndromes
Other genetic counseling issues

- Topics beyond than syndrome identification
  - Family dynamics
  - Unexpected results
  - Patient reaction to results
  - Ethical and legal considerations
Family Matters

- In hereditary syndromes, there is more than one patient
  - Results can allow for early detection and even prevention of cancers in at-risk relatives
  - Evaluate our duty to warn, especially when it is at odds with the patient’s wishes

- Genetic testing for minors is performed on a case by case basis
  - Not typically advised for adult onset conditions
Family history is tricky

- “No family history of cancer”
  - Early age of onset of initial patient — many other family members are also young and have not developed cancer YET
  - Evolution of family history — new diagnoses occur and new information is disclosed
  - Risk reducing surgery — breast cancer unaffected females s/p bilateral oophorectomy
  - Truncated history — paucity of females, adoption, only children, early death
  - De novo mutations — proband is the first person with the deleterious mutation
  - Accuracy of patient report
“Unexpected” results

- Negative/normal genetic test results in a highly suspicious family
  - Testing of other family members
  - Management?

- Variants
  - Favor Polymorphism
  - Suspected Deleterious
  - Uncertain Significance
Patient Reaction to Results

- Cancer genetic counseling is unique
  - Cancer is common → generations of health beliefs
  - How do genetic results fit into the picture?
- Special attention to results disclosure
  - Some patients are devastated to find out they have a mutation
    - Guilt for family members
    - Overwhelming to have additional cancer risks and decisions
  - Some patients WANT to have a mutation
    - Pattern of cancer in the family is reality – result is an explanation and an opportunity for prevention
    - Isolation or guilt if negative in a mutation positive family
Psychosocial Impact

- Common emotions in high risk families
  - Anger
  - Anxiety
  - Shame
  - Fear of becoming a burden
  - Loss of control
  - Fear of disfigurement
  - Negative body image
  - Isolation
  - Guilt
Informed Consent

Core elements of informed consent with regards to cancer genetic testing:

- Elicitation and discussion of a person’s expectations, beliefs, goals, and motivations.
- Explanation of how inheritance of genetic factors may affect cancer susceptibility.
- Clarification of a person’s increased risk status.
- Impact on at-risk relatives
- Potential benefits, risks, and limitations of testing technology and results.
- Costs and logistics of testing and follow-up.
- Benefits, limitations, and efficacy of medical management options.
- Possible psychological, social, economic, and family dynamic ramifications of testing or not testing.
- Alternatives to genetic testing (e.g., tissue banking, risk assessment without genetic testing).
Genetic Discrimination

- Federal and State Laws prohibit genetic discrimination
  - HIPAA
  - Genetic Information Nondiscrimination Act (GINA)
    - Positive results from predisposition testing cannot be a pre-existing condition
    - Not used to change premiums or eligibility
  - Over half a million clinical tests ordered – not one documented case of genetic discrimination

- Myth or reality?
  - Theoretical possibility
Genetic risk assessment for hereditary cancer is integral in the comprehensive care of today’s patient.

Genetic test results influence current cancer treatment as well as long term surveillance.

Genetic testing is one part of the genetic counseling process.
References and Resources

- Over 250 citations and references for this presentation
  - chorton@westclinic.com
  - 901-683-0055 x1322
- Gene Tests – collaborative reviews on many of the syndromes described
  - genetests.org
- NCCN Clinical Practice Guidelines in Oncology
  - Genetic/Familial High-Risk Assessment: Breast and Ovarian
  - Colorectal Cancer Screening