Cancer Genetics and Syndromes

Bridgette Aufmuth, MS, CGC
August 9, 2013
Objectives

- Define cancer genetic counseling
- Discuss the changing landscape of genetic testing for hereditary breast cancer
- Recognize indications for referral to genetic counseling with discussion of hereditary cancer syndromes
Cancer Genetics

- Study of hereditary and familial cancer
- Identify those at-risk to promote awareness, early detection, and prevention
- “A genetic counselor is a health care professional who is academically and clinically prepared to provide genetic counseling services to [persons] seeking information about the occurrence, or risk of occurrence, of a genetic condition...” — American Board of Genetic Counseling

National Society of Genetic Counselors
Cancer Genetic Counseling

- Obtain cancer-focused medical and family history
  - Medical and surgical history; 3-4 generation pedigree
  - Cancer: primary site, bilaterality, age at diagnosis and current age/age at death, confirm with path report if possible
  - Unaffecteds: age, prophylactic surgeries, polyps, other tumors

- Assess and educate about risk of developing cancer

- Determine if history is suggestive of hereditary cancer syndrome
Cancer Genetic Counseling

- Discuss options for genetic testing, including benefits, risks, and limitations, and the most appropriate person to test
  - Cost, technical accuracy
  - Discuss confidentiality and genetic discrimination concerns
  - +, --: True or Uninformative, Variant of Uncertain Significance
- Review medical management options including personal decisions regarding risk-reduction and prophylactic measures
- Adjust to emotional reaction of having a gene mutation
- Provide psychosocial support and facilitate communication with relatives
- Identify support resources

National Society of Genetic Counselors
J Genet Counsel Vol.15, April 2006
Cancer Family History Vital in Assessing Need for Genetic Counseling

QOPI® study finds documentation often incomplete

June 1, 2013

Family history of cancer is an important factor in assessing a patient's risk of primary and secondary cancers and need for genetic counseling. However, adequate documentation of family history is often lacking from patient records. This issue was discussed at a Pre-Annual Meeting Seminar entitled "Genetics and Genomics for the Practicing Clinician."

Family history of cancer should include at least the types of cancers in first- and second-degree relatives and their ages at cancer diagnoses, said Marie E. Wood, MD, of the University of Vermont, during her talk, "QOPI Family History Study and Recommendations."

Dr. Wood noted that family history of cancer is an integral part of screening guidelines to identify patients who are at high risk of colorectal or breast cancer and is among the referral criteria for genetic counseling and testing. In a 2003 policy statement update, ASCO recommended counseling and testing for individuals with personal or family history suggestive of genetic cancer susceptibility.
Cancer Genetic Counseling

- National Comprehensive Cancer Network
- Society of Gynecologic Oncology
- United States Preventative Task Force
- American College of Obstetrics and Gynecology
- American Gastroenterology Association
Penile Cancer
Primary Peritoneal Cancer (See Ovarian Cancer)
Prostate Cancer
Small Cell Lung Cancer
Soft Tissue Sarcoma
Testicular Cancer
Thymomas and Thymic Carcinomas
Thyroid Carcinoma
Uterine Neoplasms

NCCN GUIDELINES FOR DETECTION, PREVENTION, & RISK REDUCTION
Breast Cancer Risk Reduction
Breast Cancer Screening and Diagnosis
Cervical Cancer Screening
Colorectal Cancer Screening
Genetic/Familial High-Risk Assessment: Breast and Ovarian
Lung Cancer Screening
Prostate Cancer Early Detection

NCCN GUIDELINES FOR SUPPORTIVE CARE
Adult Cancer Pain
Referral Criteria for Hereditary Breast and Ovarian Cancer

- Known mutation in the family
- Ovarian cancer (fallopian tube/primary peritoneal)
- Breast cancer:
  - \( \leq 50 \)
  - Triple negative
  - Two breast cancers
  - Ashkenazi Jewish ancestry
  - In a male

- Breast with:
  - Pancreatic cancer, aggressive prostate cancer (Gleason \( \geq 7 \))
  - Endometrial cancer, thyroid cancer, macrocephaly, dermatologic features, hamartomas of the GI tract
  - Diffuse gastric cancer
  - Sarcoma, adrenocortical cancer, brain tumors, leukemia/lymphoma
Hereditary Breast and Ovarian Cancer syndrome (HBOC)

- Breast cancer
- Epithelial ovarian cancer (fallopian tube/primary peritoneal)
- Pancreatic cancer
- Prostate cancer
- Melanoma
- Inherited mutations in \textit{BRCA1} and \textit{BRCA2}
Testing Criteria for HBOC

- Breast:
  - ≤45 or triple negative ≤60 or ≤50 with limited family history or two primaries with 1 ≤50 or male breast cancer
  - At any age with another close relative ≤50 or 2 close relatives with breast at any age or pancreatic or aggressive prostate cancer

- Ovarian cancer at any age
- Pancreatic or aggressive prostate cancer
  - ≥2 close relatives with breast/ovarian/pancreatic/aggressive prostate cancer

- Consider testing of unaffected only if appropriate affected relative unavailable for testing
Management Guidelines

- **Breasts:**
  - CBE, mmg/MRI annually age 25 or earlier; Tamoxifen or Raloxifene; b/l mastectomy
  - Males: SBE and CBE by 35; mmg at 40

- **Ovaries:**
  - BSO age 35-40; CA-125 and TV u/s q 6 months age 30 or earlier

- **Prostate:** screening at 40

- **Pancreas:** consider research enrollment

- **Melanoma:** consider annual dermatologic evaluation

- **Reproductive options**
Case Example

Diagnosed breast ca age 36
ER/PR/Her2 +
Colon ca 70’s

Bilateral breast ca 58, 65
Fallopian tube adenoca 71

Bilateral DCIS 53, 61
Breast ca “late”

Breast ca 36

BRCA – (1998); sequencing only

Breast ca 36

BRCA – : Seq and BART
Hereditary Breast Cancer

Approximately 7% of breast cancer and 11 - 15% of ovarian cancer cases are caused by mutations in the *BRCA1* or *BRCA2* genes. When someone carries a mutation in either of these genes, they have a syndrome called Hereditary Breast and Ovarian Cancer (HBOC) syndrome.\(^1\),\(^2\),\(^3\) Myriad offers testing to determine whether a patient is a carrier of the *BRCA1* or *BRCA2* gene mutations. When assessing the risk of carrying these mutations a patient’s personal and family history is collected to investigate the risk for HBOC. Once a patient is identified as being at increased risk of HBOC, genetic test results provide the most accurate means of cancer risk assessment for a patient.
Changes in genetic testing for hereditary breast cancer

- 6/13/13: SCOTUS rules human genes are not patentable, but synthetic DNA (cDNA) is because it does not occur naturally.

- "It is ACMG's long-standing position that genes and their mutations are naturally occurring substances that should not be patented…we applaud the decision that human genes are not patentable and hope that this will eventually include cDNA also."
  
  American College of Medical Genetics
  President Gail Herman

GenomeWeb “US Supreme Court Strikes Down Gene Patents but Allows Patenting of Synthetic DNA”
# Testing Options

<table>
<thead>
<tr>
<th></th>
<th>BRCA1/2 only</th>
<th>Panel with Management</th>
<th>Expanded Panel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ambry</td>
<td>$2200</td>
<td>$3300 (6 genes)</td>
<td>$4120-$5830 (16-24 genes)</td>
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<tr>
<td>DNA Traits</td>
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<td>Myriad</td>
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<td>Prevention Genetics</td>
<td>$3290</td>
<td>$3980 (7 genes)</td>
<td>$4680 (13 genes)</td>
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<tr>
<td>University of Washington</td>
<td>$1800</td>
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<td>$3150 (40 genes)</td>
</tr>
</tbody>
</table>

Courtesy of Andrea Forman, MS, CGC
Benefits and Limitations of Testing

**BENEFITS**
- Personalized hereditary cancer risk assessment
- Information to help make medical management decisions to help reduce cancer risk
- Important information for family members to help determine their risk
- Reduced anxiety and stress

**LIMITATIONS**
- Testing does not detect all causes of hereditary cancer
- A negative result is most helpful when there is a known mutation in the family

Testing Options

There are four types of tests to look for BRCA1 and BRCA2 mutations:

- **Integrated BRACAnalysis® Testing:**
  Full examination of the most common changes of BRCA1 and BRCA2 genes and large rearrangement analysis. This test is for people who do not have any known gene mutations in the family.

- **Single Site BRACAnalysis:**
  This test is for individuals who already know a BRCA1 or BRCA2 gene mutation is in the family. Before taking this test, you should find out the name of the gene mutation from family members who have tested positive.

- **Multisite 3 BRACAnalysis:**
  This test examines the three most common BRCA1 and BRCA2 gene mutations in individuals of Ashkenazi Jewish ancestry.

- **ACAnalysis Large Rearrangement Test (BART):**
  This test examines the three most common BRCA1 and BRCA2 gene mutations in individuals of Ashkenazi Jewish ancestry. However, there are some much less common gene mutations that can only be found using a test called the BRACAnalysis Large Rearrangement Test (BART).

A doctor will decide based on your personal and family history which test is right for you.
<table>
<thead>
<tr>
<th>HBOC FOLLOW-UP</th>
<th>FAMILY STATUS</th>
<th>GENETIC TESTING</th>
<th>TEST OUTCOME</th>
<th>SCREENING RECOMMENDATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk assessment and counseling:</td>
<td>Deleterious familial BRCA1/BRCA2 mutation known</td>
<td>Recommend BRCA1/BRCA2 testing for specific familial mutation</td>
<td>Positive for familial BRCA1/BRCA2 mutation</td>
<td>See HBOC Management (HBOC-A)</td>
</tr>
<tr>
<td>Psychosocial assessment and support</td>
<td></td>
<td></td>
<td>BRCA1/BRCA2 testing not performed</td>
<td>Cancer screening as per NCCN Screening Guidelines</td>
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<tr>
<td>Risk counseling</td>
<td>No known familial BRCA1/BRCA2 mutation</td>
<td>Consider comprehensive testing of patient or if unaffected, test family member with highest likelihood of a BRCA1/BRCA2 mutation</td>
<td>Mutation found</td>
<td>See HBOC Management (HBOC-A)</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td>Not tested or no mutation found</td>
<td>Offer research and individualized recommendations (e.g., testing next family member with highest likelihood) according to personal and family history</td>
</tr>
<tr>
<td>Discussion of genetic testing</td>
<td></td>
<td></td>
<td>Variant of unknown significance found (uninformative)</td>
<td></td>
</tr>
<tr>
<td>Informed consent</td>
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</tbody>
</table>

1. Genetic counseling is highly recommended when genetic testing is offered and after results are disclosed. A genetic counselor, medical geneticist, oncologist, surgeon, oncology nurse, or other health professional with expertise and experience in cancer genetics should be involved early in counseling patients who potentially meet criteria for an inherited syndrome.

2. Comprehensive genetic testing includes full sequencing of BRCA1/BRCA2 and testing for large genomic rearrangements.

3. Genetic testing for familial BRCA1/2 in children <18 y is generally not recommended.

4. If of Ashkenazi Jewish descent, in addition to the specific familial mutation, test for all three founder mutations.

5. Testing of unaffected family members when no affected member is available should be considered. Significant limitations of interpreting test results should be discussed.

6. If more than one family member affected, first consider: youngest age at diagnosis, bilateral disease, multiple primaries, ovarian cancer, and most closely related to the proband/patient. If no living family member with breast or ovarian cancer, consider testing first- or second-degree family members affected with cancers thought to be related to BRCA1/BRCA2 (e.g., prostate, pancreas, melanoma).

7. For both affected and unaffected individuals of Ashkenazi Jewish descent with no known familial mutation, first test for the three common mutations. Then, if negative for the three mutations and ancestry also includes non-Ashkenazi Jewish relatives or other HBOC criteria is met, consider comprehensive genetic testing. If all affected family members are deceased, consider testing of paraffin-derived DNA from deceased relatives, if DNA is obtainable. For both affected and unaffected individuals who are non-Ashkenazi Jewish and who have no known familial mutation, comprehensive genetic testing is the approach, if done.

8. If no mutation is found, consider other hereditary breast/ovary cancer syndromes such as Li-Fraumeni (Li-Fraumeni) and/or Cowden syndrome (Cowden-1). For additional information on other genetic mutations associated with breast/ovary cancer risk for which genetic testing is clinically available, see GENE-1.

9. Testing family members for a variant of unknown significance should not be used for clinical purposes. Consider referral to research studies that aim to define functional impact of variant.
Case Example

Diagnosed thyroid ca age 32
Diagnosed breast ca age 43
Cowden syndrome

- Major criteria:
  - Breast cancer
  - Endometrial cancer
  - Follicular thyroid cancer
  - Macrocephaly (OFC ≥58cm in women and 60cm in men)
  - Mucocutaneous lesions
    - Trichilemmomas, mucosal papillomatosis, palmoplantar keratoses, cutaneous facial papules
  - PTEN gene mutations

- Minor criteria:
  - Colon cancer
  - Renal cancer
  - GI hamartoma or ganglieneuroma
  - Papillary or follicular variant of papillary thyroid cancer
Cowden Syndrome Management

- Breast screening same as BRCA1/2 except start imaging at 30-35
- Consider risk-reducing mastectomy and hysterectomy
- Annual PE by age 18
- Thyroid u/s annually by 18
- Colonoscopy by 35
- Annual dermatology exam

Images from Cleveland Clinic: lerner.ccf.org
Breast dx 37
ER/PR +, Her2 –
BRCA1/2 negative

Prostate dx ?

Ovarian dx 62

Breast dx 70s

PTEN mutation

Used with permission from Ambry Genetics
Case Example

Diagnosed breast ca age 45
Diagnosed peritoneal ca age 51
TP53

Walsh et al. Proc Natl Acad Sci USA. 2011; 108(44): 18032-7
Li-Fraumeni Syndrome

- Premenopausal breast cancer
- Soft tissue and osteosarcoma
- Adrenocortical carcinoma
  - Acute leukemia
- Brain tumor
  - Choroid plexus carcinoma
  - Colon cancer
  - Early-onset adenocarcinoma or childhood cancer
  - *TP53* gene mutations
LI-FRAUMENI SYNDROME TESTING CRITERIA

- Individual from a family with a known TP53 mutation
- Classic Li-Fraumeni syndrome (LFS) criteria:
  - Combination of an individual diagnosed age <45 y with a sarcoma
  - A first-degree relative diagnosed age <45 y with cancer
  - An additional first- or second-degree relative in the same lineage with cancer diagnosed age <45 y, or a sarcoma at any age
- Chompret criteria:
  - Individual with a tumor from LFS tumor spectrum (e.g., soft tissue sarcoma, osteosarcoma, brain tumor, breast cancer, adrenocortical carcinoma, leukemia, lung bronchoalveolar cancer) before 46 years of age, AND at least one first- or second-degree relative with any of the aforementioned cancers (other than breast cancer if the proband has breast cancer) before the age of 56 years or with multiple primaries at any age
  - OR
  - Individual with multiple tumors (except multiple breast tumors), two of which belong to LFS tumor spectrum with the initial cancer occurring before the age of 46 years
  - OR
  - Individual with adrenocortical carcinoma or choroid plexus carcinoma at any age of onset, regardless of the family history
- Early-onset breast cancer:
  - Individual with breast cancer ≤35 y with a negative BRCA1/BRCA2 test

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

Cancers associated with LFS include but are not limited to:
- Premenopausal breast cancer
- Bone and soft tissue sarcomas
- Acute leukemia
- Brain tumor
- Adrenocortical carcinoma
- Choroid plexus carcinoma
- Colon cancer
- Early onset of other adenocarcinomas or other childhood cancers


Patients who have received an allogeneic bone marrow transplant should not have molecular genetic testing via blood or buccal samples due to unreliable test results from contamination by donor DNA. If available, DNA should be extracted from a fibroblast culture. If this source of DNA is not possible, buccal samples can be considered, subject to the risk of donor DNA contamination.
LFS Management

- Discuss significant limitations in screening for many of LFS cancers
- Breast screening similar to BRCA1/2 but begin imaging by age 20
- Annual comprehensive PE including skin and neurologic exam
- Colonoscopy q 2-5 yr beginning by 25
- Therapeutic RT used with caution
- Consider clinical trials for other screenings
TP53 mutation

Walsh et al. Proc Natl Acad Sci USA. 2011; 108(44): 18032-7
Other Hereditary Breast Syndromes

- Peutz-Jeghers Syndrome (*STK11*)
  - 2+ PJS-hamartomas of small intestine, mucocutaneous hyperpigmentation of mouth/lips/nose/eyes/genitalia/fingers, known family history
  - Cancers of the breast, colon, stomach, pancreas, small intestine, ovary/ cervix/uterus, testes, lung

- Hereditary Diffuse Gastric Cancer (*CDH1*)
  - Diffuse gastric cancer (AKA signet ring or isolated cell-type carcinoma) with early onset
  - Lobular breast cancer in women
Breast ca 36
Bilateral DCIS
Breast ca 36
Breast ca 36
Fallopian tube adenoca 71
Colon ca 70's
Bilateral breast ca
58, 65
Breast ca “late"
BRCA – (1998); sequencing only
BRCA –: Seq and BART
BreastNext: ATM and MUTYH +
Cancer Panels

- Additional testing when family history is suggestive of >1 syndrome (when *BRCA1/2* is negative)
- Benefits:
  - Cost-effective way to screen multiple genes, up-to-date
- Limitations:
  - Unknown/ high VUS rate, lack of clinical management guidelines, uncertain cancer risks for many of the genes
- Per NCCN should only be ordered in consultation with cancer genetics professional
Case Example

Diagnosed 5 tubular adenomas age 67
Testing for Lynch syndrome:

MSH6 mutation
Hereditary CRC

- Lynch syndrome (LS) cancers:
  - Colorectal, endometrial, gastric, ovarian, pancreas, ureter and renal pelvis, biliary tract, brain, small intestinal, sebaceous gland adenomas and keratocanthsomas
  - Mismatch repair genes
    - *MLH1, MSH2, MSH6, PMS2*
    - *EPCAM*
  - Muir-Torre syndrome (skin tumors) or Turcot syndrome (glioblastoma)
Testing Criteria for LS

- Meets revised Bethesda guidelines or Amsterdam criteria
- **All CRC patients** or those diagnosed <70 and those ≥70 who meet Bethesda
- **Endometrial cancer <50**
- Known LS in family
EGAPP Recommendation

- 3% of all CRC due to LS
- Offer genetic testing for newly diagnosed CRC to reduce morbidity/mortality in relatives
- IHC: stain for protein expression of MMR gene protein products
- MSI: changes in 2 or more of 5 markers
- *BRAF* testing (V600E mutation)
- Gene testing

# Tumor Testing Results and Additional Testing Strategies

<table>
<thead>
<tr>
<th>Tumor Testinga</th>
<th>Plausible Etiologies</th>
<th>Additional Testing</th>
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<tbody>
<tr>
<td><strong>IHC</strong></td>
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<td><strong>MSI</strong></td>
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<tr>
<td><strong>BRAF V600E</strong>b</td>
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<tr>
<td><strong>MLH1 Promoter Methylation</strong></td>
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**Note:** Additional testing strategies apply to colorectal and endometrial cancers. Limited data exist regarding the efficacy of tumor testing in other LS tumors.

**Testing is not appropriate for tumors other than colorectal cancer.**

**If strong family history (i.e., Amsterdam criteria) is present, additional testing may be warranted in the proband, or consider tumor testing in another affected family member due to the possibility of a phenocopy.**

---

**N/A:** Either testing was not done or results may not influence testing strategy.

---

**Normal staining of protein**

**-** absent staining of protein
Management Recommendations
Vary by Gene

- Colonoscopy by 20-25 q 1-2 years (later/ less frequent early on with \textit{MSH6} and \textit{PMS2})
- Consider hysterectomy and BSO (not with \textit{PMS2})
- Expert opinion (\textit{MLH1/MSH2}):  
  - Annual urinalysis at 25-30  
  - Annual PE at 25-30  
  - Consider annual endometrial sampling and CA125 and TV u/s  
  - Consider EGD with extended duodenoscopy at 30-35 for some
Case Example

23 tubular adenomas
dx 41 and 44
23 tubular adenomas

Breast ca dx 60s

Colon polyps #?
Colon ca dx 60s

Breast ca dx 70s

Referred for Lynch syndrome
IHC normal
APC mutation

Dx 41 and 44
Hereditary Polyposis Syndromes: FAP

- >100 polyps (or fewer if younger if FAP in family), medulloblastoma, thyroid ca (papillary), hepatoblastoma, pancreatic, gastric, and duodenal cancers; duodenal and fundic gland polyps
- Offer testing if >10 adenomas, desmoid tumor, or known mutation in family
- Attenuated FAP: < polyps, right-sided, onset later, upper GI findings and thyroid and duodenal cancer risks similar
- APC gene
MUTYH-Associated Polyposis (MAP)

- Polyps/CRC consistent with autosomal recessive inheritance (consider if consanguinity)
- < adenomas, later-onset, duodenal cancer and polyps can occur
- Offer testing if >10 adenomas, known biallelic mutations in family, meets criteria of serrated polyposis syndrome with some adenomas
Other Polyposis Syndromes

- **Peutz-Jeghers Syndrome** (*STK11*)
  - 2+ PJS-hamartomas of small intestine, mucocutaneous hyperpigmentation of mouth/lips/nose/eyes/genitalia/fingers, known family history
  - Cancers of the breast, colon, stomach, pancreas, small intestine, ovary/cervix/uterus, testes, lung

- **Juvenile Polyposis Syndrome** (*BMPR1A* and *SMAD4*)
  - 3-5 juvenile polyps of colon or multiple in GI tract or any # with known family history
  - Colon, stomach, small intestine and pancreatic cancers
MEN syndromes

- **MEN1**: *MEN1* gene
  - 2+ of parathyroid, pituitary tumors, and well-differentiated tumors of gastro-entero-pancreatic tract; also carcinoid and adrenocrotical tumors and non-endocrine tumors

- **MEN2**: *RET* gene
  - Familial Medullary Thyroid Cancer (MTC)
  - MEN 2A:
    - MTC, Pheo, Parathyroid adenoma/hyperplasia
  - MEN 2B:
    - MTC, Pheo, oromucosal neuromas, distinctive facies, ganglioneuromatosis of GI tract, asthenic body habitus
Renal Cancer

- **Von Hippel-Lindau disease (VHL):** hemangioblastomas, renal cysts and **clear cell RCC**, pheo, pancreatic cysts and neuroendocrine tumors, endolymphatic sac tumors, epididymal and broad ligament cysts

- **Birt-Hogg-Dube syndrome (FLCN):** cutaneous manifestations; pulmonary cysts/history of pneumothorax; **renal tumors** with most common being **renal hybrids of oncocytoma and chromophobe**

- **Hereditary Leiomyomatosis and Renal Cell Cancer (FH):** cutaneous leiomyomata, uterine leiomyomata, **single renal tumor** ranging from type 2 papillary to tubulo-papillary to collecting-duct carcinomas
Other Hereditary Syndromes

- Hereditary Paraganglioma and Pheochromocytoma Syndrome:
  - PGL and Pheo
  - $SDHA, SDHB, SDHC, SDHD, SDHAF2, MAX$ genes
  - Pheo also reported in MEN, VHL, and NF1

- Melanoma
  - Familial Atypical Multiple Mole Melanoma-Pancreatic Cancer Syndrome ($p16/CDKN2A$)
  - Melanoma-Astrocytoma syndrome
Genetics in practice....

How do I diagnose the other hereditary disorders....

It’s too confusing....

I follow NCCN....

I draw a pedigree....

I refer to an expert....

Shannon KM. 2012 testing by cancer site: breast.
GYNECOLOGIC CANCER GENETICS REFERRAL GUIDE

Individuals with a total point score $\geq 10$ points should be referred to Cancer Genetics Program for genetic counseling; please fax referral form to 864-455-5897 (form at [www.ghs.org/cancergenetics](http://www.ghs.org/cancergenetics)). Please call scheduler at 864-455-1346 or genetic counselors at 864-455-5836 with questions.

ENDOMETRIAL CANCER:

<table>
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<tr>
<th>Personal history</th>
<th>Points</th>
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<tr>
<td>Endometrial cancer diagnosed $&lt; age 50$</td>
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<tr>
<td>Endometrial cancer diagnosed $50-55$</td>
<td>7</td>
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<tr>
<td>Endometrial cancer diagnosed $&gt; age 55$</td>
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<tr>
<td>Endometrial cancer and any of the Lynch syndrome cancers at any age</td>
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</tr>
<tr>
<td>Endometrial cancer with breast or non-medullary thyroid cancer, dermatologic manifestations seen in Cowden syndrome**, macrocephaly (OFC $\geq 58$ cm), hamartomatous polyps of the GI tract</td>
<td></td>
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</tbody>
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<table>
<thead>
<tr>
<th>Family history</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Close relative with endometrial cancer $&lt; age 50$</td>
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</tr>
<tr>
<td>Two or more close relatives with endometrial cancer at any age</td>
<td>10</td>
</tr>
<tr>
<td>Close relative with endometrial cancer and the same or another close relative with any of the Lynch syndrome cancers on the same side of the family at any age</td>
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<tr>
<td>Close relative with endometrial cancer and the same or another close relative with breast or non-medullary thyroid cancer or dermatologic manifestations seen in Cowden syndrome**, macrocephaly (OFC $\geq 58$ cm), hamartomatous polyps of the GI tract on the same side of the family at any age</td>
<td>10</td>
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OVARIAN CANCER (TO INCLUDE FALLOPIAN TUBE AND PERITONEAL CANCERS):

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<th>Points</th>
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<td>Epithelial ovarian cancer any age</td>
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<tbody>
<tr>
<td>Close relative with epithelial ovarian cancer at any age</td>
<td>10</td>
</tr>
</tbody>
</table>

MISCELLANEOUS FAMILY HISTORY

Close relative with invasive papillary carcinoma in a germinoma patient
Cancer Genetics Involvement

- Tumor boards
- Committee roles
- Multidisciplinary clinic
- Survivorship clinic
- Marketing
In Summary

- Genetic counselors are trained health care professionals who educate individuals about risk of cancer and hereditary risk, identify appropriate individuals for genetic testing, and discuss effect on individuals and families.
- Diagnosis of a hereditary cancer syndrome has significant implications for individual and his/her family’s medical management.
- For many cancers, genetic counseling and testing can be an integral part of medical management.
THANK YOU!

www.ghs.org/cancergenetics

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Other References and Acknowledgements

- GeneTests (genetests.org)
- OMIM—Online Mendelian Inheritance in Man (omim.org)
- NCCN (nccn.org)
- NSGC—National Society of Genetic Counselors (nsgc.org)

- Kara Bui, MS, CGC
- Andrea Forman, MS, CGC
- Cristi Radford, MS, CGC