Cancer Risk Assessment and Genetic Testing

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Conflict of Interest

• Paid consultant for Myriad Genetic Laboratories
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Background

• Genetics is an essential part of cancer care
• Level of tumor and genes
• Knowledge of a hereditary cancer risk goes back to the early 20th century
• Currently at least 54 known hereditary cancer syndromes
All Cancer Arises From Gene Mutations

**Germline mutations**
- Parent
- Mutations in egg or sperm
- Present in egg or sperm
- Are heritable
- Cause cancer family syndromes
- 5-10% of cancer

**Somatic mutations**
- Child
- All cells affected in offspring
- Somatic mutation (e.g., breast)
- Occur in non-germline tissues
- Are non-heritable
- Sporadic cancer
- 90-95% of cancer

Benefits of Identifying Individuals with Hereditary Cancer Syndromes

- **Affected**
  - Possibility to change treatment options
  - Identify risk of 2nd or 3rd cancers
  - Offer increased screening or cancer prevention
  - Identify other family members who could be at risk

- **Unaffected**
  - Identify risk
  - Offer increased screening, starting earlier
  - Discuss cancer prevention
  - Identify other family members who could be at risk
  - If diagnosed with cancer, affect approach to treatment

Cancer Risk Assessment and Genetic Counseling

- **S 2.3** Cancer risk assessment, genetic counseling, and testing services are provided to patients either on site or by referral, by a qualified genetics professional
Goals in Creating the Standard

- Differentiate cancer risk assessment/genetic counseling (CRA/GC) and genetic testing (GT)
- Identify the minimum essential elements needed when performing a CRA/GC and GT
- Identify who at a CoC-accredited institution is qualified to perform CRA/GC and GT

What is Cancer Risk Assessment/Genetic Counseling?

- CRA is the process of identifying and counseling individuals at risk for familial or hereditary cancer syndromes
- The purpose of GC:
  - Assess a patient’s personal and family medical history
  - Educate patients about their chance of developing cancers (primary or secondary cancers)
  - Review risks and genetic concepts associated with suspected syndrome
  - Explain family risks (siblings, children, etc.)
  - Perform a psychosocial assessment
  - Empower patients to make educated, informed decisions about genetic testing, cancer screening, and cancer prevention

When to Suspect a Hereditary Cancer Syndrome

- Cancer in 2 or more close relatives
  - on same side of family
- Multiple generations affected
- Early age at diagnosis (≤50)
- Multiple primary tumors
- Bilateral or multiple rare cancers
  - e.g., renal, pheochromocytoma, osteosarcoma
- Constellation of tumors consistent with specific cancer syndrome
  - e.g., breast and ovarian, colon and uterine, melanoma and pancreas
Cancer Risk Assessment/Genetic Counseling

• Collecting *relevant* information needed to assess a patient’s personal and family medical history
  – This is done in the form of a pedigree

Family History Collection

• 3-4 generation
• First, second and third degree (1st cousins and, if known, great aunts/uncles)
• Both lineages
• Ancestry/ethnicity
• Consanguinity
• Male to female ratio
• Ages of death, surgeries unrelated to cancer
• Specific questions if a syndrome is suspected
Cancer Risk Assessment/Genetic Counseling

• Evaluating Patient’s Risk
  – Cancer risk
  – Risk of a hereditary syndrome explaining the personal and/or family history

• Evaluating Patient’s Risk
  – Cancer risk
  • Combination of personal risk factors and family history
    – Epidemiologic risks
    – Family history risks

• Risk Models
  – Breast
    • Gail model
      – www.cancer.gov/bcrisktool
    • Claus model (CancerGene)
      – www.utsouthwestern.edu/cda/dept47829/files/65844.html
    • Tyrer-Cuzick
      – www.cancer.gov/bcrisktool
    • BRCAPRO (just family history based, not validated)
      – www.utsouthwestern.edu/cda/dept47829/files/65844.html
  – Colon
    • Colon Cancer Risk Assessment Tool
      – www.cancer.gov/cancersolutionscenter/
  – Melanoma
    • Melanoma Risk Assessment Tool
      – www.cancer.gov/melanomarisktool
Cancer Risk Assessment/Genetic Counseling

- Risk of a hereditary syndrome explaining the personal and family history
- Can be done based on the pedigree
- Risk models
  - BRCA1/2
    - BRCAPRO (CancerGene)
    - www.utsouthwestern.edu/utsw/cda/dept47829/files/65844.html
    - Tyrer-Cuzick
    - www.eace.rni.org/televsvaluation
    - BOADICEA
    - www.cf.ac.uk/gene/applications/boadicea_intro.html
  - Lynch syndrome
    - PREMM2
    - MBIPRO (CancerGene)
    - www.utsouthwestern.edu/utsw/cda/dept47829/files/65844.html

Example: Breast Cancer

- Hereditary Breast and Ovarian Cancer syndrome (BRCA1 and BRCA2)
  - Lifetime risk of breast cancer = ~60%
  - Lifetime risk of ovarian cancer = ~20-50%
  - Associated with
    - Prostate
    - Male breast
    - Pancreas
    - Melanoma
    - Gastric
    - Possibly colon
Example: Breast Cancer

- Hereditary Breast and Ovarian Cancer syndrome (BRCA1 and BRCA2)
  - Lifetime risk of breast cancer = ~60%
  - Lifetime risk of ovarian cancer = ~20-50%
  - Associated with prostate, male breast, pancreas, melanoma, gastric, possibly colon

- Other syndromes
  - Ataxia Telangiectasia
  - Bloom syndrome
  - Cowden syndrome
  - Familial atypical mole-malignant melanoma syndrome
  - Hereditary Diffuse Gastric Cancer
  - Li Fraumeni syndrome
  - Neurofibromatosis type 1
  - Peutz-Jeghers syndrome

- Other Genes
  - CHEK2
  - PALB2
  - RAD51C/D

Cancer Risk Assessment/Genetic Counseling

- Performing a Psychosocial Assessment
  - Assessing cancer worry, anxiety, intrusive thoughts, depression, anger, fear, guilt, family experiences with cancer, perception of risk for self and others, competence for giving informed consent, social stressors and supports
  - Effect on family

Cancer Risk Assessment/Genetic Counseling

- Educating the patient about the suspected hereditary cancer syndrome (if indicated)
  - Basic genetics concepts
    - Genes, inheritance patterns
  - Advanced genetics concepts
    - Penetrance, variable expressivity, genetic heterogeneity
  - Cancer risks associated with disorder
  - Management options if they are found to have disorder
Cancer Risk Assessment/Genetic Counseling

• Obtaining informed consent

ASCO 2003 Policy Statement on Genetic Testing

1. Information on the specific test being performed
2. Implications of a positive and negative result*
3. Possibility that the test will not be informative
4. Options for risk estimation without GT
5. Risk of passing a mutation to children
6. Technical accuracy of the test
7. Fees involved in testing and counseling
8. Psychological implications of test results (benefits and risks)
9. Risks of insurance or employer discrimination*
10. Confidentiality issues
11. Options and limitations of medical surveillance and strategies for prevention following testing
12. Importance of sharing genetic test results with at-risk relative so that they may benefit from the information

Genetic Information Non-discrimination Act (GINA)

• Federal law signed into law May 21st, 2008
  – Went into effect in 2009
• Prohibits genetic discrimination by health insurance companies and employers
• Defines genetic information as predictive genetic tests, family members’ genetic tests, and family history information
• Applies to both group and individual health insurance markets
• Prohibits the use of genetic information in underwriting
• Prohibits insurers and employers from requiring genetic testing
Limitations of GINA
- Does not apply to life insurance, long-term care insurance, disability insurance, etc.
- Only applies to individuals undergoing asymptomatic testing
  - once a person is symptomatic, health insurance companies, in theory, can use such information

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Duty to Warn
- Pate v Threlkel (Florida, 1995)
  - Ruling: Duty to warn is satisfied by warning index patient that her family members may be at risk for cancer (medullary thyroid cancer)
- Safer v Pack (New Jersey, 1996)
  - Ruling: Physician has a duty to warn other family members that they may be at risk (familial adenomatous polyposis)
- Molloy v Meier (Minnesota, 2004)
  - Ruling: Physician’s duty regarding genetic testing and diagnosis extends beyond the patient to biological parents who foreseeably may be harmed by a breach of that duty (Fragile X)
Cancer Risk Assessment/Genetic Counseling

All of these essential elements need to be addressed **PRIOR** to ordering a genetic test

- Collecting personal and family history
- Evaluation of patient’s risk
- Performing psychosocial assessment
- Education about hereditary syndrome
- Informed consent

Cancer Risk Assessment/Genetic Counseling

- Post-test counseling
  - Address questions and concerns prior to disclosure of results
  - Disclose test results with interpretation
  - Assess and provide emotional support
  - Review medical and psychological impact of results on patient and family members
  - Explain specificity, sensitivity and limitations of the test
  - Provide cancer risk assessment and medical management guidelines/recommendations (see below)
  - Refer patient to appropriate health care providers
  - Identify at-risk family member and provide patient with tools to inform and educate family members (i.e., family contact letter, website information, referrals to genetic professionals)

Importance of Cancer Risk Assessment/Genetic Counseling with Genetic Testing

- ACMG (2000, 2005)
- ACOG (2009)
- AGA (2001)
- ASCO (2003, 2010)
- ASCO/SSO (2006)
- ASBS (2007)
- ASCRS (2001)
- ATA (2009)
- ISONG (2006)
- NCCN (2011)
- NSGC (2004, 2007)
- ONS (2009)
- SGO (2007)
- SSO (1999)
- USPSTF (2005)
Who Should Perform CRA/GC

- An American Board of Genetic Counseling (ABGC) board certified (CGC)/board eligible or (in some states) a licensed genetic counselor

- An American College of Medical Genetics (ACMG) physician board certified in medical genetics

Who Should Perform CRA/GC

- A Genetics Clinical Nurse (GCN) or an Advanced Practice Nurse in Genetics (APNG), credentialed through the Genetics Nursing Credentialing Commission (GNCC)

Who Should Perform CRA/GC

- An advanced practice oncology nurse who is prepared at the graduate level (master’s or doctorate) with specialized education in cancer genetics and hereditary cancer predisposition syndromes**
  - Certification by the Oncology Nursing Certification Corporation is preferred
  - [http://www.ons.org](http://www.ons.org) or [http://www.oncc.org](http://www.oncc.org)
Who Should Perform CRA/GC

- A board-certified physician with experience in cancer genetics (defined as providing cancer risk assessment on a regular basis)
  - The Cancer Committee need to:
    - define the appropriate individuals who will provide risk assessment and counseling for major cancer disease sites (such as breast and colorectal). In addition, programs not having immediate access to formal genetic counseling services should identify resources for referral.

Who Should Perform CRA/GC

- Specialized training in cancer genetics should be ongoing
  - www.cityofhope.org/education/health-professional-education/intensive-course/Pages/default.aspx

- Educational seminars offered by commercial laboratories about how to perform genetic testing are not considered adequate training for cancer risk assessment and genetic counseling

Why these professionals?

- Ample data that most providers are not equipped to provide their own genetic counseling

- Most physicians lack time and do not have understanding of genetics concepts

- Most physicians do not obtain a detailed enough family history
  - Fam Pract 2006;25:324-31; Genet Testing 2008;12(1-2)

- Providers not sufficiently aware of current policy guidelines or laws related to genetic testing
Where to Find a Cancer Genetics Professional

- NCI – www.cancer.gov/search/genetics_services/
- International Society of Nurses in Genetics
  – www.isong.org
- American Board of Genetic Counseling
  – www.abgc.net
- American Society of Human Genetics
  – www.ashg.org/pages/member_search.shtml
- Informed Medical Decisions, Inc.
  – www.informeddna.com
- DNA Direct
  – www.dnadirect.com

Questions?

Please visit the CoC’s CAnswer Forum to post questions on this Webinar.
http://cancerbulletin.facs.org/forums/

Additional resources on the new Standards can be found at the CoC Best Practices Repository:
http://www.facs.org/cancer/coc/bestpractices.html

Login instructions can be found in an attachment posted along with the presentation handouts.

Thank you

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