Genetic Counseling and Testing for Pancreatic Cancer

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What is genetic counseling?

• Two main foci:
  – Medical
    • Helping individuals/families to understand genetic risk
  – Psychosocial
    • Helping individuals/families adjust to diagnoses
Who Should See a Genetic Counselor?

• One of your family members has tested positive for a gene mutation
• You were diagnosed with pancreatic cancer younger than 60 years old
• You were diagnosed with pancreatic cancer at any age and one of your family members has been diagnosed with any of the following (especially younger than 50):
  – Pancreatic cancer
  – Breast cancer
  – Ovarian cancer
  – Colon cancer
• You have not been diagnosed with cancer, but you have a relative who fits one of these categories and is not available to test

What happens in a genetic counseling session?

• Gather your medical history
• Gather and assess your family history
• Review basic genetics, inheritance and the genetic condition that you may be tested for
• Identify your chance to have a genetic change and what that could mean for you and your family members
• Discuss genetic testing options
• Give you support resources and make referrals
Medical History

- Age at cancer diagnosis
- Specific type of cancer
- Treatment (completed, planned, ongoing)
- Surgical history
- Cancer screening methods

For Women:
- Reproductive history
- Breast biopsy history
- Age at menarche/menopause

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Importance of Family History

• Family history taken in the form of a pedigree
  – Pedigree is a graphical representation of a family’s medical history

• Why do we take a family history?
  – To identify patterns that help us recognize what genetic condition (if any) your family may have

Family History Questions

• Information your Genetic Counselor may ask about your relatives
  – Current age/age at death; cause of death
  – Age at diagnosis
  – Type and location of primary cancer/laterality
  – Second cancer-metastatic disease vs. new primary
  – Environmental exposures
  – Other medical conditions associated with cancers (ulcerative colitis, pancreatitis etc.)
  – Ancestry (German, Irish, Native American etc.)
    • Presence of other physical findings associated with cancer syndromes (benign polyps/tumors, macrocephaly, abnormal skin pigmentation etc.)
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Pancreatic Cancer

• Pancreatic cancer affects about 1 in 65 (1.5%) individuals

• Two major types
  – 95% are exocrine (adenocarcinomas)
  – 5% are endocrine (neuroendocrine/islet cell tumors)

Pancreatic Cancer

• Sporadic- occur at older ages with little to no family history.

• Hereditary- genetic cause has been found.

• Familial- no identifiable genetic cause. Most likely a combination of genes, environment and lifestyle.
**BRCA1 and BRCA2**

- Mutations in the *BRCA2* gene
  - May account for about 10% of hereditary pancreatic cancer
  - Cause between ~10-20% lifetime chance to have pancreatic cancer
  - Cause an increase risk of breast, ovarian, and prostate cancer

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**Lynch Syndrome**

- Also known as Hereditary Non-polyposis Colorectal Cancer (HNPCC)
- May cause as much as 4% of hereditary pancreatic cancer
- *MLH1* and *MSH2* mutations can cause up to a 6% lifetime chance of pancreatic cancer
- Increases the chance of colon, uterine, ovarian, stomach and other cancers
Puetz-Jeghers Syndrome

- Rare hereditary cancer predisposition syndrome (STK11)
- Causes between 10-35% lifetime chance to have pancreatic cancer
- Causes an increased chance to have breast, colon, stomach, small intestine, gynecologic cancers, testicular and lung cancers.
- Causes freckle-like spots around and inside mouth/lips

Familial Atypical Multiple Mole Melanoma (FAMMM)

- Rare hereditary cancer predisposition
- Caused by mutations in the CDKN2A(p16) and CDK4 genes.
- CDKN2A mutations cause up to a 17% lifetime chance to have pancreatic cancer
- Cause in increased chance of atypical moles and melanoma.
Other Genes

- **PALB2** = Partner And Localizer of **BRCA2**
  - Causes about 3% of hereditary pancreatic cancers

- **PRSS1** (and others)
  - Causes hereditary pancreatitis. Chronic inflammation of pancreas increases chance to develop pancreatic cancer

- **ATM**
  - About 0.5-1% of the Western population has a mutation in **ATM**
  - Causes 2-3% of hereditary pancreatic cancers

Autosomal Dominant Inheritance
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Dad BRCA2

Mom BRCA2

Child BRCA2

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Risk Assessment

- Risk assessment is based on:
  - Your personal and family medical history
  - Known mutation in a family member
  - Autosomal dominant inheritance
  - Statistical analysis of pedigree (Bayesian statistics, BRCAPRO, etc.)

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Genetic Testing

• Test for one syndrome (i.e. Lynch) or many at the same time
• $APC$, $ATM$, $BRCA1$, $BRCA2$, $CDKN2A$, $EPCAM$, $MLH1$, $MSH2$, $MSH6$, $PALB2$, $PMS2$, $STK11$, and $TP53$.
• Results in 2-4 weeks

Types of Possible Test Results

• Positive= Mutation found
  – i.e. $BRCA2$ S1870X (6137C>A)
  – Give recommendations for cancer screening/risk reduction
  – Identify other family members who would benefit from testing
• Negative= No mutation found
  – Estimate future cancer risks and make screening recommendations based on your personal/family history
• Variant= Genetic change found
  – There is a change in your DNA but we don’t know what it means
  – Recommend screening based on current information about that exact change and your family history
Pancreatic Cancer Screening

• Research is on-going to determine the best methods and intervals
• Not recommended unless
  – the family meets the definition of familial pancreatic cancer
  – an individual has a gene mutation and a family history of pancreatic cancer

Pancreatic Cancer Screening Methods

• Magnetic resonance cholangiopancreatography (MRI-MRCP)
  – MRI done to look specifically for abnormalities in the pancreas and surrounding structures

• Endoscopic ultrasound (EUS)
  – Thin tube inserted through the mouth into the small intestine and then uses ultrasound to produce images of the pancreas.

• CA19-9
  – Blood test that can indicate pancreatic cancer
Genetic Information Non-Discrimination Act

- Prohibits discrimination by health insurance companies and employers based on “genetic information”
  - Genetic information = genetic test results, relative’s test results (up to and including 4th degree), and/or information about family history of any disease or disorder
- Group and individual health insurance plans
  - Can’t use genetic information to set eligibility, premium or contribution amounts
  - Can’t be considered a pre-existing condition
  - May not request or require a person to have a genetic test

Genetic Information Non-Discrimination Act

- Employers cannot use genetic information to:
  - Hire, fire, promote, or for job assignments
  - They also can’t request, require or buy genetic information

- Does NOT cover:
  - Manifest disease
  - Life, disability, or long-term care insurance
  - Members of the military
  - Employers with <15 people
  - People employed in law enforcement may be required to submit a DNA sample before taking part in crime scene investigation
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Patient Resources