HEREDITARY CANCER SYNDROMES: Updates and Tips for Clinical Practice

Anne Heun, MS, CGC
Certified Genetic Counselor
John Stoddard Cancer Center
Genetics Myths

- “I look like my mother and she had breast cancer, so I’m going to get breast cancer.”
- “Your dad’s family history doesn’t matter – just your mom’s matters.”
- “Cancer skips generations, so since my grandmother had it, I’m going to get it.”
- People have very deeply rooted preconceptions!
Etiology of Cancer

- Sporadic: 70-80%
- Family Clusters: 15-20%
- Hereditary: 5-10%
What is Hereditary Cancer?

In **hereditary cancer**, one damaged gene is inherited.
General Features of Hereditary Cancer

- Multiple close family members diagnosed with the same type of cancer
- Presence of related forms of cancer in the family (breast and ovarian, colon and endometrial, etc.)
- Individuals with multiple primaries (breast and ovarian)
- Early onset of diagnosis (<age 50 for breast or colon)
- Presence of rare tumors (male breast cancer, osteosarcoma, etc.)
- Ethnicity – some at higher risk of specific mutations
Hereditary Cancer Syndromes

- Attenuated/Familial Adenomatous Polyposis (Gardner syndrome, Turcot syndrome)
- Birt-Hogg-Dubé syndrome
- Carney Complex
- Cowden syndrome
- Familial Malignant Melanoma
- Hereditary Breast and Ovarian Cancer
- Hereditary Diffuse Gastric Cancer
- Hereditary Leiomyomatosis and Renal Cell Cancer
- Hereditary Paraganglioma-Pheochromocytoma syndrome
- Hereditary Mixed Polyposis syndrome
- Hereditary non-Von Hippel-Lindau Clear Cell Renal Cell Carcinoma syndrome

- Hereditary Papillary Renal Cell Carcinoma
- Hereditary Retinoblastoma
- Juvenile Polyposis syndrome
- Li-Fraumeni syndrome
- Lynch syndrome (Muir-Torre syndrome)
- Multiple Endocrine Neoplasia Type I
- Multiple Endocrine Neoplasia Type II
- MYH-Associated Polyposis
- Nevoid Basal Cell Carcinoma syndrome
- Peutz-Jeghers syndrome
- Von Hippel-Lindau syndrome
- Xeroderma Pigmentosum
Inheritance Patterns

- Most autosomal dominant

- Some autosomal recessive
Hereditary Cancer

- Pancreatic (57 yrs.)
- Stomach (41 yrs.)
- Colon (51 yrs.)
- Polyps (35 yrs.)
- Breast (55 yrs.)
- Prostate (65 yrs.)
- Lung (80 yrs.)
- Leukemia (11 yrs.)
- Lobular breast (32 yrs.)
  - 2 Polyps (33 yrs.)
- “GI” (45 yrs.)
- Ductal breast (42 yrs.)
Hereditary Cancer

- Who is appropriate for referral to genetics?
- What is the genetic counseling process/session like?
- Who should be tested?
  - And for what?
- How can genetic counseling/testing change care?
CRITERIA FOR FURTHER GENETIC RISK EVALUATION

An affected individual with one or more of the following:
- A known mutation in a breast cancer susceptibility gene within the family
- Early-age-onset breast cancer
- Triple negative (ER-, PR-, HER2-) breast cancer
- Two breast cancer primaries in a single individual
- Breast cancer at any age, and
  - ≥1 close blood relative with breast cancer ≤50 y, or
  - ≥1 close blood relative with epithelial ovarian cancer at any age, or
  - ≥2 close blood relatives with breast cancer and/or pancreatic cancer at any age
- From a population at increased risk
- ≥1 family member on same side of family with a combination of breast cancer and ≥1 of the following (especially if early onset): pancreatic cancer, aggressive prostate cancer (Gleason score ≥7); sarcoma, adrenocortical carcinoma, brain tumors, endometrial cancer, leukemia/lymphoma; thyroid cancer, dermatologic manifestations and/or macrocephaly, hamartomatous polyps of GI tract; diffuse gastric cancer
- Ovarian cancer
- Male breast cancer

An unaffected individual with a family history of one or more of the following:
- A known mutation in a breast cancer susceptibility gene within the family
- ≥2 breast primaries in single individual
- ≥2 individuals with breast primaries on the same side of family (maternal or paternal)
- ≥1 ovarian cancer primary from the same side of family (maternal or paternal)
- First- or second-degree relative with breast cancer ≤45 y
- ≥1 family member on same side of family with a combination of breast cancer and ≥1 of the following (especially if early onset): pancreatic cancer, aggressive prostate cancer (Gleason score ≥7); sarcoma, adrenocortical carcinoma, brain tumors, endometrial cancer, leukemia/lymphoma; thyroid cancer, dermatologic manifestations and/or macrocephaly, hamartomatous polyps of GI tract; diffuse gastric cancer
- Male breast cancer

For populations at increased risk, requirements for evaluation may vary (e.g., high-risk BRCA1/2 carrier; breast cancer, ovarian cancer, prostate cancer in multiple family members; macrocephaly; increased BMI; personal history of breast, ovarian, colorectal cancer; young age at breast cancer diagnosis).
What does Genetic Counseling Involve?

- Patient’s medical history
  - Cancer history, pathology, treatment
  - Carcinogen exposure
  - Patient’s reproductive health history
  - Hormone usage
  - Previous biopsies/surgeries
  - Other relevant physical features

- Family history
  - History of cancer, chemoprevention, prophylactic surgeries
  - Includes first-, second-, and third-degree relatives

- Risk counseling
- Psychosocial Assessment and Support
- Education
- Discussion of Genetic Testing
- INFORMED consent
Hereditary Breast Cancer
Half of hereditary breast cancer explained by mutations in BRCA1 and BRCA2
- 1/500 individuals

Other causes:
- Cowden syndrome
- Hereditary diffuse gastric cancer
- Peutz-Jeghers syndrome
- Li-Fraumeni syndrome
- Less well-characterized genes
BRCA1 and BRCA2
- BReast CAncer predisposition genes 1 and 2

Increased lifetime cancer risks
- Breast: 50-85%
  40-60% for second primary breast cancer
- Ovarian: 15-45% (BRCA1 > BRCA2)
- Pancreatic: 1-7% (BRCA2 > BRCA1)
- Prostate: 20% (BRCA2 > BRCA1)
- Melanoma: ~2% (BRCA2)
- Others? Perhaps uterine sarcoma, bile duct, stomach

Increased risk for early-onset cancers
- Risk of breast cancer before age 50: 30-50%
Pathology

- **Ovarian**: epithelial (usually serous adenocarcinoma)

- **Breast**:
  - 11-28% of the breast cancers in women with a *BRCA1* mutation are triple negative
    - See widely different estimates in literature – from 20-80%
    - The younger a woman is with -/-/-, the greater the risk of a BRCA mutation
  - 80% of the breast cancer in women with a *BRCA2* mutation are ER+/PR+/Her2-

- Approximately 11-40% of women with triple negative breast cancer diagnosed ≤age 40 have a BRCA mutation
NCCN added two cancer types to BRCA testing guidelines: pancreatic and aggressive prostate (Gleason score ≥7)
Less stringent ages of diagnosis of breast cancer
Medical Management

- More intensive screening protocol
  - Annual MRIs and mammograms, clinical breast exams
  - Ovarian cancer screening
  - Pancreatic cancer screening?
  - Screening for men: prostate and male breast

- Medications
  - Birth control pills
  - Tamoxifen

- Prophylactic surgeries
  - Prophylactic mastectomies: 90% risk reduction
  - Prophylactic salpingo-oophorectomies: 96% risk reduction
    - Also reduction in breast cancer risk (perhaps less so with BRCA1)
    - Prophylactic salpingectomies?
  - Prophylactic prostatectomy?
http://brcatool.standford.edu
4.5-9% of women undergoing risk-reducing salpingo-oophorectomies have occult ovarian cancers found pathologically.

One study showed 2/29 women undergoing risk-reducing mastectomies were found to have invasive breast cancer.

No surgery is 100% effective at eliminating risk.
BRCA1, BRCA2, PALB2 work together to repair DNA damage
- In individuals with BRCA mutation, this process is defective → cancer formation

PARP is one step above...causes DNA damage that BRCA1/BRCA2/PALB2 would usually repair
- Overloads cell, leading to cell death
- Selective for cancer cells (that replicate more frequently)

In clinical trials
- Have been setbacks, but new trials beginning
As part of the Affordable Care Act, BRCA testing now considered PREVENTIVE
   - Genetic counseling also should be covered

Insurance cannot apply co-pay, deductible, or co-insurance if a woman meets United States Preventive Services Task Force criteria

Same true for all USPSTF “A” and “B” recommendations
   - [http://www.uspreventiveservicestaskforce.org/uspstf/uspsabrecs.htm](http://www.uspreventiveservicestaskforce.org/uspstf/uspsabrecs.htm)

Only for women at high-risk (about 2% of adult women) and who have NOT had cancer
Non-Ashkenazi:
- 2 first-degree relatives with breast cancer, with one ≤ age 50
- 3 or more first- or second-degree relatives with breast cancer
- A combination of breast and ovarian cancer among first- and second-degree relatives
- First-degree relative with bilateral breast cancer
- 2 or more first- or second-degree relatives with ovarian cancer
- First- or second-degree relative with both breast and ovarian cancer
- Breast cancer in a male relative

Ashkenazi:
- Any first-degree relative (or 2 second-degree relatives on the same side of the family) with breast or ovarian cancer
Association for Molecular Pathology vs. Myriad Genetics

- Supreme Court case

- Myriad Genetics Laboratories lost patent to BRCA genes in June 2013
  - “isolating genes found in nature is not patentable”

- Now other labs can perform BRCA testing
  - Lower cost
  - But are they as good?
### Other Breast Cancer Syndromes

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Cancer Risks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cowden syndrome (<em>PTEN</em>)</td>
<td>25-50% breast, 10% thyroid, 5-10% endometrial, colon, renal, melanoma</td>
</tr>
<tr>
<td>Hereditary diffuse gastric cancer (<em>CDH1</em>)</td>
<td>39-52% lobular breast, 40-83% diffuse gastric, colon?</td>
</tr>
<tr>
<td>Li-Fraumeni syndrome (<em>TP53</em>)</td>
<td>Overall risk in females &gt;90%, males 73%; breast, soft tissue sarcoma, osteosarcoma, brain tumors, leukemia, adrenocortical carcinoma</td>
</tr>
<tr>
<td>Peutz-Jeghers syndrome (<em>STK11</em>)</td>
<td>39% colorectal, 32-54% breast, 11-36% pancreatic, 30% gastric, 13% small bowel, 10% cervical, 10% uterine, 15% lung, 9% testicular, 21% ovarian sex cord tumors</td>
</tr>
</tbody>
</table>

- NCCN has guidelines for Cowden syndrome and LFS
Even if no “hereditary” cause is present, a family history can lead to a higher risk of developing cancer.

- Personal risk factors:
  - Nulliparity
  - Early menarche
  - Late menopause
  - Later age at having first child
  - Long-term hormone replacement therapy

- Statistical models available to estimate risk
  - Gail, BRCAPro, Tyrer-Cuzick (IBIS), Claus, BOADICEA
### Risk Calculator

(Click a question number for a brief explanation, or [read all explanations](#).)

<table>
<thead>
<tr>
<th>Question</th>
<th>Select</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Does the woman have a medical history of any breast cancer or of ductal carcinoma in situ (DCIS) or lobular carcinoma in situ (LCIS)?</td>
<td></td>
</tr>
<tr>
<td>2. What is the woman's age?</td>
<td></td>
</tr>
<tr>
<td><em>This tool only calculates risk for women 35 years of age or older.</em></td>
<td></td>
</tr>
<tr>
<td>3. What was the woman's age at the time of her first menstrual period?</td>
<td></td>
</tr>
<tr>
<td>4. What was the woman's age at the time of her first live birth of a child?</td>
<td></td>
</tr>
<tr>
<td>5. How many of the woman's first-degree relatives - mother, sisters, daughters - have had breast cancer?</td>
<td></td>
</tr>
<tr>
<td>6. Has the woman ever had a breast biopsy?</td>
<td></td>
</tr>
<tr>
<td>6a. How many breast biopsies (positive or negative) has the woman had?</td>
<td></td>
</tr>
<tr>
<td>6b. Has the woman had at least one breast biopsy with atypical hyperplasia?</td>
<td></td>
</tr>
<tr>
<td>7. What is the woman's race/ethnicity?</td>
<td></td>
</tr>
<tr>
<td>7a. What is the sub race/ethnicity?</td>
<td></td>
</tr>
</tbody>
</table>

[![Calculate Risk](#)](http://www.cancer.gov/bcrisktool/)

- **Gail model** *(National Cancer Institute)*
- Tyrer-Cuzick Model (IBIS)
- Also calculates likelihood of BRCA mutation (reliability?)
If a woman’s lifetime risk exceeds 20% with these models, it may be appropriate for her to have more intensive screening.

- Annual mammogram\(^h\) + clinical breast exam every 6-12 mo
  - beginning at age 30 y
- Breast awareness\(^g\)
- Consider risk reduction strategies (See NCCN Guidelines for Breast Cancer Risk Reduction)
- Consider annual breast MRI
  - beginning at age 30 y

Or, if a woman is ≥35 with a 5-year risk of breast cancer at ≥1.7%, increased screening may be warranted.

- Women ≥35 y with 5-year risk of invasive breast cancer ≥1.7%\(^d\)
- OR
- LCIS (begin screening at diagnosis)
  - Annual mammogram\(^h\) + clinical breast exam every 6-12 mo
  - Breast awareness\(^g\)
  - Consider risk reduction strategies (See NCCN Guidelines for Breast Cancer Risk Reduction)
Breast Cancer Risk Assessment

- No model is perfect
  - All have strengths and limitations
  - All use certain factors to characterize risk
  - No single tool is comprehensive

- Very important that the person using the models understands strengths and limitations
Hereditary Colorectal Cancer
Majority of hereditary colorectal cancer caused by Lynch syndrome (2-3% of all colorectal cancer diagnoses)

Five known genes: MLH1, MSH2, MSH6, PMS2, EPCAM
- Gene-specific risks

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>General Population Risk</th>
<th>HNPCC Mutation Carrier Lifetime Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colon</td>
<td>5.5%</td>
<td>Up to 80%</td>
</tr>
<tr>
<td>Endometrium</td>
<td>2.7%</td>
<td>20-60%</td>
</tr>
<tr>
<td>Stomach</td>
<td>&lt;1%</td>
<td>11-19%</td>
</tr>
<tr>
<td>Ovary</td>
<td>&lt;1%</td>
<td>9-12%</td>
</tr>
<tr>
<td>Hepatobiliary tract</td>
<td>&lt;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>1-4%</td>
</tr>
<tr>
<td>Brain/central nervous system</td>
<td>&lt;1%</td>
<td>1-3%</td>
</tr>
</tbody>
</table>
Medical Management

- Colonoscopy every 1-2 years, beginning at age 25
- EGD with extended duodenoscopy every 3-5 years, beginning at age 30-35
- Annual comprehensive physical exam beginning at age 25-30
- Annual urinalysis beginning at age 25-30
- Pancreatic cancer screening?

- Women:
  - Gynecologic cancer screening
  - Consider prophylactic hysterectomy + BSO after childbearing is complete
Testing Criteria

- Always evolving and insurance-company dependent

- Amsterdam Criteria = 3-2-1 rule
  - 3 family members with Lynch-syndrome related cancers
  - 2 generations
  - 1 member diagnosed under the age of 50

- Revised Bethesda guidelines
  - CRC ≤ age 50
  - Synchronous or metachronous Lynch-related tumors
  - CRC ≤ age 60 with MSI-high histology
  - CRC with ≥ 1st degree relative with Lynch-related tumor, at least one diagnosed ≤ age 50
  - CRC diagnosed in ≥ 2 1st or 2nd degree relatives, no age specified
Tumor screening

- Tumors (usually colorectal) can be screened for Lynch syndrome
  - Immunohistochemistry for MLH1, MSH2, MSH6, PMS2
  - Microsatellite instability

- MSI-high pathology:
  - Mucinous/signet ring
  - Tumor infiltrating lymphocytes
  - Crohn’s-like lymphocytic reaction
  - Medullary growth pattern
Tumor Screening

- Tumor screening can provide a clinical diagnosis of Lynch syndrome, even if no mutation is found
  - Tumor missing MSH2 or MSH6 (or both)

- Tumor screening is 90-95% sensitive
  - Can identify people at-risk of having Lynch syndrome
  - Can also guide genetic testing

- Check out the pathology report!!!

- In Des Moines: performed for all individuals under 50 with colorectal cancer, under 60 who meet Bethesda guidelines
1% of all colon cancers associated with Familial Adenomatous Polyposis

- FAP, attenuated FAP, Gardner syndrome, Turcot syndrome = same diagnosis (on a spectrum)
  - FAP 100-1000s of polyps
  - AFAP 10-100 polyps (average 30)

- Important to differentiate between AFAP and MYH-associated polyposis
  - Recurrence risk
  - Medical management
Cancer Risks – FAP:
- Colorectal: virtually 100%
- Duodenal or peri-ampullary: 5-12%
- Gastric: <1%
- Thyroid (papillary): 1-2%
- Hepatoblastoma (by age 5): 1-2%
- Pancreatic: <1%
- Medulloblastoma: <1%

Cancer Risks – AFAP:
- Upper GI, duodenal, and thyroid risks similar
- Colorectal: 80%
FAP - Other Tumors

- Desmoid tumors
- Supernumerary teeth
- Osteomas
- Odontomas
- Epidermoid cysts
- Fundic gland polyps
- Congenital hypertrophy of the retinal pigment epithelium (CHRPE)
Medical Management (FAP)

- Annual flexible sigmoidoscopy/colonoscopy beginning at age 10-15
  - Total colectomy once polyp burden is too high
- Upper endoscopy: repeat based on findings, every 1-4 years
- Annual thyroid exam beginning in late teenage years
- Annual physical examination with abdominal palpation
- Regular small bowel screening (CT/MRI)
- Hepatoblastoma?
- Pancreatic cancer screening?
Other Colorectal Cancer syndromes

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Cancer Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>MYH-associated Polyposis (MUTYH)</td>
<td>80% colorectal, 5% duodenal</td>
</tr>
<tr>
<td>Juvenile Polyposis (SMAD4, BMPR1A)</td>
<td>Juvenile-type polyps; 40-50% colorectal, 21% gastric, pancreatic, small bowel</td>
</tr>
<tr>
<td>Hereditary Mixed Polyposis</td>
<td>No specific estimate; individuals have multiple types of colon polyps</td>
</tr>
<tr>
<td>Peutz-Jeghers syndrome (STK11)</td>
<td>See previous; risk of hamartomatous GI polyps</td>
</tr>
</tbody>
</table>

<1% of all colorectal cancers
<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Cancer Risks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Von Hippel-Lindau syndrome (VHL)</td>
<td>5-17% pancreatic neuroendocrine, 70% clear cell renal cell carcinoma; hemangioblastoma, pheochromocytoma, retinal angioma, endolymphatic sac tumor</td>
</tr>
<tr>
<td>Birt-Hogg-Dubé syndrome (FLCN)</td>
<td>13-34% renal cancer (chromophobe renal carcinoma); 84% pulmonary cysts, 80% folliculomas, renal oncocytes</td>
</tr>
<tr>
<td>Hereditary non-Von Hippel-Lindau Clear Cell Renal Cell Carcinoma</td>
<td>Clear cell renal cell carcinoma (?)</td>
</tr>
<tr>
<td>Hereditary Papillary Renal Cell Cancer</td>
<td>Type 1 papillary renal cell cancer</td>
</tr>
<tr>
<td>Hereditary Leiomyomatosis Renal Cell Cancer</td>
<td>Uterine fibroids, 15% type 2 papillary renal cell cancer</td>
</tr>
</tbody>
</table>
### Other Cancer Syndromes

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Cancer Risks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hereditary Retinoblastoma (<em>RB1</em>)</td>
<td>~100% retinoblastoma (usually bilateral); sarcomas</td>
</tr>
<tr>
<td>Familial Melanoma (<em>p16</em> or <em>CDKN2A</em>)</td>
<td>28-76% melanoma, 17% pancreatic</td>
</tr>
<tr>
<td>Multiple Endocrine Neoplasia Type I (<em>MEN1</em>)</td>
<td>10% carcinoid tumors, 40% gastrinomas; parathyroid, adrenal, pituitary tumors</td>
</tr>
<tr>
<td>Multiple Endocrine Neoplasia Type II (<em>RET</em>)</td>
<td>95-100% medullary thyroid cancer, 50% pheochromocytoma</td>
</tr>
<tr>
<td>Hereditary Paraganglioma-Pheochromocytoma syndrome</td>
<td>Paraganglioma, pheochromocytoma</td>
</tr>
<tr>
<td>Neviod Basal Cell Carcinoma Syndrome (<em>PTCH1</em>)</td>
<td>basal cell carcinoma, 5% medulloblastoma</td>
</tr>
</tbody>
</table>
Skin Manifestations

- Many hereditary cancer syndromes have skin manifestations
- Can be used to help guide testing or give a clinical diagnosis
- Other tumors (not necessarily skin) may be significant
  - Osteomas (FAP)
  - Lipomas (Cowden syndrome)
  - Desmoid tumors (FAP)
Cowden syndrome

- Trichilemmomas, papillomatous papules
Lynch syndrome

- Sebaceous keratoacanthomas, epitheliomas, adenomas
Multiple Endocrine Neoplasia Type II

- Mucosal neuromas (lips and mouth)
Peutz-Jeghers syndrome

- Mucocutaneous freckling
Hereditary Leiomyomatosis and Renal Cell Cancer

- Cutaneous (and uterine) leiomyomas
Familial Malignant Melanoma

- Multiple atypical or dysplastic moles
Birt-Hogg-Dubé syndrome

- Fibrofolliculomas, acrochordons, trichodiscomas
Former model of genetic testing: test for single most-likely syndrome, then follow up with other testing (if needed)

New model of genetic testing: test initially for mutations in many different genes
- Some genes not well understood or characterized

Panels similar in cost (or sometimes CHEAPER) than single-gene testing

What do we do???
<table>
<thead>
<tr>
<th>Panels</th>
<th>Genes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comprehensive Cancer Panel (35 Genes)</td>
<td>APC, ATM, AXIN2, BARD1, BLM, BMPR1A, BRCA1, BRCA2, BRIP1, CDH1, CDK4,</td>
</tr>
<tr>
<td></td>
<td>CDKN2A, CHEK2, EPCAM, FAM175A, FANCC, HOXB13, MLH1, MRE11A, MSH1,</td>
</tr>
<tr>
<td></td>
<td>MSH2, MSH6, MUTYH, NBN, PALB2, PALLD, PMS2, PTEN, RAD50, RAD51C, RAD51D,</td>
</tr>
<tr>
<td></td>
<td>SMAD4, STK11, TP53, VHL, XRCC2</td>
</tr>
<tr>
<td>Breast/Ovarian Cancer Panel (26 Genes)</td>
<td>ATM, BARD1, BLM, BRCA1, BRCA2, BRIP1, CDH1, CHEK2, EPCAM, FAM175A,</td>
</tr>
<tr>
<td></td>
<td>FANCC, HOXB13, MLH1, MRE11A, MSH1, MSH2, MSH6, NBN, PALB2, PMS2, PTEN,</td>
</tr>
<tr>
<td></td>
<td>RAD50, RAD51C, RAD51D, STK11, TP53, XRCC2</td>
</tr>
<tr>
<td>Breast Cancer High Risk Panel (6 Genes)</td>
<td>BRCA1, BRCA2, CDH1, PTEN, STK11, TP53</td>
</tr>
<tr>
<td>Colorectal Cancer Panel (18 Genes)</td>
<td>APC, ATM, AXIN2, BLM, BMPR1A, CDH1, CHEK2, EPCAM, MLH1, MSH1, MSH2,</td>
</tr>
<tr>
<td></td>
<td>MSH6, MUTYH, PMS2, PTEN, SMAD4, STK11, TP53, XRCC2</td>
</tr>
<tr>
<td>Lynch/Colorectal High Risk Panel (7 Genes)</td>
<td>APC, EPCAM, MLH1, MSH2, MSH6, MUTYH, PMS2</td>
</tr>
<tr>
<td>Pancreatic Cancer Panel (18 Genes)</td>
<td>APC, ATM, BRCA1, BRCA2, CDK4, CDKN2A, EPCAM, FANCC, MLH1, MSH1, MSH2,</td>
</tr>
<tr>
<td></td>
<td>MSH6, PALB2, PALLD, PMS2, STK11, TP53, VHL, XRCC2</td>
</tr>
<tr>
<td>Endometrial Cancer Panel (11 Genes)</td>
<td>BRCA1, BRCA2, CHEK2, EPCAM, MLH1, MSH2, MSH6, MUTYH, PMS2, PTEN, TP53</td>
</tr>
</tbody>
</table>
## Other Genes

<table>
<thead>
<tr>
<th>Gene</th>
<th>Tumor Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATM</td>
<td>Female Breast (25-30%), Colon, Pancreatic</td>
</tr>
<tr>
<td>CHEK2</td>
<td>Female Breast (28-38%), Male breast (1%), Colon (~10%), Prostate (24-50%), Thyroid, Renal, Uterine (serous), Ovarian</td>
</tr>
<tr>
<td>PALB2</td>
<td>Female Breast (25-50%), Male Breast (0.5%), Ovarian, Pancreatic (10%)</td>
</tr>
<tr>
<td>AXIN2</td>
<td>Female Breast, Colon</td>
</tr>
<tr>
<td>BARD1</td>
<td>Female Breast, Ovarian</td>
</tr>
<tr>
<td>BLM</td>
<td>Female Breast, Colon</td>
</tr>
<tr>
<td>BRIP1</td>
<td>Female Breast, Ovarian</td>
</tr>
<tr>
<td>CDK4</td>
<td>Breast, Pancreatic, non-melanoma skin cancer</td>
</tr>
<tr>
<td>FAM175A</td>
<td>Female Breast</td>
</tr>
<tr>
<td>FANCC</td>
<td>Female Breast, Pancreatic</td>
</tr>
<tr>
<td>HOXB13</td>
<td>Female Breast, Prostate</td>
</tr>
<tr>
<td>MRE11A</td>
<td>Female Breast, Ovarian</td>
</tr>
<tr>
<td>NBN</td>
<td>Female Breast, Melanoma, Non-Hodgkin lymphoma, Colon</td>
</tr>
<tr>
<td>PALLD</td>
<td>Pancreatic</td>
</tr>
<tr>
<td>RAD50</td>
<td>Female Breast</td>
</tr>
<tr>
<td>RAD51C</td>
<td>Female Breast, Ovarian</td>
</tr>
<tr>
<td>RAD51D</td>
<td>Female Breast, Ovarian</td>
</tr>
<tr>
<td>XRCC2</td>
<td>Female Breast, Colon, Pancreatic</td>
</tr>
</tbody>
</table>
Issues for Patients

- Meaning of results
- Telling other family members, including children
- Fear of developing cancer (perhaps again)
- Differing knowledge levels among healthcare providers
- Life, long-term care, disability insurance issues
- Health insurance coverage for increased screenings
- “Survivor guilt”
- Need unique support
How to Identify Patients at Risk

- Strong family history
- Unusual tumor type
- Unusual pathology
- Skin manifestations

- Use NCCN guidelines
- Call us!
You already had a wonderful talk on this subject!

NOT a test for determining if someone has a hereditary cancer syndrome

“Genetic” test on the tumor
- Genetic mutations in tumor usually somatic

Used for treatment decisions
Questions?

- Thank you very much!
- Anne Heun, MS, CGC
  (515)241-4232
  Anne.Heun@unitypoint.org