Breast Cancer

- Major global problem
- Reduction in mortality rates Western Countries
- Incidence of breast cancer increased
- Diet changes
- Reproductive patterns have changed
- Increased incidence of BRCA1 and BRCA2 mutations

Breast Cancer factors

- One in 8 to one in 12 lifetime risk
- Gender
- Age
- Family history
- Endocrine factors
- Breast Density
- Hx of proliferative breast disorders
### Decisions Regarding Prevention

- Accurate and individualized risk assessment
- Risk falls into two categories
- Mutations and non-mutations

### Family History

- Necessary to assess the likelihood of hereditary genes
- Identify patients at risk for mutations
- Negative for BRCA, a genomic deletion of other mutations genes is 5%.
- High risk is 10% or higher for mutations

### Exceptions

- Cowden Syndrome is...
- Hereditary disorder mutations in the PTEN tumor suppressor
- Macrocephaly
- Multiple tumor-like growths
- Increased risk of certain types of cancer
- One of those if breast cancer
- Lets go more in-depth
Cowden syndrome (CS) is part of the PTEN hamartoma tumor syndrome. Hamartomas are benign, meaning noncancerous, tumor-like growths. Other clinical syndromes that are part of the PTEN hamartoma tumor syndrome are Bannayan-Riley-Ruvalcaba syndrome (BRR; diagnosed in children), Proteus syndrome, and Proteus-like syndrome. CS is characterized by a high risk of both benign and cancerous tumors of the breast, thyroid, endometrium (uterus), colorectal, kidney, and skin (melanoma).

Other key features of CS are skin changes, such as trichilemmomas (skin tags) and papillomatous papules, and macrocephaly, meaning larger than average head size.

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**Cowden Syndrome PTEN Gene Testing Criteria**

- People with a personal history of:
  - A family with a known PTEN gene mutation
  - Meeting clinical diagnostic criteria for CS
  - Bannayan-Riley-Ruvalcaba syndrome (BRR)
  - Adult Lhermitte-Duclos disease (cerebellar tumors)
  - Autism spectrum disorder and macrocephaly
  - Two or more biopsy-proven trichilemmomas
  - Two or more major criteria (one must be macrocephaly)

Models

- Different models have been developed
- Different models produce different results
- Calibrated for accuracy for estimation on the population
- Improvements in models need to be revalidated.
What is epidemiology?

- **Epidemiology** is the study and analysis of the patterns, causes, and effects of health and disease conditions in defined populations. It is the cornerstone of public health, and shapes policy decisions and evidence-based practice by identifying risk factors for disease and targets for preventive healthcare.

Models

- For clinicians, it is very important that a good risk assessment tool has good ability.
- An appropriate preventative treatment can be tailored.
- Good balance between sensitivity and specificity.
- Let's talk about sensitivity and specificity...
Sensitivity (Is it there) (True positive)
The sensitivity of a test refers to how many cases of a disease a particular test can find. A very sensitive test is likely to give a fair number of false-positive results, but almost no true positives will be missed. In mammography, sensitivity is the probability of finding a cancer when the cancer exists. Diagnosing a patient correctly.

Specificity (what is it) (True Negative)
The specificity of a test refers to how accurately it diagnoses a particular disease without giving false-positive results. In mammography, the probability of a normal mammogram when no cancer exists.

Empirical Models
- Estimate the probability genetic testing will detect BRCA1, BRCA2
- Includes early models such as Shattuck-Eidens model also known as Myriad I model.
- Couch model which was updated to Upenn or Penn model.
- Now Penn model is updated to Penn II model.
Models

- Penn II model is a more comprehensive personal and family cancer histories information.
- More validation is needed and not yet published.

Other empirical models include tabular scoring systems like Myriad II also known as the Frank model.
The Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm (BOADICEA) is a computer program that is used to calculate the risks of breast and ovarian cancer in women based on their family history. It is also used to calculate the probability that they are carriers of cancer-associated mutations in the BRCA1 or BRCA2 gene. The latest version of BOADICEA (BWA v3) is described by Lee et al. (2013). You can run BOADICEA risk calculations using the BOADICEA Web Application.

BOADICEA is a user account, which you can setup online in a minute. To date, more than 5000 healthcare professionals have registered to use BWA v3, based in more than 100 countries worldwide. In the United Kingdom, it is recommended as a risk assessment tool in the National Institute for Health and Care Excellence clinical guideline CG164 and has been incorporated in the guidelines of several countries for the management of familial breast cancer.
The BOADICEA Web Application is an example of translational research, where scientific software has been developed further for use by healthcare professionals. For technical reasons, the BOADICEA Web Application is not currently available to members of the public. If you are concerned about your family history of cancer you are advised to consult your GP. The program is available to health care providers as normal.

A Known model

- IBIS also known as Tyer Cruzick model for above average risk.
- IBIS international breast cancer interventional study

Most known Model

- BCRAT is breast cancer risk assessment tool
- BCRAT also known at Gail model
- BCRAT is breast cancer risk assessment tool
- Used for average risk patients
Gail model

- Looks at ....
- Personal medical history
- Family and reproductive history
- Previous bx’s especially with atypical hyperplasia
- Menarche
- Number of pregnancies and birth
- Endocrine history

Gail Model

- Did not include racial or ethnic differences
- Did not include previous breast cancers
- Did not include endocrine therapy
- Had underestimation of many risk factors
- Now the model has been modified by U of Texas Southwestern Medical Center.

Gail Model

- Newly incorporated into the Gail risk model is ...
- Alcohol consumption
- Racial characteristics
- African American, Asian, and Hispanics have a higher risk
- Dietary habits, no more Twinkies !!!
What is the Angelina Effect?

Why her mastectomies raise key issues about genes, health, and risk.
Each woman is different and has different ideas about body perception.
Each decision is carefully thought out and decided with family, friends, and counseling.
Is not having surgery worth the chance?

What country has the most known BRCA mutations?
Additional Options….

Chemoprevention

- Tamoxifen
  - Reduces the risk of developing breast cancer by 50 percent in women who are at an increased risk.
  - Testing is still being done for women with BRCA1 and BRCA2.
  - Raloxifene is also being tested to help reduce risk for the mutation genes.

WHAT IS GENETIC DISCRIMINATION?

- This occurs when people are treated differently by insurance companies or employers because they have a gene mutation that increases their risk of a disease, such as cancer. However, in 2008, Genetic Information Nondiscrimination Act (GINA) was enacted to protect U.S. Citizens against discrimination based on their genetic information in relation to health insurance and employment.
  - The law does not cover life insurance, disability insurance, and long-term care insurance. In addition, the law does not cover members of the military.
  - Employers cannot refuse to hire or fire based on their genetic information. Also they cannot base the employee’s salary because of genetic information.

GENETIC COUNSELING

- A person who is considering genetic testing should speak with a professional trained in genetics before deciding whether to be tested. These professionals may include doctors trained in genetics, genetic counselors, and/or other health care workers that specialize in genetics.
Genetic Counseling

The results of gene sequencing and large rearrangement testing of 9 genes associated with hereditary forms of cancer indicated no detectable mutations. Testing included analysis of BRCA1, BRCA2, EPCAM, MLH1, MSH2, MSH6, PMS2, PTEN, and TP53. This result is considered an uninformative negative result. We regard this result as uninformative given it has not explained the history of cancer seen in Ms. H's family. It is possible there may be a mutation not detectable by current technology or there may be other genes involved. It may also be that there was a hereditary form of cancer in her family for which she did not inherit. Based on this, we discussed genetic testing for her brother.
My Facility

- We have a clinic just for Risk Assessment
- Dr. Teresa Bevers is in charge
- She helped to start the program for both men and women
- Cancer prevention is the key to finding diseases early while they are curable.
- Women get assessment in the categories of breast, cervical, uterine, skin, and colon and lung.
- Men get assessment in the categories of prostate, testicular, skin, and colon and lung.
- If assessment has a high risk, psychiatry and genetic counselors are available.

Let’s get some NCI percentages......