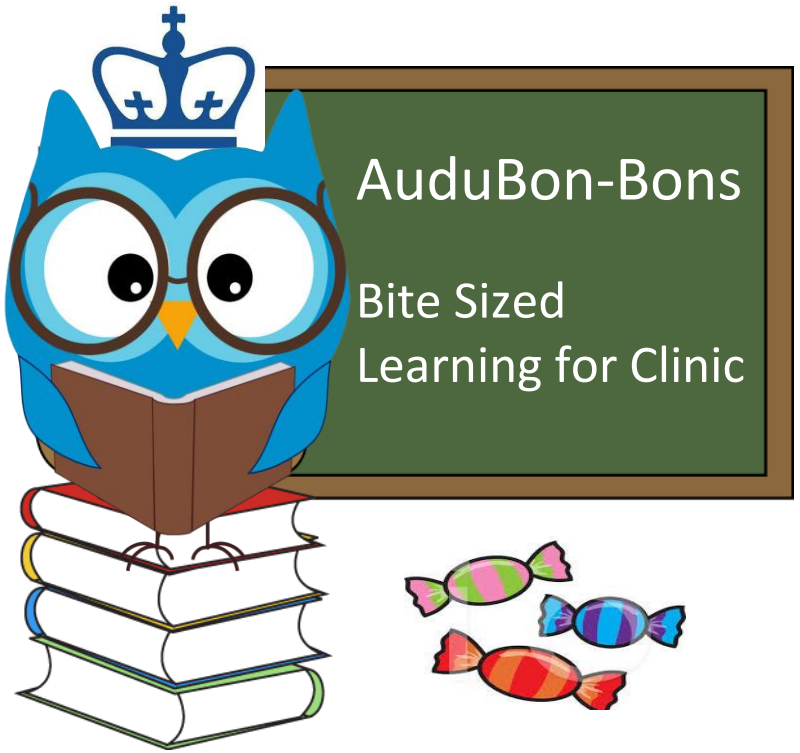
# HEREDITARY BREAST AND OVARIAN CANCER (HBOC) SYNDROME




Week 96

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Reading Assignment:
ACOG Practice Bulletin No. 182: Hereditary Breast and Ovarian Cancer Syndrome

# LEARNING OBJECTIVES 

- Review the common genes implicated in hereditary breast and ovarian cancers (HBOC)
- Understand the criteria for genetic testing referrals
- Discuss cancer risks for BRCA1 and BRCA2
- Review screening and risk reducing strategies for patients with HBOC syndromes

# CASE VIGNETTE

- A 26 yo G1P1 woman presents for her annual GYN exam. She had one uncomplicated NSVD 18  months ago. She has normal monthly menses since she stopped breastfeeding 9 months ago, and she is using OCPs for contraceptives which she is very happy with. She has no complaints, but discloses her mother has recently died from breast cancer. She is appropriately tearful, but feels very supported by her friends and family.

# FOCUSED HISTORY

- **PMH:** None
- **PSH:** Tonsils and adenoids at age 14
- **POBH:** NSVD in 6/2018, FC, 3250g, no complications
- **PGYNH:** No abnormal Paps, most recently in 2019, no STIs, no cysts, fibroids or ovarian masses
- **MEDS:** **Cryselle (OCPs)**, PNV
- **ALL:** None
- **SOCIAL:** Graphic designer, soc EtOH use, no tobacco use, rare MJ use, lives with partner and 18 month old daughter, exercises 5 days a week

# HISTORY CONTINUED

- **What other history do you want to ask her about?**
  - Family history!
    - Mother diagnosed at age 44
    - Maternal aunt with ovarian cancer diagnosed at age 38
    - Maternal aunt with breast cancer at age 40, and subsequent ovarian cancer
- Given the concerning family history, you send her for genetic testing and it returns:
  - **BRCA1 positive**

# PERTINENT PHYSICAL EXAM FINDINGS

**What elements of this patient's physical exam are most relevant?**

- **General:** Well-appearing woman
- **Pulm/CV:** CTAB, RRR
- **Abdominal Exam**: +BS, non-tender to palpation in all four quadrants, no hepatosplenomegaly
- **Breasts:** examined in two positions, no visible/ palpable masses, no skin retraction or dimpling. No LAD. No nipple discharge.
- **Pelvic:** Normal external female genitalia
  - **Spec:** normal vaginal mucosa, no blood in vault, physiologic discharge, cervix with no lesions
- **BME:** no CMT, mobile AV small uterus, no adnexal masses

- **What are t… …netic testing for HBOC?**

**TABLE 1** National Comprehensive Cancer Network (NCCN) guidelines for genetic testing include.[23]

| Personal history of breast cancer and one or more of the following: | Family member with the following: |
|---|---|
| ■ Age at diagnosis < 45 years<br>■ Age at diagnosis 46-50 with:<br>• Additional primary breast cancer<br>• 1 or more close relative(s) with breast, pancreatic, or prostate cancer<br>• Unknown family history<br>■ Age at diagnosis < 60 years with:<br>• Triple negative breast cancer<br>■ Diagnosis at any age with:<br>• 1 or more close relative(s) with breast cancer diagnosed at < 50 years<br>• 2 or more close relatives with breast cancer at any age<br>• 1 or more close relative(s) with invasive ovarian cancer<br>• 2 or more relatives with pancreatic cancer<br>• Male relative with breast cancer<br>• Ashkenazi Jewish ancestry<br>■ Personal history of invasive ovarian cancer<br>■ Personal history of male breast cancer<br>■ Personal history of high-grade prostate cancer and 1 or more close relative(s) with breast, ovarian, pancreatic or prostate cancer<br>■ Personal history of pancreatic cancer with 1 or more close relative(s) with invasive ovarian or pancreatic cancer or 2 more more close relatives with breast or prostate cancer | ■ Family member with known deleterious genetic mutation related to increased breast cancer risk<br>■ First- or second-degree blood relative who meets any of the individual criteria<br>■ Third-degree blood relative with breast and/or invasive ovarian cancer with 2 or more close relatives with breast and or invasive ovarian cancer |

https://www.contemporaryobgyn.net/view/nccn-guidelines-genetic-testing

# HBOC

- BRCA germline mutations:
  - Account for 9-24% of epithelial ovarian cancer
  - 4.5% of breast cancer
  - Tumor suppressor genes involved in DNA repair process
  - 1 in 300-800 individuals carry BRCA germline mutation
  - Increased risk in certain groups (Ashkenazi Jews, French Canadians, Icelanders)
- BRCA1: on chromosome 17
- BRCA2: on chromosome 13

# HBOC

**Table 1.** Genetic Mutations Associated With Hereditary Breast and Ovarian Cancer Syndrome

| Gene | Breast Cancer Risk | Ovarian Cancer Risk* | Other Cancer Risk |
|---|---|---|---|
| *ATM* | Increased | No increased risk | Insufficient evidence |
| *BRCA1* | Increased | Increased | Prostate |
| *BRCA2* | Increased | Increased | Melanoma, pancreas, prostate |
| *BRIP1* | No increased risk | Increased | Insufficient evidence |
| *CDH1* | Increased | No increased risk | Stomach |
| *CHEK2* | Increased | No increased risk | Colon |
| Lynch Syndrome Genes: *MSH2, MLH1, MSH6, PMS2, and EPCAM* | Insufficient evidence | Increased | Colon, uterine, renal pelvis, small bowel, and others |
| *PALB2* | Increased | No increased risk | Unknown |
| *PTEN* | Increased | No increased risk | Cowden Syndrome |
| *RAD51C* | No increased risk | Increased | Unknown |
| *RAD51D* | No increased risk | Increased | Unknown |
| *STK11* | Increased risk | Increased risk of sex cord stromal tumors | Peutz–Jehger Syndrome |
| *TP53* | Increased | No increased risk | Li–Fraumeni Syndrome |

*Includes fallopian tube cancer and primary peritoneal cancer.

Data from National Comprehensive Cancer Network. Genetic/familial high risk assessment: breast and ovarian. Version 2.2017. NCCN Clinical Practice Guidelines in Oncology. Fort Washington (PA): NCCN; 2016. Available at: https://www.nccn.org/professionals/physician_gls/pdf/genetics_screening.pdf.

# BRCA1

- **57%** risk (45-85%) of developing **breast cancer** by age 70
- For those with breast cancer, risk of subsequent ovarian cancer is 12.7%
- Typically triple negative breast cancer
- **39-46%** risk of **ovarian cancer** by age 70
  - Typically high-grade, serous or endometrioid
  - Growing data support fallopian tubes as cancer origin site

# BRCA2

- **49%** risk (45-85%) of developing **breast cancer** by age 70
- For those with breast cancer, risk of subsequent ovarian cancer is 6.8%
- Typically ER/PR receptor positive
- **10-27**% risk of **ovarian cancer** by age 70
  - Typically high-grade, serous or endometrioid
  - Growing data support fallopian tubes as cancer origin site
- **7**% lifetime risk of **pancreatic cancer**
- Increased risk of melanoma, and prostate cancer

# BACK TO THE PATIENT

- What screening will you recommend for the patient?
  - **Ovarian cancer**:
    - CA-125 or TVUS is NOT recommended for surveillance
    - May be appropriate for women between 30-35 until they undergo rrBSO
  - **Breast Cancer**:
    - Age 25-29: breast cancer surveillance q6-12 months with clinical breast exam and MRI with contrast
    - > 30: surveillance q6 months with alternating mammo and MRI

# BACK TO THE PATIENT…

- **What risk-reducing agents exist for ovarian cancer?**
  - **OCPs**
    - 33-80% risk reduction for ovarian/endometrial cancer  with 1 year of use for BRCA1
    - 58-63% risk reduction for ovarian/endometrial cancer with 1 year use for BRCA2
    - No clear increased risk for breast cancer with BRCA mutation carriers with OCP use
- **What surgical risk reducing strategies exist for ovarian cancer?**
  - **BSO**
    - Reduces risk of ovarian, fallopian tube, or peritoneal cancer by 80% in BRCA mutation carriers
    - BRCA1 – typically between 35-40 due to higher risk of premenopausal ovarian cancer than BRCA2 (40-45)
    - **Timing individualized by patient's genetic mutation, family history, and fertility plans**
    - Must counsel on adverse events including early menopause and risk of surgical comps
  - **BS**
    - Trials are currently underway for risk reduction as bridge to future oophorectomy for RR for ovarian cancer
    - No added protection for breast cancer risk

# BACK TO THE PATIENT…

- **What risk reducing strategies will you recommend for breast cancer?**
  - Chemoprevention
    - **Tamoxifen**: reduces risk by ~ 62% in BRCA2 mutation carriers
      - No reduced risk in BRCA1 mutation carriers
      - Adverse events: vasomotor sx, vaginal dryness, increased risk VTE, and endometrial cancer
  - Surgical:
    - **Bilateral mastectomy**
      - Reduces risk by 85-100%
        - 3-59% risk of surgical complications, 64-87% risk of postsurgical physical symptoms
        - 70% of women satisfied with decision
    - **BSO**:
      - Decreases risk of breast cancer by 37-100%

# SOCIAL DETERMINANTS OF HEALTH

HBOC: What factors impact access to genetic testing?

| Provider impact | Patient impact | Payer impact | Diagnostic Delay |
|---|---|---|---|
| ▪ Minority-serving physicians less likely to order genetic testing and refer patients for genetic counseling | ▪ Blacks and Latinos are less likely to request genetic testing<br>▪ Distrust in how info is used<br>▪ Less knowledge of own pedigree | ▪ Private insurance more likely to cover genetic testing | ▪ Decreased or missed window for implementing screening and prevention strategies |

Blacks and Latinos are less likely to access genetic testing than non-Hispanic whites

# EPIC .PHRASE

**.BBonHBOC**

## Description: HBOC Syndrome Counseling

Discussion was had about reasons for referral for genetic testing for hereditary breast and ovarian cancer syndromes. The patient ***accepts/declines genetic counseling referral. She was counseled about both benefits and potential adverse outcomes from genetic testing including false positive results from genetic testing.

We discussed screening and risk reducing strategies for breast and ovarian cancers for patients who are HBOC mutation carriers including medical and surgical management options.

# CODING/BILLING

- Z80.3- Family history of malignant neoplasm of breast
- Z80.41- Family history of malignant neoplasm of ovary
- Z15.01- Genetic susceptibility to malignant neoplasm of breast
- Z84.81- Family history of carrier of genetic disease

# REFERENCES


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