

The background features a vertical gradient from light purple at the top to light blue at the bottom. Scattered throughout are several realistic water droplets of various sizes, some with highlights and shadows, giving them a three-dimensional appearance.

GENETICS AND BREAST CANCER

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- ONLY 5-10% OF WOMEN WITH BREAST CANCER HAVE AN INHERITED GENE MUTATION
- GENETIC TESTING HAS CHANGED SIGNIFICANTLY OVER THE PAST 5 YEARS (MY TEXTBOOK IS NOT HELPFUL)
 - PANEL TESTING
 - HIGH RISK VERSUS MODERATE RISK GENES
- THE FIRST BREAST CANCER GENES TO BE DISCOVERED WERE.....

30 YO FEMALE WITH NO HISTORY OF CANCER

- WHICH FAMILY HISTORY WOULD BE MOST CONCERNING FOR BRCA 1/2 MUTATION?
 - TWO MATERNAL AUNTS HAD BREAST CANCER AT AGE 50.
 - TWO PATERNAL AUNTS HAD OVARIAN CANCER AT AGE 50.
 - MOTHER HAD BREAST CANCER AT AGE 50.
 - MOTHER HAD COLON CANCER AT AGE 50.
 - A MATERNAL AUNT HAD BREAST CANCER AT AGE 50 AND A PATERNAL AUNT HAD BREAST CANCER AT AGE 50.

SV

- 60 MALE WITH HISTORY OF LEFT BREAST CANCER
- SHOULD HE UNDERGO GENETIC TESTING? IF SO, WHICH GENES?

- BRCA 1/2
 - PATIENT HAS A 14% CHANCE OF TESTING POSITIVE
 - ALL MEN WITH BREAST CANCER SHOULD BE TESTED FOR THESE GENES

A 52-YEAR-OLD WOMAN PRESENTS WITH AN ABNORMAL MAMMOGRAM, AND SHE IS CONCERNED THAT SHE MIGHT CARRY A BRCA MUTATION. AS YOU ANALYZE THE POSSIBILITY THAT THIS COULD BE THE CASE, WHICH OF THE FOLLOWING CLINICAL OR PATHOLOGIC FEATURES WOULD CONTRIBUTE THE LEAST TO INCREASING YOUR LEVEL OF SUSPICION?

- THE PRESENCE OF MULTIPLE SEPARATE CANCERS WITHIN THE SAME BREAST
- INVASIVE BREAST CANCER DEMONSTRATING A TRIPLE-NEGATIVE PHENOTYPE
- EXTENSIVE LOBULAR CARCINOMA IN SITU (LCIS) FOUND IN THE RIGHT BREAST, WITH A PREVIOUS HISTORY OF LCIS IN THE LEFT BREAST
- HISTORY OF PANCREATIC ADENOCARCINOMA IN THE PATIENT'S FATHER
- A HISTORY OF DUCTAL CARCINOMA IN SITU (DCIS) IN THE PATIENT'S SISTER AT THE AGE OF 44

A 41-YEAR-OLD WOMAN WITH NO HISTORY OF MALIGNANCY IS FOUND TO CARRY A MUTATION IN BRCA1. HER MOTHER HAD BREAST CANCER AT 46, AND HER MATERNAL AUNT WAS RECENTLY DIAGNOSED WITH OVARIAN CANCER AT 68. THE PATIENT IS DONE WITH CHILD-BEARING, AND IS CONSIDERING A RISK-REDUCING SALPINGO-OOPHORECTOMY (RRSO). WHICH OF THE FOLLOWING STATEMENTS WOULD NOT BE INCLUDED IN YOUR RECOMMENDATIONS FOR HER RISK MANAGEMENT?

- OCCULT MALIGNANCY CAN BE FOUND IN THE OVARIES OR FALLOPIAN TUBES IN 2-10% OF BRCA-POSITIVE PATIENTS UNDERGOING RRSO.
- RRSO MAY REDUCE HER FUTURE BREAST CANCER RISK BY AS MUCH AS 50%.
- THIS SURGERY CAN BE SAFELY DELAYED UNTIL SHE IS 58, OR 10 YEARS YOUNGER THAN THE YOUNGEST OVARIAN CANCER AGE IN HER FAMILY.
- HYSTERECTOMY IS CONTROVERSIAL IN THIS SETTING, BUT MAY ALLOW HER TO SAFELY TAKE ESTROGEN REPLACEMENT UNTIL AGE 50 OR SO.
- AFTER REMOVAL, THE TUBES AND OVARIES SHOULD BE SERIALY SECTIONED AT 2- TO 3-MM INTERVALS.

YOU HAVE DEMONSTRATED A BRCA2 MUTATION IN A 42-YEAR-OLD WOMAN WHO WAS RECENTLY DIAGNOSED WITH INVASIVE DUCTAL CANCER. THERE IS A STRONG FAMILY HISTORY OF BREAST CANCER, BUT SHE IS THE YOUNGEST WOMAN IN HER FAMILY TO BE DIAGNOSED WITH CANCER. HER 21-YEAR-OLD DAUGHTER IS SUBSEQUENTLY FOUND TO CARRY THE SAME MUTATION, AND THE DAUGHTER CONSULTS YOU REGARDING MANAGEMENT OF HER CANCER RISKS. **YOUR ADVICE INCLUDES WHICH ONE OF THE FOLLOWING STATEMENTS?**

- GIVEN HER MOTHER'S AGE AT DIAGNOSIS, THIS PATIENT SHOULD PLAN TO HAVE BILATERAL PREVENTIVE MASTECTOMY BY THE AGE OF 32.
- SHE SHOULD START ANNUAL SCREENING WITH BREAST MRI AT AGE 32.
- SHE SHOULD AVOID THE USE OF ORAL CONTRACEPTIVE PILLS, WHICH WILL EXACERBATE HER BREAST CANCER RISK.
- SCREENING MAMMOGRAMS MAY MISS MORE THAN 50% OF BRCA-RELATED BREAST CANCERS.
- SHE SHOULD TRY TO GET PREGNANT AS SOON AS POSSIBLE IN ORDER TO LOWER HER BREAST CANCER RISK.

A 40-YEAR-OLD PREMENOPAUSAL WOMAN HAS RECENTLY UNDERGONE A RISK REDUCING BILATERAL TOTAL MASTECTOMY FOR A BRCA1 MUTATION. **SHE NOW SEEKS YOUR ADVICE REGARDING HER OVARIAN CANCER RISK AND ITS MANAGEMENT.** YOUR ADVICE INCLUDES WHICH OF THE FOLLOWING STATEMENTS?

- HER LIFETIME RISK FOR OVARIAN CANCER IS APPROXIMATELY 20%.
- ORAL CONTRACEPTIVE USE CAN SIGNIFICANTLY LOWER THE RISK FOR THESE CANCERS.
- TRANSVAGINAL ULTRASOUND, PELVIC EXAMINATION, AND SERUM CA-125 LEVELS TWICE YEARLY REPRESENT A HIGHLY EFFECTIVE APPROACH FOR SCREENING FOR OVARIAN CANCER.
- RISK-REDUCING SALPINGO-OOPHORECTOMY WILL SIGNIFICANTLY REDUCE HER RISK FOR A LOCAL RECURRENCE OF HER DCIS.

INDICATIONS FOR BRCA TESTING

- BREAST CANCER UNDER AGE 50
- TRIPLE NEGATIVE BREAST CANCER UNDER AGE 60
- MULTIPLE BREAST CANCERS
- MALE BREAST CANCER
- BOTH BREAST AND OVARIAN CANCER IN PATIENT OR IN HER FAMILY
- 2 OR MORE PRIMARY TYPES OF BRCA 1/2 CANCERS IN FAMILY
- ASHKENAZI JEWISH HISTORY
- CONSIDER FOR DCIS < 45

BRCA CANCERS

- BRCA 1

- BREAST (55-65%)
- OVARIAN (39%)
- FALLOPIAN TUBE/PERITONEAL
- MALE BREAST (LESS THAN BRCA 2)
- PROSTATE CANCER
- PANCREATIC CANCER

- BRCA 2

- BREAST (45%)
- OVARIAN (11-17%)
- MALE BREAST CANCER
- PROSTATE CANCER
- PANCREATIC CANCER

BRCA AND PARP INHIBITORS

- BRCA PLAYS A ROLE IN PROTEIN STABILITY AND HOMOLOGOUS DNA REPAIR
- PARP REPAIRS SSDNA BREAKS
- COMBINATION OF BRCA AND PARP INHIBITORS = LOTS'O'PROBLEMS REPAIRING DNA
- “OLYMPIA: A RANDOMISED, DOUBLE-BLIND, PARALLEL GROUP, PLACEBO-CONTROLLED MULTI-CENTRE PHASE III STUDY TO ASSESS THE EFFICACY AND SAFETY OF **OLAPARIB** VERSUS PLACEBO AS ADJUVANT TREATMENT IN PATIENTS WITH GERMLINE BRCA1 /2 MUTATIONS AND HIGH RISK HER2 NEGATIVE PRIMARY BREAST CANCER WHO HAVE COMPLETED DEFINITIVE LOCAL TREATMENT AND NEOADJUVANT OR ADJUVANT CHEMOTHERAPY”

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- 50 YO FEMALE WITH NEW DX OF LEFT BREAST CANCER
- RECENT DX OF ENDOMETRIAL CANCER, HX OF THYROID CANCER
- MACROCEPHALY
- PTEN MUTATION = COWDEN SYNDROME

COWDEN SYNDROME

- INCREASED RISK OF BREAST (85%), THYROID (35%), ENDOMETRIAL CANCER (28%)
- OTHER CANCERS: COLON, KIDNEY, MELANOMA
- OTHER CHARACTERISTICS:
 - MACROCEPHALY
 - COLONIC POLYPS
 - BENIGN THYROID DISEASE
 - LHERMITTE-DUCLOS DISEASE

40 YO FEMALE WITH HX OF ILC, FAMILY HX OF GASTRIC CANCER

- CDH1 (E-CAD)
- STK11 (LKB1) (PEUTZ-JEGHER)
- PTEN
- P53
- PALB2

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OTHER GENES OF INTEREST

- ATM
 - BREAST + PANCREATIC CANCER
 - RISK OF BREAST 24 – 69% ?
- CHEK2
 - BREAST + COLON + PROSTATE
 - 2X LIFETIME RISK OF BREAST CANCER

FAMILY HISTORY IMPORTANT TO EVALUATE ACTUAL RISKS

BREAST CANCER RISK ASSESSMENT TOOLS

- GAIL MODEL BASED ON:
 - AGE
 - RACE/ETHNICITY
 - AGE AT MENARCHE
 - AGE AT FIRST LIVE BIRTH
 - NUMBER OF PRIOR BREAST BIOPSIES
 - PERSONAL HISTORY OF ATYPICAL HYPERPLASIA
 - FAMILY HISTORY OF BREAST CANCER IN FIRST-DEGREE RELATIVES (FEMALE)
 - **THE BEST VALIDATED BREAST CANCER RISK ASSESSMENT MODEL**

BREAST CANCER RISK ASSESSMENT TOOLS

- TYRER-CUZICK
 - SIMILAR TO GAIL RISK MODEL
 - NOT WELL VALIDATED
- BRCAPRO
 - BASED ON MENDELIAN MODELS
 - ESTIMATES BREAST CANCER RISK BASED ON THE PROBABILITY THAT THE INDIVIDUAL CARRIES A MUTATION IN A MAJOR BREAST CANCER SUSCEPTIBILITY GENE, SUCH AS BRCA1 OR BRCA2.
- CLAUUS
 - BASED ON FIRST AND SECOND DEGREE RELATIVES ONLY

OPTIONS FOR HIGH RISK PATIENTS

- INCREASED SCREENING WITH MAMMOGRAM AND MRI
- TAMOXIFEN
- BILATERAL PROPHYLACTIC MASTECTOMY