

Hereditary Breast & Ovarian Cancer (BRCA)

BRCA gene mutations break the body's ability to fix damaged DNA in cells. When DNA repair fails, cells can grow out of control and form breast or ovarian cancers.

THE ONE-LINE TRUTH

BRCA mutations disable critical DNA repair mechanisms, allowing cancer-causing genetic errors to accumulate unchecked in breast and ovarian tissues.

The chain — how it unfolds

1. Germline BRCA mutation inherited at conception — why: Every cell in the body carries one defective BRCA gene, reducing baseline DNA-repair capacity and setting the stage for cancer if the second copy is lost.
2. Hormonal exposure amplifies DNA damage in target tissues — why: Estrogen and progesterone drive repeated cycles of cell division in breast and ovarian tissue over decades, and estrogen metabolites (breakdown products) create oxidative DNA damage that requires BRCA-mediated repair.
3. Second hit eliminates remaining BRCA function in one cell — why: Random mutation, spontaneous deletion, or accumulated oxidative stress knocks out the last working BRCA gene copy in a single epithelial cell (lining cell) in the breast duct or ovarian surface.
4. Genomic instability triggers mutation cascade — why: Without homologous recombination, every cell division produces new DNA breaks that are repaired incorrectly, rapidly accumulating dozens to hundreds of mutations in growth-control and DNA-damage-response genes.
5. Loss of cell-cycle checkpoints (especially TP53) — why: Mutations disable p53 protein (the 'guardian of the genome') and other checkpoint proteins that normally stop defective cells from dividing, allowing the cell to replicate despite carrying dangerous genetic errors.
6. Uncontrolled proliferation and tumor formation — why: The cell ignores normal stop signals, divides continuously, and forms a microscopic tumor cluster (carcinoma in situ) that may remain contained for months to years before breaking through the basement membrane (thin barrier around ducts or ovarian surface).

7. Invasion and metastasis — why: Accumulated mutations allow tumor cells to produce enzymes that dissolve surrounding tissue, enter blood vessels or lymphatic channels, and travel to distant sites—lymph nodes, bones, liver, lungs, or brain.
8. Widespread metastatic disease and organ failure — why: Metastatic tumors disrupt organ function by replacing normal tissue, consuming nutrients, and causing complications like bone fractures, liver failure, fluid around the lungs (pleural a fluid collection (effusion)), or brain swelling, ultimately leading to multi-organ failure and death if untreated.

Spot it — what you see, and why

- No symptoms (often discovered through genetic testing): BRCA1 or BRCA2 gene mutations increase cancer risk but do not cause symptoms until cancer develops
- Family history of early-onset breast cancer (before age 50): BRCA mutations are inherited in autosomal dominant pattern (50% chance each child gets the mutation) causing breast cancer at younger ages
- Family history of ovarian cancer at any age: BRCA mutations impair DNA repair allowing ovarian cancer cells to grow; 40-50% lifetime risk in BRCA1 carriers
- Male relative with breast cancer: BRCA2 mutations give men 6-7% lifetime breast cancer risk; BRCA1 gives 1% risk
- Multiple family members with breast or ovarian cancer on same side of family: Autosomal dominant inheritance means mutation passes through generations on maternal or paternal side
- Ashkenazi Jewish ancestry with family history: 1 in 40 Ashkenazi Jews carry founder mutations (specific BRCA changes common in this population)

Red flags — act now

- Family history of breast cancer before age 50 or ovarian cancer at any age (suggests hereditary mutation requiring genetic counseling)
- Male relative with breast cancer or personal/family history of pancreatic cancer (strongly suggests BRCA2 mutation)
- New breast mass, persistent nipple discharge, or palpable axillary lymph nodes (requires urgent imaging within 2 weeks)
- Abdominal bloating, pelvic pain, early satiety, or increased abdominal size in BRCA carrier (ovarian cancer symptoms requiring urgent ultrasound and CA-125)

Treat it — in this order

1. Risk-reducing bilateral mastectomy (removing both breasts) → Reduces breast cancer risk by 90-95%; does not eliminate risk because small amount of breast tissue remains
2. Risk-reducing bilateral salpingo-oophorectomy (removing fallopian tubes and ovaries) after childbearing complete, age 35-40 → Reduces ovarian cancer risk by 80-90% and breast cancer risk by 50% if done before menopause; most effective intervention
3. Chemoprevention with tamoxifen (20 milligrams daily for 5 years) in premenopausal women → Reduces estrogen-receptor-positive breast cancer risk by 40-50% but does not reduce triple-negative breast cancer common in BRCA1 carriers
4. Enhanced surveillance without risk-reducing surgery (patient choice) → Increases early cancer detection so treatment can start at earlier stage with better survival; does not prevent cancer
5. Genetic counseling for family members → Identifies other at-risk relatives who can benefit from testing and prevention; 50% of first-degree relatives carry mutation

Your top priorities at the bedside

1. Identify patients with strong family history of breast, ovarian, pancreatic, or prostate cancer for genetic counseling referral — why: BRCA mutations (changes in genes that increase cancer risk) are inherited; early identification allows cascade testing (testing family members) and risk-reducing interventions before cancer develops.
2. Support patients through genetic testing decision-making and informed consent process — why: Testing has profound implications for the patient and blood relatives; informed consent must address psychological impact, insurance discrimination concerns under GINA (Genetic Information Nondiscrimination Act), and family disclosure.
3. Coordinate multidisciplinary care including medical oncology, surgical oncology, and reproductive specialists — why: BRCA carriers need individualized surveillance (regular monitoring for cancer), risk-reducing surgeries (mastectomy or oophorectomy), and fertility preservation counseling before preventive oophorectomy (removal of ovaries).