CANCER RISK REDUCTION LIFESTYLE: IT MAY BE EASIER THAN YOU THINK (FEATURING BREAST CANCER)

15TH ANNUAL INTEGRATIVE MEDICINE CONFERENCE

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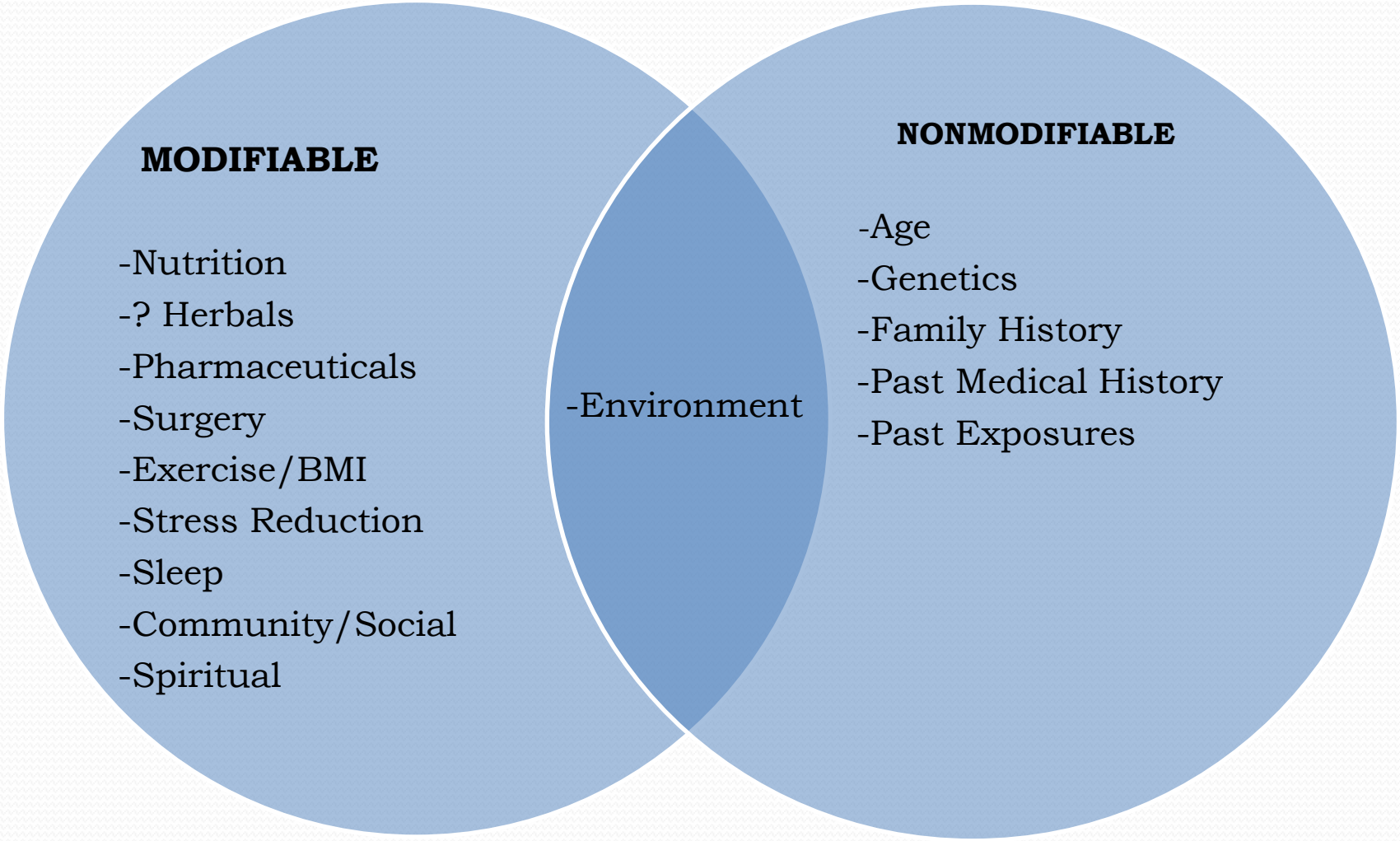
CANCER RISK REDUCTION



BREAST CANCER RISK

- What factors increase risk?
- Common in US, strikes 1 in 8 women by age 80.
- 1 in every 36 women in US die of breast cancer.
- Not a single disease, but a collection; different causes and poorly understood risk factors.
- Strongest risk factors involve inherited defects in DNA repair ability.
- Other risk factors involve signaling pathways related to sex steroids, inflammation, nutrient-sensing, and energy balance.

BREAST CANCER RISK

- Risk factors are classified as major, moderate, or minor based on the strength of their effect, and whether they are modifiable or non modifiable.
- Moderate risk factors are “reproductive risk factors” because of connection to female endocrine system.
- Effects of minor risk factors are seen in large populations, and are difficult to quantify in individuals, and degree of risk can depend on individual genetic variation.

BC RISK FACTORS: MAJOR

MAJOR	2-10 FOLD RISK INCREASE
• Gender	• F:M 100:1
• Age	• Incidence peaks age 70
• BRCA 1 and 2 mutations	• Triple negative tumors assoc with BRCA1
• BC in 1st degree relative under 40	
• BC in 3 or more close relatives any age	
• Personal hx invasive BC	
• Personal DCIS, LCIS, atypia	
• Dense breast tissue on mammogram	• Study screening MRI/US

BC RISK FACTORS: MODERATE

MODERATE

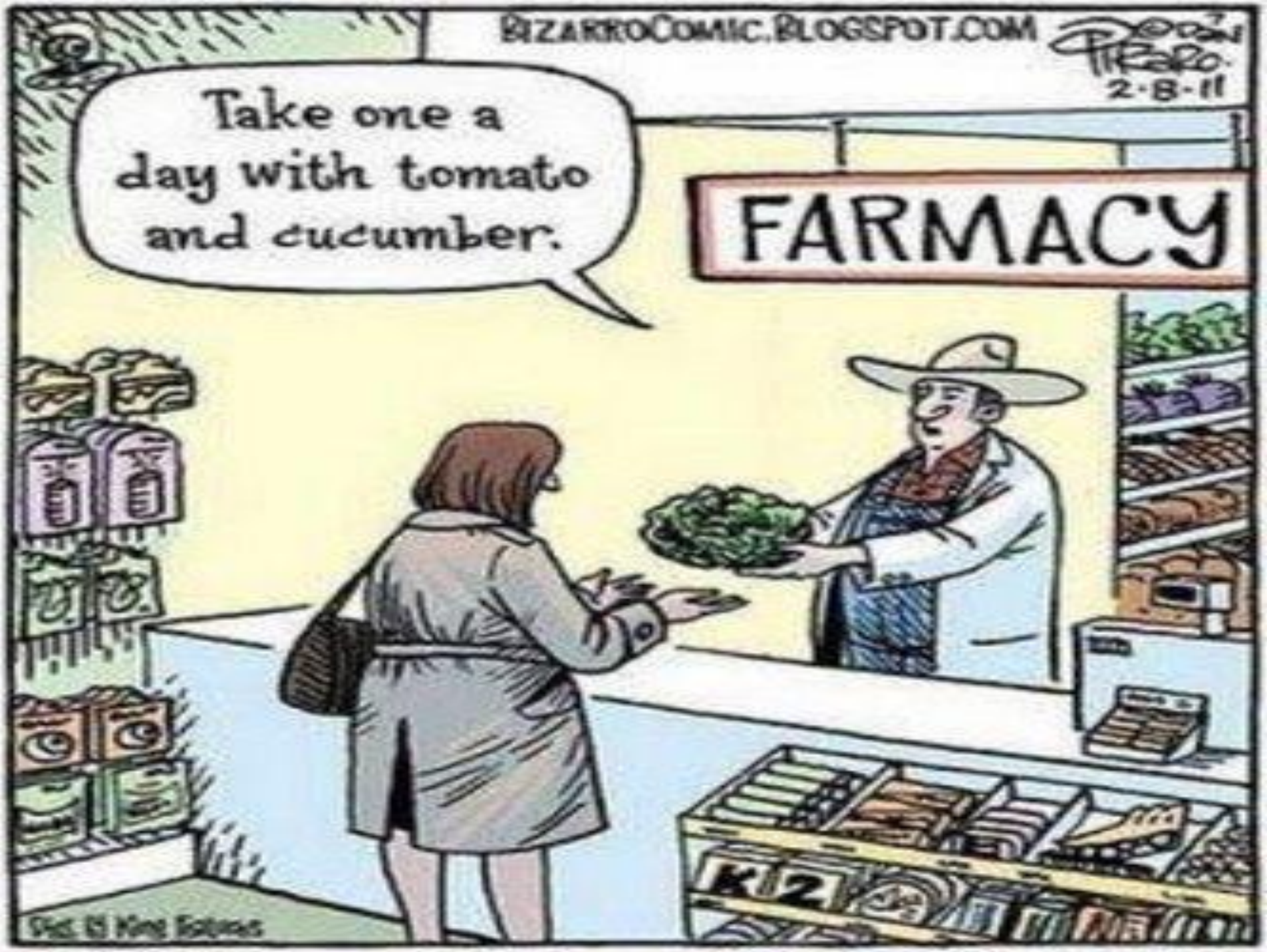
- Early menses and/or late menopause
- Older age first pregnancy or nulliparity
- Lactation
- Hormone Replacement Therapy

1.5-2-FOLD RISK INCREASE

- Increased HR+ tumors
- Increased risk in pts with variants in insulin and angiogenesis genes
- Inverse association

BC RISK FACTORS: MINOR

MINOR	INDETERMINATE RISK INCREASE
• Alcohol	• Effect seen: 1 drink/day
• Race/ethnicity	• European heritage: more HR+ disease; African A:more triple negative
• Environmental toxin exposure	• Food, plastics, pesticides, cosmetics, etc.
• Physical activity	• Inverse risk
• Height, weight, fat distribution, weight changes, obesity	• Complex interactions
• Shift work (circadian disruption)	• Increased risk depending on genetic variants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2-8-11
Take one a day with tomato and cucumber.
FARMACY
K2

RISK REDUCING NUTRITION

- High intake fruits/vegetables beneficial for risk reduction: antioxidants/phytonutrients and fiber
- Plant-based diet (Anti-inflammatory), non-processed, organic (fish, meat), O6:O3, no transfat
- Cruciferous vegetables (BC)
- Fatty fish (herring, mackerel, tuna, salmon, sardines); minimize mercury; 2-3x/week; vs algae
- Hydration esssential for detoxification
- Green tea: rich in antioxidants (BC)
- Minimize alcohol (esp BC)
- Mushrooms (shitake, white button)
- Spices (garlic, onions, pepper, ginger, turmeric)
- Consideration of soy
- Flaxseed (especially BC)

FASTING

- Intermittent fasting: may be helpful in risk reduction, especially for BC; animal studies show reduced caloric intake inhibits cancer initiation and progression.
- Valter D. Longo, PhD: cell biologist; animal and early human trials on role of starvation/nutrient response genes on cell protection in aging and in disease.
- Longo 2015 mouse studies: bimonthly 4 day fasts: increased lifespan, immune system, cognition, and decreased cancer, inflammation, bone density loss.
- Pilot human trial: decreased risk factors for aging, DM, CVD, and cancer; no adverse side effects.
- Low calorie, not water fasts; contraindicated in DM
- Short fasts during chemo: decreased side effects.

JAMA ONCOLOGY PUBLICATION

- "PROLONGED NIGHTLY FASTING AND BREAST CANCER PROGNOSIS", by Catherine R. Marinac, BA, et al, March 31, 2016.

- FINDINGS: Cohort of 2413 patients with history of early stage breast cancer, nightly fasting for less than 13 hours was associated with a 36% increased risk of breast cancer recurrence compared with nightly fasting more than 13 hours.
- CONCLUSIONS: Prolonging the length of nightly fasting interval may be a dietary strategy to reduce risk of breast cancer recurrence in women.

CARBOHYDRATE RESTRICTION: BREAST CANCER

- The Woman's Healthy Eating and Living (WHEL) trial: carb restriction led to 5x reduction in BC recurrence in 50% of patients expressing IGF-1 receptor; no benefit in women with IGF-1 negative tumors. Testing of breast tumors for IGF-1 however not yet routinely available in clinical practice.
- Elevated blood glucose levels after a meal, and elevated fasting insulin levels are associated with poor BC prognosis.

HERBALS

- Many plants contain **phytochemicals** with antioxidant, anti-inflammatory, immune- and hormone- modulating, detoxifying, and adaptogenic effects which antagonize cancer.
- Few of these, when isolated as “supplements”, have undergone phase III clinical trial testing to demonstrate cancer risk reduction, yielding insufficient data for specific recommendations on formulas, doses, and duration of use.
- We DO have some in-vitro, animal, and small human trial data on certain supplements which can reduce risk of breast cancer.

HERBALS/SUPPLEMENTS

- **Ashwagandha (Withania somnifera)**: in vitro, reduces BC cell proliferation, increases cell death in ER+ and ER- human BC cells.
- **Black cohosh**: 2 observational human studies in BC patients: decreased recurrence risk.
- **Curcumin**: decreases BC tumor growth in animal and in-vitro studies (mixed data: adria).
- **Fermented wheat germ extract (Avemar)**: animal studies, enhances tumor destruction, synergistic with hormone Rx.
- **Flaxseed lignans**: cell and animal studies, decreased tumor growth/mets; human trials: reduced risk of BC.

HERBALS/SUPPLEMENTS

- **Green tea**: inhibits cancer cell growth and invasion, in vitro and human data (Stage I BC pts 57% decreased recurrence with 5 cups/d).
- **Indole-3-carbinole**: in cruciferous veggies; diverts estrogen metabolites to noncarcinogens; controversy if synergizes vs harm with Tamoxifen.
- **Iodine**: down regulates BC cell growth stimulated by ER, causes tumor cell death, increases body breakdown of estrogen; give if deficiency.
- **Melatonin:** in vitro, reduces BC invasiveness and mets; humans: decreases BC risk; is an AI.
- **Mushrooms**: PSK extended survival in Stage II ER negative BC pts at 3 grams per day.

HERBALS AND SUPPLEMENTS

- **Omega-3-fatty acids**: flax, algae, fish oils: decreases BC growth in animal models
- **Proanthocyanidins (ex: resveratrol)**: grape skins, seeds, fruits, veggies: kills BC cells in vitro.
- **Probiotics**: in-vitro and animal studies: may slow growth of BC cells.
- **Vitamin D**: low serum vitamin D level at time of BC Dx predicts a worse outcome; studies ongoing to see if correcting a low level after diagnosis improves survival (and ? prevention).

RISK-REDUCING PHARMACEUTICALS

- Certain patients at increased risk for BC may benefit from medications (chemoprevention) to reduce risk.
- Breast Cancer Risk Assessment Tool (Gail Model): to calculate a woman's magnitude of increased BC risk (increased risk: age over 60, LCIS or atypical ductal or lobular hyperplasia; women between 35 and 59 with calculated 5 year risk of developing breast cancer of 1.66 percent or higher).
- Preventive meds interfere with effects of estrogen.
- SERMS (Tamoxifen and Raloxifene): block estrogen effects on breast tissue; adverse reactions.
- ?Aromatase Inhibitors (Anastrozole and Exemestane: decreased BC risk; joint pain; await FDA approval.

PHARMACEUTICALS UNDER STUDY

- **Metformin:** used to treat non-insulin dependent diabetes; may also inhibit breast cancer cell growth. Studies show 43-49% reduction in cancer mortality (included liver and lung cancer as well as breast).
- **Aspirin/NSAIDS:** studies show 21% decreased breast cancer risk with aspirin use daily and 49% decreased risk with ibuprofen use.
- **Statins:** Observational and retrospective studies suggest 51% decreased BC risk, need randomized clinical trials
- **Deslorelin:** inhibits estrogen from ovaries, can decrease breast density; more study needed.
- **Fenretinide:** vitamin A derivative, 50% BC reduction in women with prior BC; further study needed.

RISK-REDUCING SURGERY

- In BRCA-1 or -2 mutation positive women, National Comprehensive Cancer Network guidelines recommend these patients be offered prophylactic mastectomies and/or bilateral salpingoophorectomies (BSO) (as long as child-bearing is complete with BSO).
- Not 100% elimination of risk.
- Clinical decision making is complex, requires genetic counseling, and involves choice of surveillance only, risk-reducing surgery, or chemoprevention (SERMS, AI's).

EXERCISE

- Observational studies: vigorous physical activity is strongly associated with lower risk of BC and improved survival after diagnosis.
- Energy balance (calories in, calories expended) affect estrogen, insulin, IGF-1, inflammation, and immune pathways (all implicated in BC risk).
- Lifespan exercise (especially exercise in early life) is associated with lower BC risk.
- Exercise after a BC diagnosis shows improved survival at 10 years.

EXERCISE/BMI

- Exercise for 30-60 min at least 5 days a week (more than 3 hours per week) is recommended (especially aerobic with strength resistance).
- During and after cancer treatment, exercise benefits mood, strength, weight control, energy levels, immunity, overall health and well being, survival, prevention of recurrence, and QOL.
- BMI is linked to BC; overall weight gain raises risk of BC and death after Dx of BC
- Obesity is BMI $\geq$ 30.

STRESS REDUCTION

- Scientific data: stress does not ***cause*** cancer, but there is evidence that chronic stress can ***promote*** growth of tumors already present.
- Excess *sympathetic tone* (norepinephrine surge) caused by emotional stress can decrease cancer survival.
- Observational studies: decreased BC mortality with use of beta-blockers, which decrease sympathetic tone (Barron, et al, 2011).
- Clinical trials of beta-blockade in metastatic breast cancer have been started.

STRESS REDUCTION

- Non-pharmaceutical interventions that decrease sympathetic tone and increase parasympathetic tone ("relaxation response") such as massage, meditation, yoga, hypnosis/guided imagery, and heart-rate variability training (and others): helpful for BC.
- Acupuncture: helpful for BC-related fatigue, decreased anxiety and depression, improved QOL (Molassiotis, et al, 2012).
- Art and music therapy, dance and movement, journaling, and aromatherapy: decreased anxiety and depression.

SLEEP/CIRCADIAN DISRUPTION

- Strong evidence: night shift work, with disruption of circadian rhythm, increases BC risk.
- Melatonin (produced at night), is anti-inflammatory and suppresses estrogen activity (protective vs. BC).
- Light exposure at night increases BC risk due to decreased melatonin release, and this promotes release of estrogen.
- Japan study 23,995 women: short sleeping time, increased BC risk.

SLEEP/CIRCADIAN DISRUPTION

- Shift workers display symptoms of immune suppression; this is a mechanism of increased BC risk, independent of melatonin.
- Greater the sleep deprivation, the higher the risk.
- Good sleep and continuous darkness during sleep time are preventive means for cancer.
- Melatonin reduces cancer cell proliferation. Supplemental melatonin can improve circadian rhythms ; dose is 1-3 mg at bedtime, up to 20 mg (one study: 20-40 mg improved survival in metastatic BC patients).

SOCIAL CONNECTION

- Strong data: social isolation and depression promote tumor growth (Lutgendorf, et al 2011). Robust social support should be part of every BC recovery program.
- Early study: metastatic BC patients in support groups lived longer; further studies could not confirm, but did confirm enhanced mood and decreased pain (Goodwin, et al, 2001). Also improved coping and less stress.
- Vogt, et al 1992 showed that social networks are more effective in supporting recovery after BC occurred than in prevention.

SPIRITUALITY/RELIGION

- No clear evidence that religion or spirituality can impact cancer progression or mortality (Stefanek, et al 2004), but clear link between spirituality and QOL, adjustment, and symptom management (Meraviglia, 2006).
- Cancer survivors who draw on spiritual resources report more personal growth related to trauma of Dx (Carpenter, et al, 1999).
- Spiritual struggle is associated with poorer QOL and life satisfaction (Manning, et al 2005).


BLEACH

BREAST CANCER RISK AND ENDOCRINE DISRUPTORS

- Many environmental chemicals act as **endocrine disruptors**, which are chemicals that interfere with the body's endocrine system and produce adverse reproductive, neurological, and immune effects in humans and wildlife.
- Xenoestrogens are a subclass of such disruptors that specifically have estrogen-like effects; they are not biodegradable and are stored in our fat cells, and have been implicated in many conditions such as breast, prostate and testicular cancer, obesity, infertility, endometriosis, early onset puberty, miscarriages and diabetes.

BC AND ENVIRONMENTAL EXPOSURES

- Environmental chemicals and toxicant exposures during vulnerable periods (in utero, breast feeding, childhood, and puberty) play a large role in development of BC later on.
- Most data linking toxins to BC is based on animal studies (hard to study in humans).
- As of 2007, 216 chemicals in animal tests have been linked with BC causation (consumer products, contaminants in food, pesticides, etc).
- BPA (in plastics), Atrazine (herbicide), DES (used in past in pregnancy), and DDT (pesticide): all linked to BC incidence.

BC AND ENVIRONMENTAL EXPOSURES

- Early puberty (BC risk factor) is triggered by exposure to endocrine disruptors found in skin care products and cosmetics (phthalates).
- Exposure to polycyclic aromatic hydrocarbons in combustion gases and PCB's: increase BC incidence in women genetically susceptible.
- Exposure to dioxins and solvents increases BC risk.
- Women in the following work environments with increased BC risk: nurses, motor vehicle manufacturing, ceramic/cement/stone manufacturing, agriculture, food canning, and metal working.

TOXIN EXPOSURE REDUCTION SUGGESTIONS

- Eat organic food; hormone free meat and dairy.
- Reduce consumption of animal fat.
- Eat fish low in mercury.
- Minimize eating canned foods (can lining BPA).
- Wash hands often with plain soap and water.
- Test well water for harmful substances and use a water filtration system that removes chemicals. (http://water.epa.gov/drink/info/well/faq.cfm)
- Use stainless steel or glass containers.
- Do not microwave in plastic containers.

EXPOSURE REDUCTION SUGGESTIONS

- Remove shoes before coming in the home.
- Wet mop floors regularly and vacuum with HEPA filter.
- Avoid carpeting/furniture with flame retardants.
- Avoid pesticide use/application in and around the home or on pets.
- Use no or low-VOC paint products.
- Don’t burn trash.
- Test homes for radon.
- Eliminate phthalate-containing household items (PVC plastic), toys.

EXPOSURE REDUCTION SUGGESTIONS

- Eliminate products containing “fragrance”.
- Use nontoxic cleaning products.
- Avoid chemical-based dry cleaning.
- Avoid car exhaust and gasoline fumes.
- Use personal care products free of parabens and phthalates.
- Use mineral-based cosmetics.
- Use aluminum-free deodorant.
- Websites: goodguide.com, cornucopia.org
- Apps: skin deep, think dirty


Cancer
MoonShot
2020

CANCER MOONSHOT PROGRAM

- November 2015: formation of National Immunotherapy Coalition formed by private sector (pharmaceutical, biotech, and academic medicine communities): aim to develop a vaccine-based immunotherapy to combat cancer by 2020.
- January 2016: development of White House Cancer Moonshot Task Force; Vice President Joe Biden in charge; President Obama asks Congress for $1 billion to “send cancer to the moon”.
- Program focuses on immune/vaccine cancer therapies

MOONSHOT CRITICISM

- Public health experts say Cancer Moonshot Program ignores prevention:
- "We are concerned that the initiative may be undervaluing the vital role that public health and prevention have played…in reducing cancer incidence and mortality…the massive reductions in lung, cervical, colorectal, and gastric cancer mortality rates are almost entirely due to a focus on public health and prevention approaches."
- "…history has shown that the greatest impact in reducing cancer mortality rates has come from preventing cancers".
- Need to support prevention as well as treatment.

"I'll have an ounce of prevention."