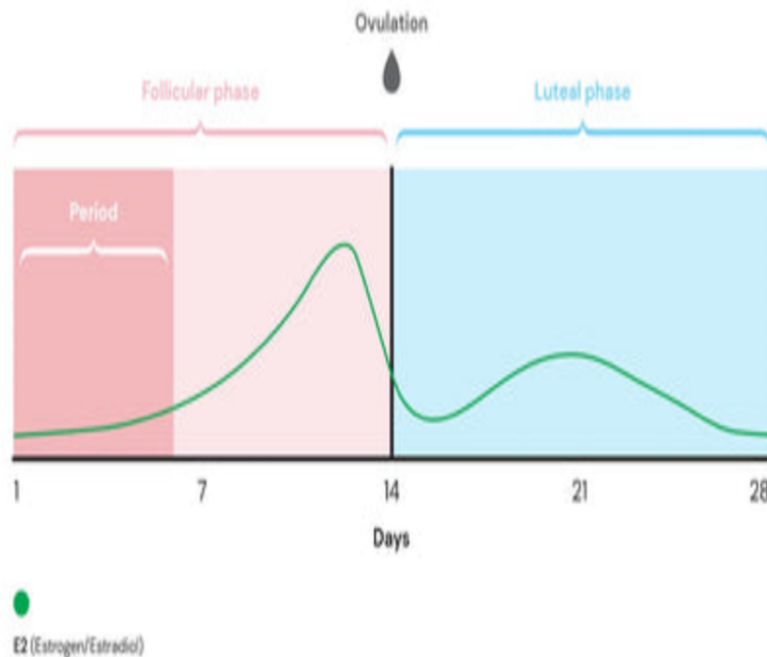


## Estrogen

Everyone knows that estrogen is a primary hormone for women. Beyond effects on sexuality and fertility, it is a major player contributing to moods, bone strength, and cardiovascular health. There are three types of estrogen:

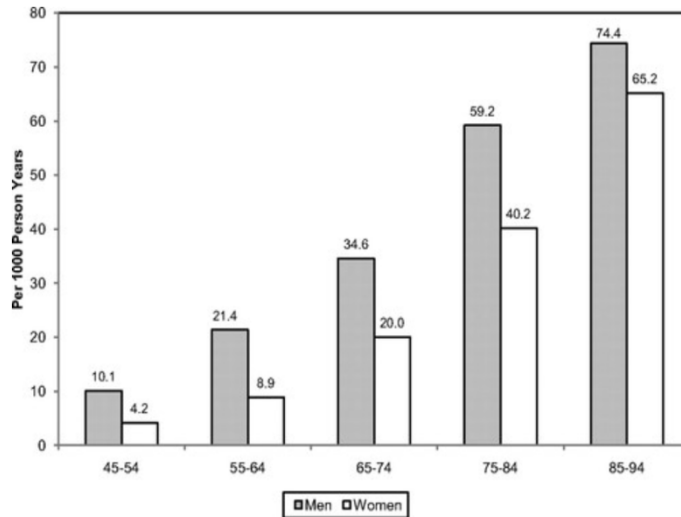
- ❖ estradiol (E2) which is the major estrogen during childbearing years. It has the strongest effect on your body's estrogen receptors. It is primarily made in the ovaries. How much is produced varies over the course of a woman's monthly period.
- ❖ estrone (E1) is the second most common form of estrogen during childbearing years. It is weaker than estrogen as to its effects on hormone receptors. It is made mostly by converting male hormone (androgen) into estrone and it occurs primarily in fat cells and muscle. A little estrone is produced in the ovaries. After menopause estrone is the only type of estrogen still made.
- ❖ estriol (E3) is known as being the form found during pregnancy. It is produced by the placenta and fetus. It is barely present at any other time outside of pregnancy. It has the weakest effect on hormone receptors. Research has found that estriol protects against a number of inflammatory autoimmune diseases such as reducing relapse rates for MS. During pregnancy relapse rates of MS decreased when estriol levels were at their highest, and rebounded after giving birth.



Estrogen's role in sexual development includes the growth and continued development of reproductive anatomy including the vagina and uterus, along with the breasts. It is involved with pubic and armpit hair during puberty. It is responsible for building up the uterine lining during the monthly cycle in preparation for pregnancy. It thins cervical mucus around ovulation making it easier for sperm to reach the egg. With menopause the massive decrease in estrogen leads to hot flashes, vaginal dryness, mood changes, and night sweats.

Estrogen is important for healthy bone development and what is called bone turnover (making new bone) and protects against bone loss. More bone loss can occur during menopause leading to osteoporosis due to the protective effect of estrogen being decreased during this phase of life. Increased risk of hip fracture results from such bone loss. It also has an impact as to sensitivity to pain and motor coordination.

Estrogen also plays a major role in cardiovascular wellbeing by keeping blood vessels healthy, decreasing inflammation, and controlling cholesterol levels. It also increases blood flow in the brain and stimulates nitric oxide release which leads to vasodilation (which can contribute to preventing stroke or high blood pressure). During menopause such benefits of estrogen are lost and there is increased risk of heart disease.



Graph showing annual number of adults having a diagnosed heart attack or fatal coronary heart disease by age and sex. American Heart Association, [Circulation](#), "Heart disease and stroke statistics – 2011 update, a report from the AHA" VL Roger et al.

Estrogen's effects on mood and the brain are also major. Mood is affected by impacting neurotransmitters including serotonin, dopamine, acetylcholine, and noradrenaline. It also has antidepressant effects.

It is believed to impact how the structures of the brain are wired together, how brain cells communicate with each other, and even the shape of the brain. It helps maintain healthy mitochondria (the energy source for cells).

Estrogen also seems to prevent or delay memory and cognitive problems such as from Alzheimer's, Lou Gehrig's, or Parkinson's by attacking free radicals and fighting against DNA damage. It has a positive effect on learning, verbal memory, and spatial ability. For older women who use hormone replacement therapy (HRT) there is a lower rate of death by Alzheimer's compared to those who do not use hormone replacement therapy. Conversely, women after menopause have a higher incidence of Alzheimer's, with the ratio to men being roughly 2:1. It used to be thought that more women developed it due to living longer. There is new research suggesting that it is due to lower estrogen levels after menopause. Males can still convert testosterone into estrogen through the enzyme aromatase as they age. The areas of the brain in women that are lost due to Alzheimer's overlap with the areas affected by estrogen.

It also helps form new brain cells through BDNF (brain derived neurotrophic factor) and insulin-like growth factor (IGF-1). It may also help prevent cells committing suicide (apoptosis) as to the process that removes unneeded or damaged cells.

Estrogen promotes the production of serotonin which is a neurotransmitter that has effects on mood. When estrogen levels are low serotonin levels will decrease too and this may be the cause of postpartum and menopausal depression.

One surprising fact is that males actually have more estrogen than females early in life. Even as fetuses the testicles are producing a large amount of testosterone that is converted into estrogen through aromatase. This estrogen then makes its way to the brain through the circulatory system. Girls' ovaries are relatively quiet until puberty and so their brains develop differently from boys' due to the absence of hormonal influence. Differences in how the brain develops in the genders includes in the hypothalamus where different regions that impact male and female sexuality are larger for the attendant gender.

Low estrogen levels can occur in women for reasons other than menopause. It can result from thyroid problems, removal of the ovaries (oophorectomy), hysterectomy, autoimmune disorders, chemo and radiation for cancer treatment, excessive caffeine intake, or from those who have a low body-fat percentage such as resulting from being very athletic or anorexic.

Low estrogen levels can cause

- ❖ decreased sexual desire
- ❖ infrequent or disrupted periods
- ❖ sleep issues
- ❖ mood swings
- ❖ dry skin
- ❖ hot flashes, night sweats
- ❖ menstrual migraines
- ❖ UTIs
- ❖ infertility
- ❖ cardiovascular disease
- ❖ poor concentration, memory
- ❖ bone loss

High estrogen levels ('estrogen dominance') can result from use of hormonal birth control, hormone replacement therapy for postmenopausal women, constipation, excessive weight, and can occur in women with a higher body-fat percentage. Use of antibiotics can increase levels too.

One of the major causes of estrogen dominance is food such as commercially raised animals that are injected with hormones to make them grow bigger and faster or to increase milk production.

Another cause is an imbalance in the gut microbiome (SIBO, small intestinal bacterial overgrowth). The gut bacteria help regulate estrogen through an enzyme and with SIBO it cannot properly metabolize estrogen leading to higher levels of the hormone.

HRT was billed for decades as being a good approach for treating postmenopausal symptoms. A study in 1998 (HERS, Heart & Estrogen Replacement Study) found there were serious risks

associated with HRT. In 2002 there was the largest randomized clinical trial of HRT through the Women's Health Initiative and WHI Memory Study (WHIMS). Estrogen was found to decrease the risk of hip fracture and colorectal cancer and prevent hot flashes. But there was increased risk of breast cancer, stroke, pulmonary embolism, and coronary heart disease. Estrogen increases inflammation and blood clotting which obviously creates risk of heart disease and stroke. The increased risk of cardiovascular disease was felt to outweigh the benefits of HRT.

There has been more recent research since 2002 which has found that HRT is safer and can help with

- ❖ hot flashes
- ❖ vaginal dryness
- ❖ night sweats
- ❖ lowering risk of osteoporosis
- ❖ lowered risk of colon cancer
- ❖ lowered risk of diabetes
- ❖ modest improvement in joint pain

but there is continuing debate on the point. Current research suggests that there is still risk especially if it is begun at or after the age of 60, or more than 10 years from menopause onset. If it is started before age 60 or within 10 years of menopause it is thought the benefits outweigh the risk. There are still problems that are at increased risk such as

- ❖ endometrial cancer
- ❖ blood clots and stroke
- ❖ gallbladder/gallstone problems
- ❖ increased risk of dementia if HRT is started after midlife. If it is started during midlife it is associated with a reduced risk of Alzheimer's and dementia
- ❖ breast cancer with long-term use

There is bioidentical hormone replacement therapy (BHRT) that uses lab produced hormones that are derived from plants. They are identical to the hormones produced by your body vs. the traditional HRT that are synthetic, and can be made from other sources like Premarin – an abbreviation for where it came from – pregnant mare urine. Because they are chemically different how the body reacts to them can vary from those made by your system. Some of the more common BHRTs are for estrogen, progesterone, and testosterone. They can come in various forms such as pills, creams, patches, implanted pellets, gels, and IV injections. How fast they take effect varies, but a few weeks to a few months should be expected.

**Table. FDA-approved Bioidentical Hormone Therapy Products**

Composition	Product Name
Oral 17 $\beta$ -estradiol	Estrace Various generics
Oral estradiol acetate	Femtrace
17 $\beta$ -estradiol matrix patch	Alora Climara Esclim Fempatch Menostar Vivelle Vivelle-Dot Various generics
17 $\beta$ -estradiol reservoir patch	Estraderm
17 $\beta$ -estradiol transdermal gel	EstroGel Elestrin Divigel
17 $\beta$ -estradiol topical emulsion	Estrasorb
17 $\beta$ -estradiol transdermal spray	Evamist
17 $\beta$ -estradiol vaginal cream	Estrace vaginal cream
17 $\beta$ -estradiol vaginal ring	Estring
Estradiol acetate vaginal ring	Femring
Estradiol hemihydrates vaginal tablet	Vagifem Vagifem LD
Estradiol valerate injection	Delestrogen
Estradiol cypionate injection	Depot-estradiol
Oral micronized progesterone	Prometrium
Vaginal progesterone cream	Crinone*
Vaginal progesterone ovules	Endometrin*

\*FDA approved for infertility, not menopausal hormone therapy.  
Complete information available on the NAMS website at [www.menopause.org/bioidenticalcharts.pdf](http://www.menopause.org/bioidenticalcharts.pdf).<sup>15</sup>

Some say that BHRT is safer because they are 'natural' and identical to the body's own hormones. Large-scale reputable studies have not confirmed the claim of their being safer. Some have passed FDA standards, and others have not.

Side effects of BHRT can include:

- ❖ weight gain
- ❖ blurred vision
- ❖ tiredness
- ❖ acne
- ❖ increased facial hair
- ❖ headaches
- ❖ breast tenderness
- ❖ spotting
- ❖ cramping
- ❖ bloating
- ❖ mood swings

There are also BHRT that are 'compounded' by a pharmacist where they mix together different ingredients. Compounded BHRT are not FDA-approved. Nor are they tested for effectiveness or safety. Long-term side effects are also unknown. Various medical groups such as the American College of Obstetricians & Gynecologists, the Endocrine Society, and the North American Menopause Society have come out against compounded BHRTs.

Symptoms of high estrogen can include

- ❖ weight gain especially in the hips, waist, and thighs
- ❖ changes in one's period such as light or heavy bleeding
- ❖ worsening of PMS, cramps
- ❖ fibrocystic breast lumps
- ❖ uterine fibroids
- ❖ fatigue
- ❖ lower sex drive
- ❖ anxiety or depression
- ❖ hormone-related cancers
- ❖ vaginal yeast infections
- ❖ thyroid problems

One of the major reasons for estrogen dominance is chronic stress and trauma. Another potential cause of high estrogen are xenoestrogens that are often found in personal care products, plastic ware, and the environment. Such 'endocrine disrupting chemicals' (EDCs) include:

- ❖ phthalates, which makes plastic more flexible. They can be found in squeeze bottles, plastic wrap, food wrap, plastic containers, medical tubing, detergents, candles, cosmetics (in 'fragrance'), powders, skin creams, hair spray, nail polish along with enamels and base coats, aftershave, perfume, and cologne. It is also found in air fresheners and kids' toys made from PVC plastic. Phthalates may contribute to PCOS, endometriosis, miscarriage, and placental problems with higher rates of low birth weight, premature birth, and fetal loss (at least in lab animals). They can also lower testosterone and estrogen that are important for female sex drive. There is some research showing that phthalates cause gender confusion in kids exposed to them. One study found that metabolites of these chemicals being elevated in mothers' prenatal urine was associated with their sons being less likely to play with male-typical toys like trucks or guns, and more likely to play with dolls. It has been hypothesized that phthalates may lower fetal testosterone production during a critical window - somewhere within 8-24 weeks of gestation when the testes begin to function, and thereby altering brain sexual differentiation. Such research is still in the early stages.
- ❖ BPA and other bisphenols which can be found in plastics, food wrap, storage containers, and cash register receipts. i.e. 'BPA-free' is not necessarily indicative that a product is safe because a substitute bisphenol may be just as bad if not worse as to its effects. Early research shows that BPF and BPS have the same activity as BPA. BPS in pregnant mice affects maternal behavior and how the brain is 'wired' (as laid out in an article called 'The Plastic Mother'). Bisphenol may contribute to PCOS, elevated risk of miscarriage during the first trimester, poor egg quality, and premature ovarian insufficiency leading to menopause occurring at an earlier age. The best way to avoid bisphenol intake is to avoid canned food.
- ❖ dioxins which are a byproduct of paper bleaching and herbicide production, and PCB's (a chemical banned in the 1970s but still in the environment today as to its persistence) can be found in meat and fish, and may be one cause of girls hitting puberty at younger ages.
- ❖ triclosan which is in anti-microbial and personal care products like liquid body wash, foaming soaps, underarm deodorants, mouthwash, laundry detergents and fabric softeners, some toothpaste, and even in baby toys. It can enter the body through oral mucosa from teeth brushing and skin through hand soaps etc., and affect hormones. Colleen Rogers, a lead microbiologist at the FDA has said "there currently is no evidence that antibacterial soaps are more effective than plain soap and water" (<https://www.fda.gov/consumers/consumer-updates/antibacterial-soap-you-can-skip-it-use-plain-soap-and-water?source=govdelivery>). It interferes with estrogen, androgen, and thyroid hormones, and increases the risk of breast cancer due to its estrogenic nature. It may also interfere with sperm production and affect sperm and testicular health. If you avoid getting it into your body what is in your system can be eliminated in something like a week or so.

- ❖ mercury (such as from eating fish that contain it). It is ranked third by the US government's Agency for Toxic Substances and Disease Registry (behind lead and arsenic). It may disrupt the pituitary, thyroid, adrenal glands, and pancreas. Hormones most affected by it are thought to be insulin, estrogen, testosterone, and adrenaline. Toxic levels of the metal in the pituitary can lead to low function of the gland and appears to be a major factor in teens and others committing suicide. It causes hormone imbalance by lowering progesterone and raising estrogen levels.
- ❖ parabens which can be found in personal care products like
  - lotions
  - sunscreens
  - face and skin cleansers
  - toothpaste
  - moisturizers
  - concealers
  - blush
  - mascara
  - shampoo and conditioners
  - shaving gels and cream
  - some deodorants
  - makeup

Parabens can also be found in some baked goods, beverages, syrups, jellies, jams, and preserves. They can affect fertility and might make it into the bloodstream and affect a fetus and birth outcomes such as premature birth and low birth weight. They can mimic estrogen and bind to those receptors on cells, and in some case increase breast cell division and growth of tumors and hence increase breast cancer risk. Environmental Working Group (EWG) also says they can cause changes in the menstrual cycle, decrease sperm production and lower testosterone levels (at least in animal studies), cause skin irritation and rashes. Females, adults under age 60, and non-Hispanic Blacks were found to have the highest levels in their urine based on a CDC study in 2006. Wearing less makeup helps avoid this chemical. A study found that adolescent girls who wore makeup daily had significantly higher levels of propylparaben in their urine compared to those who rarely wore makeup ([Journal of Exposure Science & Environmental Epidemiology](#), "Personal care product use as a predictor of urinary concentrations of certain phthalates, parabens, and phenols in the HERMOSA study" Kimberly Berger et al, Jan 2019).

- ❖ polystyrene (plastic #6) better known as Styrofoam as in the coffee cups, also can cause problems. It can leach from products like cups and containers into hot drinks and foods especially if microwaved; temperature is said to play a major role in the chemical leaching from such cups. The chemical mimics estrogen and can lead to thyroid and menstrual problems. Mouse research has found an association between the chemical and

spontaneous abortions, and it being embryotoxic even beyond the levels of benzene, toluene, or xylene. The FDA says it is safe to use for food products.

- ❖ there is some evidence that for women who take antidepressant drugs the probability of becoming pregnant may be reduced by 25%. SSRIs, antipsychotics and antiseizure drugs may also cause amenorrhea, meaning menstrual irregularities.

Males also have estrogen which is produced in the testes. Plus, testosterone can be converted into estradiol through aromatase. Estradiol is used for regulating the male sex drive, achieving erections, producing sperm, and testicular function. According to the Endocrine Society adult males should have 10-40 pg/ml of estradiol, and 10-50 pg/ml of estrone. Too much estrogen in men can cause gynecomastia ('man boobs'), infertility, erectile dysfunction and depression. Low estrogen levels in men can decrease sex drive, increase fat around the belly, contribute to bone loss and lead to osteoporosis.

There are natural ways to lower or raise estrogen levels in women and men. Levels can be lowered, such as to help reduce breast cancer risk, through means including

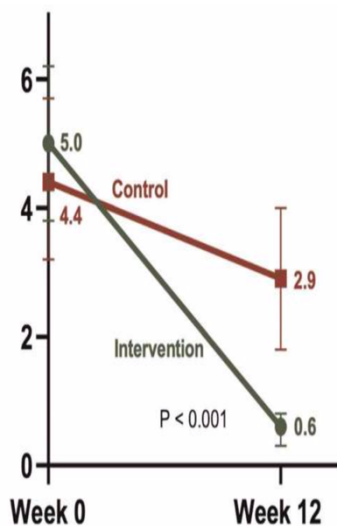
- ❖ soy. It has gotten a bad rap for years as to it promoting cancer due to phytoestrogens in the food. It turns out there are two types of estrogen receptors, with one being alpha that sits on cancer cells. And then there are beta receptors, with soy isoflavones having 1,600% greater affinity for them. Beta's activity includes shutting down alpha receptors which turns off a fuel for cancer. And it goes to aromatase which sits with fat cells and turns it off thus lowering estrogen levels.

Why has soy gotten such a bad reputation for promoting cancer? Prior to 2009 there was no research done on people and instead they were done on animals like mice. Soy promotes cancer in mice. But women are not mice, and in this case such mouse findings do not translate to people. One study on premenopausal women in Texas had them drink 3 cups of soy milk/day for a month, and the study looked at estrogen levels before and after. Blood levels of estrogen dropped between 30-80% in all of them and stayed lower for 2-3 months more after the study ended. Another study called the Shanghai Breast Cancer Survival Study on over 5000 breast cancer survivors was done on women ages 20-75. Those with the highest soy intake had a 29% decrease in total mortality and 32% decrease in cancer reoccurrence compared to those with the lowest soy intake, with a follow-up averaging about 4 years (JAMA Network, "Soy food intake and breast cancer survival" Xiao Ou Shu et al, 12/9/09). Another study looked at Asian-American women and their soy intake during childhood, adolescence, and adulthood. The greatest benefit was for high soy intake in childhood with a 60% reduction in breast cancer, and a 20% and 24% reduction for the other age groups, respectively. (Cancer Epidemiology, Biomarkers & Prevention, "Childhood soy intake and breast cancer risk in Asian American Women" Larissa Korde, et al, 4/2009).

A study in 2020 looked at 52,795 adult women in the Adventist Health Study-2 and followed them for about 8 years (International Journal of Epidemiology, "Dairy, soy and risk of breast cancer: those confounded milks" Gary Fraser et al, 2/25/2020). Over 1,000 developed breast cancer by the time the study was finished. The researchers suggested that the biggest benefit of



soy milk relative to breast cancer is not from the soy itself but from the exclusion of dairy. Drinking as little as a quarter to a third cup of dairy milk/day was associated with an increased breast cancer rate of 30%. Drinking one cup/day was associated with a 50% increase in risk. Those having 2-3 cups/day increased risk of breast cancer by 70-80%. There was little difference between nonfat, low and full fat milk. Cheese and yogurt did not have significant associations either. Consuming soy milk did not increase cancer risk. Substituting dairy for soy milk led to a 32% drop of breast cancer. It is suspected that sex hormones in dairy milk increase hormonal levels in women.



There was another study on soy called WAVS (Women's Study for the Alleviation of Vasomotor Symptoms). It found that a plant-based diet rich in soy reduced moderate to severe hot flashes of menopause by 88% (as seen in the graph), and also helped the women lose an average of 8 pounds in 12 weeks. The study entailed 84 postmenopausal women who were getting two or more hot flashes a day. They were randomly assigned to a low fat, vegan diet including a half cup of cooked soybeans per day, or a control group that had no dietary changes. The study ran for 12 weeks, and the combination of avoiding animal products, reducing fat, and adding soy mirrored the results found in pre-Westernized Japan and the Yucatan peninsula where soy is more prevalent and postmenopausal women have fewer symptoms like hot flashes. Physicians Committee for Responsible Medicine

Another study looking at about 2000 women who were on Tamoxifen, having already been diagnosed with estrogen-driven breast cancer, and they were followed for more than six years. Looking at high vs. low soy consumption in postmenopausal women there was approximately a 60% drop in cancer reoccurrence. The researchers concluded that "soy isoflavones consumed at levels comparable to those in Asian populations may reduce the risk of cancer reoccurrence in women receiving tamoxifen therapy and appears not to interfere with tamoxifen efficacy." (Breast Cancer Research & Treatment, "Soy isoflavones and risk of cancer recurrence in a cohort of breast cancer survivors: life after cancer epidemiology (LACE) study." Neela Guha et al, Nov. 2009).

Other ways to lower estrogen include:

- ❖ cruciferous veggies and leafy greens (e.g. broccoli, cauliflower, Brussels sprouts, bok choy, cabbage) through DIM which is a phytochemical that binds to estrogen receptors as well as inhibiting aromatase. Sulforaphane is another chemical found in this group of veggies and which is especially prevalent in broccoli sprouts. It also reduces excess estrogen. DIM content of some foods include:

	mg
Brussel sprouts	104 (1/2 cup)
Garden cress	98 (1/2 cup)
Mustard greens	79 (1/2 cup chopped)
Kale	67 (1 cup, chopped)
Turnip	60 (1/2 cup, cubed)
Kohlrabi	31 (1/2 cup, chopped)
Red cabbage	29 (1/2 cup, chopped)
Broccoli	27 (1/2 cup, chopped)
Horseradish	24 (1 T)
Cauliflower	22 (1/2 cup, chopped)
Bok choy	19 (1/2 cup, chopped)

- ❖ ground flax seeds. They have 100 times the lignans of other foods which are good for lowering estrogen (and they have other benefits such as decreasing inflammation and stopping cancer development by blocking growth of new blood supply that tumors need).
- ❖ increasing intake of dietary fiber (fruits, veggies, 100% whole grains, nuts & seeds, legumes). It binds estrogen in the GI tract so that it can be eliminated. (Other benefits include improving regularity, and improving insulin sensitivity. The GI microbiome also love fiber and release healthy chemicals, 'postbiotics,' that reduce the risk of inflammation and cancer.) Estimates are that about 3% of Americans get enough fiber each day.
- ❖ mushrooms, and especially white buttons and oyster, block aromatase. (Half a button mushroom/day dropped breast cancer rates by 64% in Chinese mushroom eaters vs. those that did not have any in one study.)
- ❖ tomatoes. One factor in their being helpful is they contain melatonin which reduces aromatase activity such as in the breast and thereby decreasing estrogen production. Another ingredient, naringenin, also inhibits estrogen positive breast cancer cell growth and migration in the presence of estradiol.
- ❖ apples have insoluble fiber that binds to estrogen in the small intestine which stops it from being absorbed by the body. Two servings a day are recommended.
- ❖ seaweed by way of its fiber helps bind up and lower estradiol. One study found that the effective dose of seaweed for lowering the hormone would be about 75 mg/kg of body (about 4.5 g for a 132 lb. woman).
- ❖ red grapes (especially the ones with seeds) by way of the resveratrol and other polyphenols, along with quercetin.

- ❖ green tea which also inhibits aromatase such as through a chemical abbreviated EGCG. One study found that green tea was linked to lower levels of total estrogens (Nutrition Journal, “Green tea intake is associated with urinary estrogen profiles in Japanese-American women” Barbara Fuhrman et al, Feb. 2013). (A squeeze of lemon into green tea boosts EGCG absorption by 5-fold.)
- ❖ pomegranates contain a compound that inhibits the enzyme that converts estrone into estradiol. They also contain something called ellagittanins that block androgens being converted into estrogen.
- ❖ magnesium can help lower estrogen by supporting an enzyme, COMT, in the liver that clears excess amounts of the hormone, and it may be a treatment for PMS too.
- ❖ other foods that contain aromatase inhibitors (e.g. artichokes, arugula, blueberries, sour or tart cherries, corn, cranberries, grapes, horseradish, kale, lemons and limes, mustard, oats, oranges and tangerines, radishes, rice [black, red, purple], turnips, walnuts, watercress). Aspirin and metformin can also inhibit aromatase.
- ❖ iodine which helps maintain estrogen balance in favor of estriol (E3, that has been shown to protect against estrogenic cancers, and decreases the risk of fibrocystic breasts, and even help with estrogen-related weight gain as to losing some pounds). It may also reduce risk of prostate cancer by reducing the production of estrogen. It can also increase testosterone and reduce prostate size. However, this is not to advocate gulping down handfuls of iodine pills or teaspoons of iodized salt. Getting a lab test to see where your iodine level is at and rectifying it if it is low is being advised.

Estrogen levels can be raised by determining what is causing it to be low (such as EDC's, low body fat, heavy metal poisoning, excessive physical training, an eating disorder, or menopause).

One side effect of estrogen, such as in birth control pills, is that it can cause magnesium deficiency so teen girls and women may have such an issue. Estrogen also effects copper, potassium, and calcium levels and this leads to mineral imbalances as to elevated ratios of sodium: potassium, and calcium:magnesium.