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Health Concerns Faced by Women Today
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An Introduction to the HPG Axis
The hypothalamic–pituitary–gonadal axis (HPG axis) plays an important role in the development and regulation of a number of the body’s systems involved in women’s health.

Menopause Parts 1 & 2:
Natural substances such as phytoestrogens can help to balance hormones and ease the transition into menopause. Lifestyle and dietary modifications can also be both helpful and healthful in managing or eliminating these symptoms.

Is it Really My Thyroid? Hypothyroid Explored
Thyroid health is a key ingredient to managing energy, weight, aging, and overall well-being. Hypothyroid (low-thyroid) conditions can benefit from food sourced nutrients as well as supplemental support.

The Breast Cancer-Estrogen Connection
The risk of breast cancer is thought to be closely related to the balance of estrogen hormones in a women’s body; there are several ways to reduce this risk.

Hidden Dangers in Our Modern World
Xenoestrogens are a significant source of estrogen that can affect a women’s hormone balance. Supporting the body’s detoxification processes and reducing exposure is important.

Control PCOS: Control Your Life
PCOS is a poorly understood condition that is also linked to other concerning health problems. Learn more about how you can evaluate and control PCOS.
An Introduction to the Hypothalamic–Pituitary–Gonadal Axis

The hypothalamic–pituitary–gonadal axis (HPG axis) plays an important role in the development and regulation of a number of the body’s systems, such as the immune and reproductive systems. Fluctuating hormone levels cause changes in the hormones that are produced by each gland and as a result have a variety of widespread and local effects in the body. The HPG axis can be influenced by lifestyle and dietary factors such as stress, inadequate sleep, illness, the use of certain medications including hormones, as well as poor dietary habits. This axis can also be subject to disorders such as hypothalamic–pituitary failure or dysfunction, as occurs in ovulation disorders, one example being PCOS (polycystic ovary syndrome). Female hormones affect reproductive organs and also influence several other body functions by interacting with major neuroendocrine systems including thyroid hormones, stress hormones, and the autonomic nervous system. The HPA (hypothalamic-pituitary-adrenal) axis is affected by similar factors as the HPG axis and involves the hypothalamus, pituitary and adrenal glands as well as the hormones CRH (corticotropin-releasing hormone), ACTH (adrenocorticotropic hormone) and the stress hormone known as cortisol which is necessary to survive. Therefore, a lack of normal functioning of the female reproductive system impacts a wide variety of other emotional and physical health conditions.

HPG axis refers to the effects of the hypothalamus, pituitary gland, and gonads as if these separate endocrine glands were a single entity acting as a whole. Since the glands often function in cooperation, endocrinologists and physiologists find it more simple and descriptive to refer to them as a single system. The HPG axis controls reproduction, development, and aging. The hypothalamus produces gonadotropin-releasing hormone (GnRH). The anterior portion of the pituitary gland produces luteinizing hormone (LH) and follicle-stimulating hormone (FSH), and the gonads produce estrogen and testosterone.

The hypothalamus is located in the brain and secretes GnRH. GnRH moves down the anterior portion of the pituitary and binds to the secretory cell receptors of the anterior pituitary.
In response to stimulation from GnRH, these cells then produce LH and FSH, which enters into the blood stream. These two hormones have a significant role in communicating to the gonads. FSH and LH act primarily to activate the ovaries to produce estrogen and inhibin and to regulate the menstrual cycle and ovarian cycle in females.

**Symptoms of HPG Axis Dysfunction**

The most common cause of hot flashes in menopausal women is changing levels of estrogen in the body. Diminished amounts of estrogen have a direct effect on the hypothalamus, the part of the brain responsible for controlling appetite, sex hormones, sleep, and body temperature. Lowered levels of estrogen confuse the hypothalamus, causing it to inaccurately sense that the body is overheating. This provokes an internal chain of reactions that women experience as “hot flashes”. Sudden weight gain in women may also be caused by hormone imbalance. Since the hypothalamus is responsible for metabolism and body temperature, when the hypothalamus isn’t functioning normally, this can slow metabolism, also causing the thermogenic process for fat burning to slow, thus causing significant weight increase.

**HPG Axis’ Role in Female Reproduction and Development**

One of the most important functions of the HPG axis is to regulate reproduction by influencing the ovarian and uterine cycles. In females, a positive feedback loop between luteinizing hormone and estrogen assists in preparing the follicle in the ovary and the uterus for ovulation and implantation. At the time the egg is released, the ovary starts to produce progesterone to inhibit the hypothalamus and the anterior pituitary, therefore stopping the estrogen-LH positive feedback loop. If conception does occur, the fetus will assume the role of secreting progesterone; causing the mother to be unable to ovulate again. If conception does not occur, reduced progesterone excretion will allow the hypothalamus to restart secretion of GnRH. These hormone levels also influence the menstrual cycle initiating the proliferation phase to prepare for ovulation, the secretory phase after ovulation, and menstruation when conception does not occur. HPG axis activation in both males and females during puberty also causes individuals to gain secondary sex characteristics.

HPG axis activation and deactivation also helps to regulate life cycles. FSH and LH levels are elevated at birth, and females have a lifetime supply of the primary cells from which an egg develops (oocytes). These levels decrease and remain lower throughout childhood. At puberty the HPG axis is activated by estrogen secreted from the ovaries or testosterone from the testes. Physiological and psychological changes are caused by the activation of estrogen and testosterone. After being activated, the HPG axis functions in men for the rest of their life but becomes deregulated in women which leads to menopause. The deregulation is caused mainly by the reduction in oocytes that normally produce estrogen to create the positive feedback loop. Over many years, HPG axis activity decreases and women cease to be fertile. Balancing the HPG axis throughout life is important since it significantly affects temperature regulation, metabolism, weight control, mood and also the aging process. Lifestyle factors and dietary choices as well as supplements and medications can all profoundly affect the functioning of this system.
Menopause is a normal, natural and inevitable event that affects all women reaching middle to late adulthood. In a very basic sense, menopause occurs as a result of aging. Changes in the structure and function of the female ovaries lead to a drastic drop in estrogen levels and permanent cessation of menses. Unfortunately, its associated symptoms can make this process quite uncomfortable for many women and can negatively impact their social life, psychological health and overall well-being.

The most common concern in postmenopausal women are hot flashes; these cause an episodic feeling of heat, intense sweating and flushing of the face and chest and are experienced by as many as 75% of menopausal women. Night sweats and difficulty sleeping appear to be the next most common concerns, although psychological distress, anxiety, mood changes, concentration difficulties and bone loss are all frequent concerns as well. The average age of onset is 51, but there is quite a wide age range (40-58 years of age) for any individual woman to enter menopause.

The most common conventional treatment used to address the concerns of menopause is hormone replacement therapy (HRT). While this therapy may provide relief for symptoms such as hot flashes and night sweats and protection against bone loss, evidence exists to suggest that HRT may also increase the risk of heart attacks, coronary attacks, strokes and even breast cancer (see page 17 for information on breast cancer). An online survey of 166 menopausal women showed that 27% of respondents stopped or didn't use HRT at all because of these safety concerns.

With all of this in mind, it's no surprise that menopausal women experiencing discomfort want safe and alternative solutions. The good news is that there are many effective options. Let's take a closer look at some of the best alternative therapies available for the most common menopausal symptoms:
Exercise

Exercise has long been considered a beneficial treatment for easing the transition into menopause, most notably through reducing the frequency and intensity of hot flashes. It is proposed that the exercise-induced production of beta-endorphins (the “happy” chemical associated with a sense of euphoria) combats the natural decrease in β-endorphins seen with decreasing estrogen levels in aging women. These peptides act on many areas of the brain and ultimately may help to stabilize the thermoregulatory centre of the hypothalamus, an area crucial to temperature regulation. Multiple studies have reported that physical activity has positive effects on various menopause-related symptoms and overall health. As many people are aware, these improved health outcomes include better cognitive function, sleep patterns, mood, bone density, cardiovascular function and energy levels. Observational studies confirm this notion.

In a survey of over 66,000 menopausal women in Italy, those that reported the lowest level of regular exercise were significantly more likely to experience more severe symptoms such as hot flashes. A recent 2012 study found that symptoms of anxiety and depression experienced by menopausal women could be alleviated by a controlled physical exercise regimen. A 2008 study examined the effects of physical exercise and HRT on “health-related quality of life” (HR-QOL) in 44 post-menopausal women. Only 3 hours per week of moderate aerobic exercise led to an increased HR-QOL and decreased severity of menopausal symptoms (including hot flashes, insomnia, nervousness, headaches and joint pains) after a period of six months. While the groups receiving only HRT and no exercise showed similar decreases in menopausal symptoms, they did not experience the similar increase in HR-QOL that exercising women exhibited.

Finally, there is also strong evidence that menopausal symptoms such as hot flashes may be reduced and a more positive mental outlook obtained with the increased sense of accomplishment and self-esteem associated with
exercise. This is supported by the idea that yoga, an exercise form that equally requires physical activity and mental focus, has also been suggested to improve menopausal symptoms when practiced regularly. Regardless of the mechanism, all forms of regular exercise should be considered safe and effective methods to reduce the frequency and intensity of hot flashes, improve sleep and balance mood throughout menopause.

Diet

It's no secret that diet affects many aspects of our health. Menopausal symptoms are no exception to this rule and many women have seen firsthand that dietary factors can influence menopausal symptoms for better or for worse. A very recent 2013 prospective cohort study found this exact association between diet and menopause symptom complaints by monitoring 6040 women over a period of 9 years (from 2001 to 2010). After gathering baseline dietary data, researchers were able to define six distinct dietary patterns and allocated each woman into a category for subsequent analysis. Both night sweats and hot flashes were assessed for each woman every 3 years throughout the follow-up.

Findings of this study identified one specific type of diet that appeared to aggravate menopause symptoms, and two diet types that decreased the risk of menopause symptoms. Diets high in fat and sugar noticeably worsened hot flashes, while diets higher in fruit and diets closely resembling a Mediterranean diet (greater proportions of garlic, peppers, mushrooms, salad greens, pasta and red wine) appear to be protective of the same symptom. Diets high in meat, dairy and vegetables did not show any trend in either direction.

Other studies have also found that high fibre and low fat intakes may be associated with reduced menopause symptoms. Many other modifiable lifestyle factors that are closely tied to diet have shown to be risk factors for increased vasomotor symptoms as well. Specifically, women with a higher body mass index (BMI, a measure of body weight relative to height) are at an increased risk. A 2012 study actually showed that menopausal women who lost 10 lbs or more through increased fruit and vegetable intake and reduced fat intake were more likely to eliminate their hot flashes and night sweats completely after 1 year. Interestingly, many women who adopted this new dietary regimen but did not lose weight also found some benefit in the form of reduced hot flashes and night sweats. This shows that dietary interventions and weight loss both independently improve these menopause concerns.

As a final note on dietary and lifestyle factors, women who smoke cigarettes regularly and those with a higher consumption of alcohol have both been shown to be at an increased risk for experiencing hot flashes. If you have been trying to quit smoking or reduce
your alcohol consumption, here is yet another reason why it may be time!

Black Cohosh

Black Cohosh (also known as *Actaea racemosa* or *Cimicifuga racemosa*) is one of the most promising herbal preparations for reducing menopausal symptoms and which also has a long history of use in traditional medicine for treating menstrual irregularities and pain associated with childbirth. Unlike other commonly used herbs to treat menopausal discomforts, black cohosh is not just a phytoestrogen (see page 10 for an explanation of Phytoestrogens) but rather a substance that increases dopamine and serotonin levels in the body. Additionally, it appears that black cohosh has an affinity for bone protection as it selectively activates estrogen receptors in the skeletal system.

In a randomized, double-blind, placebo-controlled trial involving 304 healthy, postmenopausal women in Germany, a standardized extract of black cohosh was found to be beneficial in alleviating menopausal concerns after 12 weeks of treatment. Specifically, improvements in sleep disorders, hot flashes, memory, irritability, depression and vaginal dryness were seen. It should be noted that concomitant use of HRT or any other herbal supplements were prohibited during the study. With this in mind, the positive results can be solely attributed to the black cohosh.

The safety profile of black cohosh has been a controversial issue over the years, with previous case reports suggesting a possible relationship between black cohosh use and liver toxicity. However, review of these reports has determined that these cases were not properly assessed for causality and, in fact, there were many confounding variables present that may have been responsible for the unwanted side effect. A much larger body of evidence exists to suggest that black cohosh is extremely safe, however, the monitoring of liver health by physicians prescribing black cohosh is still a prudent approach.

Other interventions for treating menopausal concerns

**Acupuncture:** A systematic review on acupuncture and menopausal symptoms suggest that acupuncture is an effective treatment option for vasomotor symptoms and improving health-related quality of life.

**Massage:** Both aromatherapy massage and non-aroma massage have been shown to benefit overall menopausal symptoms after only 4 weeks of 30-minute treatment sessions twice a week. While both massage forms provided relief, aromatherapy massage was most beneficial.

**Omega-3 Fatty Acids:** Eight weeks of supplementation with Eicosapentaenoic acid (EPA) leads to improvements in psychological distress and depressive symptoms of menopausal women. Supplementation did not, however, show any benefit over placebo in menopausal women suffering from a major depressive episode.

**Ginseng:** *Panax ginseng* produced significant benefit over placebo for menopausal depression and overall well-being (according to the Psychological General Well-Being Index [PGWB]).

**Qigong:** A 12-week study found that menopausal symptoms and sleep quality improved as women practiced and became better versed in this form of meditative exercise.
Menopausal women searching for safe and effective alternatives to hormone replacement therapy (HRT) will inevitably come across “phytoestrogens”, either in their whole food form or as a concentrated extract in a supplement. But what exactly are phytoestrogens and how do they work in the human body? Are they even safe? Many answers remain unknown to the general public and the literature can offer mixed results as well. Let’s clear up some of the confusion.

The term “phytoestrogen” can literally be translated into “plant estrogen”. In the 1950’s, this estrogenic activity was discovered in plants when researchers investigated the cause of infertility in a specific group of Australian sheep. Researchers noticed that these infertile sheep were grazing in pastures of clover, subsequently labeling genistein as the active ingredient and the constituent responsible in clover for having estrogen-like activity. Since this discovery, hundreds of foods have been identified as phytoestrogens, each possessing varying potencies. Soy, hops, flaxseeds, legumes, lentils, chickpeas, beans, alfalfa sprouts and red clover are now commonly known phytoestrogen sources, although when it comes to natural health products, their labels will often only list the active phytoestrogenic ingredient from each plant. See Figure 1 for a list of common phytoestrogenic plants, their corresponding Latin names and their most active estrogenic constituents.

Despite the literal translation to “plant estrogen”, it’s important to note that no actual estrogen exists in phytoestrogenic plants (the principle human estrogen, 17β-estradiol, is not present). Instead, plants that are described as phytoestrogens simply have effects in the human body similar to the effects of our bodies’ natural estrogen. In the

**References**

most basic sense, all phytoestrogenic plants contain active ingredients with a similar chemical structure to estrogen. The ingredients actually interact with and activate estrogen receptors. The human body interprets this chemical signal in the same way that it would if natural estrogen had triggered the receptor. In other words, the switch gets turned on regardless of what initiated the action.

It is also very important to recognize that, even though phytoestrogens activate estrogen receptors, they do so in a much weaker manner. Using our on/off switch analogy, phytoestrogens simply turn on fewer switches than true estrogen because they don’t bind strongly enough to the switch.2 This results in similar physiological responses that are much milder.

Lastly, to fully understand the action of phytoestrogens we must recognize that there are two different types of estrogen receptors in the body: alpha-estrogen receptors (ER-α) and beta-estrogen receptors (ER-β). Each receptor is distributed more heavily in certain tissues (for example bone versus breast tissue). This is important because all phytoestrogens are actually “selective estrogen receptor modulators” (SERMs), meaning they affect either the ER-α or ER-β preferentially.2

Research examining the ability of phytoestrogens to alleviate menopausal ailments is positive, yet still mixed. Beneficial results have been shown for improving hot flashes, vaginal dryness, sleep disturbances, cognition and bone density in menopausal women. However, many studies have also shown very little or no effect of phytoestrogens on menopausal symptoms. With this in mind, it’s important to know that there is a tremendous amount of variability in terms of the amount of active ingredient used in each study. Moreover, individual differences in intestinal microflora can further lead to mixed results by altering the ability to break down and use phytoestrogens in the human body.2

Let’s take a closer look at some of the most popular and most potent phytoestrogens:

### Hops

Hops (Humulus lupulus) can be considered a relatively “new” phytoestrogen as the active estrogenic ingredient, 8-prenylnaringenin (8-PN) was only recognized in 1999.3 While the hops plant is now acknowledged for its ability to influence menopausal symptoms and other conditions of estrogen imbalance, traditionally hops has been used for its sedative properties.3

Comparison against the active ingredients found in other phytoestrogens (such as genistein and daidzein from soy) show that 8-PN is actually one of the most potent!3 Moreover, 8-PN actually binds ER-α stronger than it binds ER-β, a quite unique property when comparing phytoestrogenic activities.1 Perhaps this partially explains why hops has shown such positive research for menopausal concerns.

Two clinical studies using standardized hops extracts have been conducted, both of which elucidated the rapid and effective relief of hot flashes. One study examined the effects of supplemental hops for 12 weeks in 67 menopausal women while the most recent study in 2010 only examined 36 menopausal women, but over a longer duration of 16 weeks. Both studies measured scores on a modified Kupperman Index (an assessment tool to rate the intensity of hot flashes, insomnia, headaches, vaginal dryness etc.) on a patient questionnaire.4

While the relatively small number of participants in each study may be considered a limitation, the various assessment tools all revealing beneficial effects in such a short duration shows great promise for hops as a treatment intervention. Considering the large proportion of menopausal women with sleep disturbances and hot flashes, hops is an ideal ingredient to target this population for its estrogenic and sedative properties.4 In addition, 8-PN has been shown to exhibit estrogenic effects on bone metabolism, thereby providing another menopausal benefit by possibly reducing bone loss.4 Nevertheless, more research is needed to fully reveal all of the benefits that hops have to offer for menopausal women.

### Soy

Soy is one of the most well-known phytoestrogens, the most researched and also the most controversial. Many research studies have found soy (or the active ingredients isolated from soy; see figure 1) to have no benefit over placebo on menopausal hot flashes.5,6 Yet, other studies show great benefit in specific populations. For example, one study found that soy derived isoflavones improved mood and hot flashes in menopausal women with high body mass index (BMI) measurements.7 Another study found that genistein decreased all severities of hot flashes in women entering menopause within the past 12 months with higher BMI’s.8

A 2011 report by the North American Menopause Society states that soy-based isoflavones are “modestly effective in relieving menopausal symptoms”.9 This statement is significant because the report literally evaluated hundreds
Advances of studies using soy supplementation for menopause and found benefit for its use. Specifically, better results were found in whole food consumption and in products that provided high proportions of genistein. To add support to the argument that isoflavone supplementation does play a positive role in alleviating menopausal symptoms, a comprehensive 2013 review evaluating the efficacy of isoflavones, coumestans and lignans found that current research sufficiently concludes that the findings are positive.

Increased dietary soy consumption has also been shown to decrease endometrial and breast cancer risk in observational studies, perhaps making soy a more attractive option for treating menopause. In addition, possible protective effects on the cardiovascular system, cognition and bone health have been suggested, although research in these areas is much farther from being conclusive.

Flaxseed
Of all the known phytoestrogenic plants, flaxseeds contain the highest amount of lignans, the active ingredient responsible for their estrogenic activity. However, lignans must be converted by the bacteria in the human digestive tract in order to become “activated.” These active metabolites actually help the liver to make sex-hormone binding globulin (SHBG), a hormone that decreases the clearance of circulating estrogens, and the metabolites also act as SERM's with an affinity for ER-α. The end result of both of these processes is more estrogen activity in the body.

Almost all trials assessing the effectiveness of flaxseeds or lignans alone in the treatment of hot flashes have produced insignificant effects. To be more specific, research has found quite a large proportion of flax interventions to reduce hot flashes, but the corresponding placebo groups have proven to be so powerful that there is actually very little difference in the efficacy between groups. However, one study examining the use of isoflavones in conjunction with lignans found significant improvements in hot flashes after 12 months. This suggests that perhaps a synergistic effect is present between the two phytoestrogens. This is supported by the fact that vaginal atrophy has also shown improvement through the combined use of lignans and flaxseeds.

Lignans and flaxseeds have shown improvements in the areas of cognition and bone health, while also possibly showing a protective effect against breast cancer. Specifically, high dietary lignan intake has been associated with better performance in processing capacity, processing speed and executive function, while the alpha-linolenic acid (an omega fatty acid) content of flaxseeds are theorized to benefit bone health by decreasing prostaglandin synthesis. The suggested protective effect of lignans on breast cancer has only been observed in dietary observational analysis and therefore the proposed benefit is plausible but far from definitive.

A major shortcoming of the use of flaxseeds clinically is that there is currently no long-term research evaluating their efficacy as a sole intervention. Perhaps studies of duration longer than 12 weeks would ascertain whether flaxseed is indeed beneficial or not in alleviating menopausal symptoms.

Are phytoestrogens safe?
One of the greatest attributes of phytoestrogens is their extremely high safety profile. A literature review in 2010 analyzed twenty years of soy research and found that there were no serious side effects – only a slightly higher incidence of gastrointestinal disturbances (such as gas or bloating) in those consuming higher amounts of dietary soy. Similarly, there have been studies examining the safety of soy consumption for up to 3 years in length that failed to expose any serious adverse effects. Research on the use of lignans from flaxseeds, 8-prenylnaringenin from hops and coumestrol from both alfalfa and red clover have all shown comparable safety profiles.
Some research has raised concerns surrounding the use of soy and its possible negative effects on thyroid health.\textsuperscript{14} It’s important to clarify that: research has only shown that genistein from soy can exacerbate low thyroid function in individuals with pre-existing suboptimal thyroid function (specifically deficient in iodine).\textsuperscript{14} There is currently no evidence to suggest that healthy people consuming soy are at increased risk for hypothyroidism.

As aforementioned, HRT has also raised various concerns regarding their use and possible risk of increased blood clotting, liver disease and certain cancers. Interestingly, phytoestrogens have been found to decrease the risk of endometrial cancer, but also some studies actually suggest a possible protective effect for this type of cancer.\textsuperscript{2,9} Also, soy consumption has actually been found in many human populations to be protective against breast cancer.\textsuperscript{2,9}

All in all, phytoestrogens appear to be a very safe substitute for HRT that can alleviate women’s health concerns and aid their transition into menopause. Still, to be cautious, it is advised to only utilize phytoestrogens for shorter-term use and at reasonable dosages, as long-term use over a period of years of high-potency extracts have not been explicitly studied.

In summary, there are many different phytoestrogens, in varying capacities, that have shown to be beneficial for menopausal complaints including hot flashes, vaginal dryness, sleep disturbances, cognition and bone density and the safety profile for phytoestrogens is good.

Phytoestrogens in dietary form or standardized extracts may be beneficial for your menopausal symptoms. However, as the mixed evidence suggests, each phytoestrogen doesn’t necessarily work for everyone – it’s clear that the type and potency of phytoestrogen alters the physiological effects on the body. Numerous active ingredients, inadequate potency and variations in individual metabolisms may lead to mixed results, but many women have found tremendous relief from menopausal ailments by using phytoestrogens, and much of the research supports this claim. You must find the combination or product that works best for you.

References
Is it Really my Thyroid? Hypothyroidism Explored

Hypothyroid is also known as low or underactive thyroid. This condition occurs when the gland fails to produce proper amounts of the thyroid hormones (T3 and T4) to meet the body’s needs. Thyroid disease is estimated to affect 200 million people worldwide, with recent studies showing that as many as 1 in 10 Canadians are affected. Of those affected with thyroid dysfunction the majority are women, of which an estimated 50% remain undiagnosed.

There are numerous factors that may contribute to low thyroid function including:
- Autoimmune disease (known as Hashimoto’s thyroiditis)
- Hyperthyroid treatment (using radioactive iodine or thyroid suppressing medications)
- Thyroid surgery
- Radiation therapy of the head and neck regions
- Medications such as birth control, hormone replacement, and antidepressants
- Pregnancy
- Iodine deficiency
- Pituitary tumor
- Congenital defects

In addition to the many contributing factors for hypothyroid, the list of potential symptoms is also numerous. Please see Table 1. Symptoms and Disorders Associated With Hypothyroidism.

Conventional testing for hypothyroid involves a blood test that primarily investigates TSH (thyroid stimulating hormone). If this measurement is elevated (>5.5 mlU/L), then a diagnosis of hypothyroid is given and patients are usually placed on thyroid medication; this shuts down the stimulation of the hypothalamus/pituitary, decreases your TSH, and “normalizes” your blood test (see Figure 1). While this can be helpful for some individuals, two main issues are left unaddressed. The first is that the laboratory values for appropriate thyroid level are based on a bell curve of diseased individuals, and not what a healthy optimum level should be. Second, the blood test does not investigate potential roots of the problem concerning hypothyroidism.

Six Patterns of Hypothyroid to Consider
1. Pituitary dysfunction – caused by chronic stress during which high levels of cortisol¹ are secreted, pregnancy, low blood sugar or insulin resistance. These stressors tax the pituitary so it no longer signals the thyroid to release hormone. With this pattern, individuals will experience hypothyroid symptoms but have a normal to low normal TSH (1.8–3.0 mlU/L).

2. Underconversion of T4 to T3 – T4 (thyroxine) is the inactive form of the hormone and it must be converted to T3 (triiodothyronine) before it can be used in the body. Common reasons for underconversion are inflammation and high cortisol levels. Inflammatory chemicals (cytokines) damage the cell membranes and impair the conversion of T4 to T3. Elevated cortisol also suppresses the conversion of T4 to T3. This results in hypothyroid symptoms but normal values of TSH, T4 and a low T3 reading (if tested).

3. Elevated TBG – TBG (thyroid binding globulin) is the protein transporter for thyroid hormone. When thyroid hormone is bound to TBG, it is inactive and unavailable to the tissues. Elevated TBG can be caused by high estrogen levels (from estrogen-containing birth control pills, or hormone replacement therapy). Thus, with high TBG, levels of unbound thyroid hormone will be low, leading to hypothyroid symptoms. With this pattern, TSH and T4 will be normal. T3 if tested will be low and TBG will be high.

4. Decreased TBG – the reverse of above. When TBG levels are low, free thyroid levels are high. Intuitively you would think this would cause high thyroid function, but with high thyroid levels circulating, the tissues develop a resistance, causing hypothyroid symptoms instead. Decreased TBG can be caused by high testosterone levels, often associated with PCOS (polycystic ovarian syndrome) in women. This pattern reveals normal TSH and T4 and high T3.

5. Thyroid resistance – in this pattern both the thyroid and pituitary are functioning, but the hormones are
Advances

levothyroxine (synthroid). Additional options are triiodothyronine and desiccated thyroid compounds. While these medications may be clinically effective and relieve symptoms, there are also some natural compounds worth considering. They are all found in the AOR product ThyroSupport. This formula is designed to provide nutrients needed by the thyroid and to help in the stimulation and production of thyroid hormones. It does not act like a drug and take over for an underfunctioning thyroid, but rather provides the necessary nutrients to ensure your body’s own thyroid success.

Subclinical Hypothyroid
This means that with respect to laboratory testing, your values are within range. However, your clinical history and physical symptoms may all point to hypothyroid; therefore a course of thyroid treatment should still be considered.

Basal Body Temperature
Patients with suspected hypothyroidism that have normal lab values may get additional information about their condition by measuring basal body temperature. This test is performed by placing a thermometer deep in the armpit for 10 minutes, immediately upon waking and before getting out of bed. Typically the temperatures are taken over 5 days and the results are averaged. Women should begin taking their temperature on the second day of menstruation, which is the time in the cycle when the body temperature is the lowest. If the temperature averages below 36°C, then this could be a clue that a hypothyroid condition is possible. Basal body temperature is an estimate of basal metabolic rate, which is intimately linked to thyroid function.

Treatment Options
Conventional treatment for hypothyroid is almost unanimously levothyroxine (synthroid). Additional options are triiodothyronine and desiccated thyroid compounds. While these medications may be clinically effective and relieve symptoms, there are also some natural compounds worth considering. They are all found in the AOR product ThyroSupport. This formula is designed to provide nutrients needed by the thyroid and to help in the stimulation and production of thyroid hormones. It does not act like a drug and take over for an underfunctioning thyroid, but rather provides the necessary nutrients to ensure your body’s own thyroid success.

Tyrosine: An amino acid that when combined with iodine, makes thyroid hormone. It is interesting to note that tyrosine is also the building block for the stress hormones epinephrine and norepinephrine. Thus, when under stress, thyroid production can be reduced, as tyrosine is utilized for the production of stress hormones instead.

Iodine: Numerous studies have shown that normal thyroid status is dependent on the presence of many trace elements for both the synthesis and metabolism of thyroid hormones. Iodine is most important as a component of the hormones thyroxine and 3,3',5-triiodothyronine (T3), and iodine deficiency can be a key factor in hypothyroidism.
**Coleus Forskohlii:** The Ayurvedic herb *Coleus forskohlii*, and its active constituent forskolin, can raise the production and release of thyroid hormones in animal and *in-vitro* studies.8

**Bacopa monnieri:** Studies in male mice showed that Bacopa possesses beneficial thyroid-stimulating effects, increasing T4 concentration by 41% after supplementation for 15 days when compared to non-treated mice.9

**Copper:** Copper plays an important role in thyroid metabolism, especially in hormone production and absorption. Copper stimulates the production of the thyroxine hormone (T4), and prevents over-absorption of T4 in the blood cells by controlling calcium levels in the body.

**Zinc:** Zinc plays an essential role in thyroid hormone function. In fact, without the presence of zinc, the thyroid gland cannot transform the inactive hormone T4 into the active hormone T3. Furthermore, the hypothalamus also requires zinc to make the hormone it uses to signal the pituitary gland to activate the thyroid. All of this means that people with insufficient zinc levels are likely to have an underactive thyroid gland.

**Selenium:** Is essential for normal thyroid hormone metabolism, it is a cofactor for various iodothyronine deiodinases (enzymes) that control the synthesis and degradation of the biologically active thyroid hormone, T3.10

Thyroid health is a key ingredient to managing energy, weight, aging, and overall well-being. Low thyroid function can be something that may fly under the radar of regular medical checkups, or may be tested and deemed fine by laboratory standards. This article has attempted to highlight that this screening is not always sufficient, and your physical and emotional symptoms should be taken into account with equal consideration as there may be other factors at play.

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**Table 1. Symptoms and Disorders Associated with Hypothyroidism**

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<thead>
<tr>
<th>General</th>
<th>Psychiatric</th>
<th>Cardiovascular</th>
<th>Gynecological</th>
<th>Dermatological</th>
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<td>Cold intolerance</td>
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<td>Muscle aches</td>
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<td>Constipation</td>
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<td>Cold intolerance</td>
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<td>Typing</td>
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</table>

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Breast cancer is the most common cancer in North American women. It makes up almost 30% of all female cancers and is the leading cause of death among women 40-55 years old.1 There are numerous risk factors that are associated with breast cancer. However, one of the most well established is increased exposure to estrogen.2 Women that experience early menarche and a later onset menopause have a higher risk of breast cancer due to the lengthened exposure to estrogen during their lifetime.1 External sources of estrogen such as hormone replacement therapy and the birth control pill have also been linked to increased breast cancer rates.3 Awareness about the impact and importance of estrogen is quickly growing because there are so many factors that can lead to increased exposure. Not only is estrogen made within the body, many chemicals found in the environment act like estrogen and also prevent its proper breakdown and metabolism. Fortunately, there are a number of dietary factors that promote the healthy function and metabolism of estrogen and other hormones. This article will discuss the positive and negative forms of estrogen including phytoestrogens and xenoestrogens and how they relate to breast cancer. It will also address key dietary factors that help reduce breast cancer risk and promote hormonal balance.

Understanding estrogens

Estrogens are an essential family of hormones that regulate many important functions, especially in the female reproductive system. While they are important, estrogen receptors often become saturated and over stimulated due to excess production, poor metabolism and exposure to environmental chemicals that have similar functions. This leads to the excessive promotion of cell growth, which ultimately contributes to cancer cell growth. To fully understand the role of estrogen in breast cancer development, we must look at the various forms and their actions since there is wide range of functions and levels of activity. Estrogens exist in the body in 3 different primary forms, estrone (E1), 17β-estradiol (E2), and 16α-estriol (E3).4 E2 is produced in the ovaries and is considered the most potent estrogen. E2 is approximately 12 times more potent than E1 and over 80 times more potent than E3.4 Estrone (E1) is produced primarily in adipose tissue, especially after menopause. Estriol (E3) is formed in the liver through the conversion of E2 and E1.4 Unfortunately, a number of harmful foods, environmental toxins, and chemicals can block this conversion and therefore result in increased levels of E2, which can promote breast cancer growth.2 Since E3 is the weakest form of estrogen, it acts in a similar fashion to a plant phytoestrogen and blocks the estrogen receptor from being stimulated by the more potent E2 or xenoestrogens. Higher levels of E3 have been associated with lower breast cancer risk, while higher levels of E2 have shown increased cancer risk.4

During the metabolism of E2 and E1 in the liver, 3 main estrogen metabolites are formed: 2-hydroxyestrone (2-OHE1), 4-hydroxyestrone (4-OHE1), and 16α-hydroxyestrone (16α-OHE1).5 See Figure 1 for a diagram of estrogen metabolism in the liver. The 16α-OHE1 metabolites have a very potent stimulatory effect on estrogen receptors and they promote cell growth, which increases cancer risk.5 4-OHE1 accumulates in the breast tissue and causes DNA mutations and suppresses the activity of p53, an anti-cancer gene.5 2-hydroxyestrone opposes the effects of the other 2 estrogen metabolites and appears to have a protective effect in breast cancer.5 Recent studies have looked at the ratio of 2-OHE1 to 16α-OHE1 in urine and have found that higher ratios may have protective effects in breast cancer, but more studies are needed to confirm this ratio as a risk assessment tool.6,7

Xenoestrogens

Xenoestrogens are a group of environmental chemicals which mimic estrogen in the body. This family of molecules has been linked
to the development and promotion of hormonally sensitive cancers. As of 2003 there were over 160 xenoestrogens that may be involved in breast cancer development. For a list of the most common xenoestrogens and where they are found please see Table 1 on page 23. Cancer types associated with environmental chemical exposure and that have been well documented in literature include those of the reproductive system, breast, lung, kidney, pancreas, and brain. There is evidence that the xenoestrogens play a role in all phases of cancer development including initiation, transformation, and invasion. For example, a number of studies have now confirmed that a chemical (a polycyclic aromatic hydrocarbon) produced during meat frying and grilling strongly increases DNA damage in breast cells and promotes breast cancer growth. There is still more research to be done to fully understand the broad health impact of xenoestrogens, but the emerging evidence is very concerning due to their widespread prevalence and pervasiveness in our food products, water supply, and environment. As part of a hormonal balancing and breast cancer prevention plan, it is paramount to consider reducing the exposure to these compounds that contribute to detrimental estrogenic activity in the body.

**Phytoestrogens and breast cancer**

It is impossible to talk about breast cancer and estrogen without briefly discussing phytoestrogens. There is a fair amount of confusion about the safety and effectiveness of phytoestrogens, even among medical professionals. Phytoestrogens are a group of compounds found in certain plants that have an estrogen-like effect in the human body. These compounds interact with estrogen receptors, but they are much weaker than estradiol (E2) or most xenoestrogens. Due to their relative weakness, phytoestrogens may actually bind to the estrogen receptor without actually activating it, therefore preventing E2 or xenoestrogens from activating the receptor. This would explain the fact that the majority of studies have shown phytoestrogens to be protective against breast cancer, while elevated levels of human or synthetic estrogen increases the risk. It is also important to recognize that there are two different types of estrogen receptors in the body: alpha-estrogen receptors (ER-α) and beta-estrogen receptors (ER-β). This is important because most phytoestrogens bind more strongly to ER-β than ER-α. ER-β receptors have been linked to increasing cancer cell apoptosis and are often down regulated in hormone sensitive cancers. Conversely, many xenoestrogens activate ER-α, which are present on 75% of breast cancer tumors. The fact that plant compounds such as quercetin selectively bind ER-β receptors suggests that some phytoestrogens may be useful in promoting cancer cell death.

A large number of population studies that assess soy consumption found that higher intakes do not increase breast cancer risk. Some studies even showed a protective effect. After considering all the studies, a daily intake of 10g of soy protein had the optimal protective effect. These results are opposed by a number of test tube studies that have shown phytoestrogens in soy to stimulate estrogen receptors and breast cancer cell growth. The difference in the results highlights the complexity in phytoestrogen activity. One important point to consider is that individual differences in intestinal microflora in humans promote the formation of various phytoestrogen metabolites such as equol, which has a noted cancer protective effect. New data suggests that equol could possibly enhance the effect of tamoxifen in the prevention of breast cancer. These factors are not considered in test tube studies and may be responsible for the negative results.

While there still is more research to be done, population studies suggest that moderate dietary consumption does not increase the risk of breast cancer. It may even be protective, especially if the person has consumed soy since childhood. It’s also important to remember that not all phytoestrogens are the same and some may offer a greater protective effect than others.

**The Influence of Diet on Estrogen and Breast Cancer Risk Reduction**

From a dietary perspective, cruciferous vegetables have demonstrated the most powerful anti-cancer effect. One study found that increasing the cruciferous vegetable intake of healthy postmenopausal women for four weeks increased urinary 2-OHE1:16α-OHE1.
ratios, suggesting that high intakes of cruciferous vegetables can shift estrogen metabolism. Theses vegetables contain a group of natural compounds called glucosinolates (which are later converted to biologically active isothiocyanates) that support liver detoxification and hormone elimination pathways. Two of the most promising isothiocyanates with potential hormonal balancing activity include indole-3-carbinol (I3C) and sulforaphane.

**Sulforaphane**

Sulforaphane is a compound with a unique ability to stimulate the phase 2 liver detoxification system. The phase 2 pathway is very important since it is the final stage for the removal of harmful compounds, detoxification products, and excess estrogens. Sulforaphane also has an impressive range of anti-cancer activity beyond stimulating phase 2 detoxification including stimulation of cancer cell suicide, preventing replication, reducing tumor spreading and inhibiting blood supply to cancer cells. Numerous studies have shown that sulforaphane can prevent the growth of various cancer cells of the prostate, colon and breast. Perhaps the most exciting recently discovered action is that it may actually inhibit breast cancer stem cells which are responsible for continued tumor growth and disease relapse. Another promising anti-cancer effect is the ability of sulforaphane to reduce inflammation right at the genetic level by stimulating a control protein called nuclear factor 2 (Nrf2).

From a practical perspective, cruciferous vegetables contain high amounts of glucoraphanin (also referred to as sulforaphane glucosinolate or SGS), which is then converted to biologically active sulforaphane by an enzyme called myrosinase. Myrosinase is released when the plant is chewed or processed or produced in the gut by bacteria. See Figure 2 for a diagram of sulforaphane breakdown. Unfortunately, cooking partially destroys this enzyme, limiting sulforaphane production. Glucoraphanin is abundant in broccoli, cauliflower, cabbage, and kale, with the highest concentration found in broccoli and broccoli sprouts. Studies show that just 1 cup of raw broccoli sprouts contains enough sulforaphane (200 µmol) to penetrate breast tissue and stop cancer growth.

**Indole-3-Carbinol (I3C)**

I3C is another compound found in the cruciferous vegetable family, which has an impact on estrogen levels and breast cancer risk. Like sulforaphane, I3C possesses multiple anti-cancer mechanisms including the up-regulation of detoxification enzymes and increasing the 2-OHE1 form of estrogen in the liver. In controlled clinical trials, oral supplementation with 300–400 mg/day of I3C has consistently increased urinary 2-OHE1 levels and urinary 2-OHE1:16α-OHE1 ratios in women. I3C supplementation also reversed a form of early cervical cancer after just 12 weeks of supplementation.

Once I3C is ingested it forms several metabolites, but the majority is converted to diindolylmethane (DIM), which is considered the most active metabolite. Like I3C, DIM has also demonstrated an improvement in estrogen metabolism, however it does not have the same volume of clinical research as I3C does. A number of cell studies have shown that it prevents the growth of breast cancer cells.

Supplementation with 108 mg/day of DIM also increased urinary 2-OHE1 levels in postmenopausal women suggesting that is has a positive effect on estrogen balance. One advantage DIM has over I3C is that it is a more stable molecule which leads to enhanced biological activity.

**Essential Fatty Acids**

The omega-3 and omega-6 class of polyunsaturated fatty acids exert a modulating action on estrogen metabolism. High intake of omega-6 fatty acids - linoleic acid (LA) and arachidonic acid (AA) - interferes with the detoxification of estrogens. Omega-3 fatty acids refer to a group of three fats: alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). Hydroxylation is an important biochemical process necessary for detoxification. EPA has been shown to increase 2-hydroxylation of E2 at the expense of C-16α hydroxylation, while DHA decreases the binding of estrogens to the ERs.

**Dietary Fibers**

Dietary fibers are parts of a plant that do not break down in our stomach, and pass through our system undigested. Soluble fibers dissolve in water, while insoluble fibers do not. Insoluble fibers...
such as lignins are found in flaxseeds and in the bran layer of grains, beans, and seeds. Fruits and vegetables provide most of the soluble fibers. Both types of fibers are equally important for health, digestion, and preventing various diseases. Soluble fibers are readily fermented in the colon into gases and physiologically active byproducts, while insoluble fibers increase bulk, soften stool, and shorten transit time through the intestinal tract.

Recent studies demonstrate that 16α-OHE1 levels are affected by fiber intake. Soluble fibers favorably modulate the 2/16α ratio while insoluble fibers sequester endogenous estrogens within the gut, decreasing their circulation within the body, their resulting availability to target tissues, and improving their elimination via feces.

Current recommendations from the United States National Academy of Sciences, Institute of Medicine suggest that adults consume 20–35 grams of dietary fibers per day, but the average American’s daily intake of dietary fiber averages only 12–18 grams. Partially hydrolyzed guar gum (PHGG) constitutes an excellent way to increase soluble fibers in your diet, and a good alternative to other highly allergenic alternatives such as wheat fibers or corn-based products. This tasteless, odourless supplement dissolves completely in water and it has been better tolerated and preferred by patients in clinical trials.

**B vitamins**

The important role of vitamins B6, B12, and folate as cofactors for enzymes involved in the methylation of catechol estrogens (2-OHE1 and 4-OHE1) to less harmful metabolites has already been mentioned. However, obtaining B vitamins solely from the diet can represent quite a challenge, especially for the increasing number of individuals adhering to a gluten-free diet. A significant portion of the population presents single nucleotide genetic polymorphisms (SNPs) which interfere with their ability to metabolize certain vitamins to their active form utilized by the body. For example, it is estimated that between 10 and 15% of North American Caucasians, and >25% of Hispanics present a polymorphism affecting 5,10-methylenetetrahydrofolate reductase (MTHFR), the enzyme needed for the conversion of folate to 5-methyltetrahydrofolate (5-MTHF), the primary circulating form of folate. Since SNPs can affect any other enzymes involved in the metabolism of vitamins, choosing a nutritional supplement containing the metabolically active form of folate (5-MTHF) and other B vitamins (P-5-P, methylcobalamin, etc.) will help ensure that you obtain adequate levels of these crucial nutrients.

**Green Tea**

Green tea has a large range of potential anti-cancer actions including reducing the growth of cancer cells and the blood vessels that feed them. For a more detailed discussion on green tea and cancer please see the article in Advances: Cancer. A recent study added another benefit to the long list when it found that green tea actually blocked breast cancer growth associated with a powerful xenoestrogen called PhIP (found in grilled or fried meats). This is so important because xenoestrogens may be responsible for up to 85% of spontaneous breast cancers.

**Glucaric Acid**

Glucaric acid is found in many fruits and vegetables, with the highest concentrations in oranges, apples, grapefruit, and cruciferous vegetables. Oral supplementation of calcium-D-glucarate (a salt form of glucaric acid) has been shown to inhibit beta-glucuronidase, an enzyme produced by gut bacteria that prevents phase II liver detoxification. Elevated beta-glucuronidase activity is associated with an increased risk for various cancers, particularly hormone-dependent cancers such as breast, prostate, and colon cancers. Calcium-D-glucarate’s inhibition of beta-glucuronidase activity allows the body to excrete hormones such as estrogen before they
certain forms of estrogen have been shown to lower serum estrogen levels in rats by 23 percent.\textsuperscript{31} 

**Pulling it all together**

There is little doubt that estrogen plays a large role in breast cancer development and growth. Certain forms of estrogen normally produced in the body or found in the environment have been linked to higher breast cancer risk. Increasing elimination and lowering exposure to these forms should be a primary goal in reducing risk and achieving healthy estrogen balance. Various natural substances found in plants and vegetables can promote healthy estrogen balance by binding estrogen receptors and increasing the elimination of excess estrogen. Cruciferous vegetables, organic soy products and green/white tea stand out in the research as the most beneficial. Incorporating these foods into your diet can help to promote healthy estrogen balance and to help reduce breast cancer risk.

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## References

Xenoestrogens: Hidden Dangers in our Modern World

Xenoestrogens or "foreign estrogens" are chemical compounds that mimic the effects of estrogen in our bodies. Sources come from almost all walks of our modern lives, from industry, water sources, agriculture, clothing/textiles, furniture, home cleaning products, make-up, skin care products, contraceptives, sunscreens, insecticides, food dyes, electrical oils, emulsifiers, paints; the list is almost endless. An additional list of common sources of xenoestrogens can be seen in Table 1.

While these chemicals have systemic effects in our bodies, there are certain areas that will concentrate xenoestrogens and demonstrate more significant issues due to exposure. These areas include the brain (pituitary, hypothalamus), thyroid, cardiovascular system, breasts, pancreas, ovaries, uterus and adipose tissue.

With targeted uptake of chemical concentration into these tissues, conditions such as hypothyroid, heart disease, diabetes, early puberty, fibroids, endometriosis, fibrocystic breast disease, polycystic ovarian syndrome, and cancers have shown a relationship to xenoestrogen exposure. While there are numerous factors that will govern how significant these exposures will be to your health, here are five worth consideration:

1. Age at exposure - it has been shown that exposure to these chemicals in utero or as a child has the potential for more harm than if exposed as an adult.
2. Latency due to exposure - there can be a time lag between exposure and manifestation of symptoms which may make it difficult to determine when or where the exposure occurred.
3. Mixed exposure - due to contamination of environment, we are rarely exposed to just one of these chemicals. Thus the effects of multiple xenoestrogens may be additive and possibly synergistic.
4. Dose response dynamics - It has been shown that even minute exposure to these chemicals can cause endocrine or reproductive harm if they happen at a critical developmental stage. In addition, the strange cases of some of these chemical compounds are shown to be more toxic at low dose exposure rather than high dose exposures.
5. Transgenerational (epigenetic) effects - perhaps the scariest to consider, these chemicals may not only affect those exposed, but the children born in subsequent generations.

All of this information can be daunting and potentially depressing, however there are ways to minimize your exposure to xenoestrogens as can be seen in Table 2.

To utilize all of the ideas in this table may not be feasible, however any movement to apply even some of these suggestions will go a long way to reducing overall exposure level. In addition there are some natural compounds that will also work synergistically with these suggestions. *Sulforaphane* - This natural compound is found in cruciferous (green, leafy) vegetables and has been
shown to protect our DNA from toxic chemicals, act as an anticancer agent, stimulate our immune system and activate our phase II liver detoxification enzymes.\(^6\)

*Calcium-D-glucarate - Shown to inhibit the detoxification enzyme beta-glucuronidase, allowing toxins to be effectively neutralized and excreted from the body before they can do significant damage.\(^7\)

**Milk Thistle** - A liver protector and detoxifier, this herbal remedy acts to neutralize the harmful chemicals we are exposed to and also protects the liver from damage even in cases of hepatitis and cancer.\(^8\)

**N-acetyl cysteine (NAC)** - The amino acid precursor to glutathione (body's premier antioxidant) NAC demonstrates protection against toxins and poisons.\(^9\)

*Diindolylmethane (DIM) - Another natural compound from cruciferous vegetables like broccoli, DIM promotes the production of the healthy "2-OH" estrogen, and reduces the production of unhealthy "16-OH" estrogen. This aids in reducing the formation of reproductive system diseases and estrogen sensitive cancers.\(^10\)

**Hops** - The active ingredient 8-prenylnaringenin (8PN), may help to reduce breast cancer metastasis as well as tumor formation.\(^11\)

**Choline** - A natural compound shown to support the liver via its contribution as a cofactor in the methylation process of detoxification - a key detoxification pathway for dealing with xenoestrogens. In addition, it may also be associated with the reduction of breast cancer.\(^12\)

These natural compounds can be found in the AOR products Cellular Detox, Liver Support and Estro Adapt.

*For additional information on these compounds please see the article on page 17.

In our modern world, chemical exposure is part of life. If we can make conscious decisions to limit our xenoestrogen exposure as best we can by making clean choices with our diet, how we clean and care for our bodies and our homes, as well as by utilizing some natural compounds as mentioned above to assist in detoxification, we limit our total chemical load and thereby reduce the potential for complications with our health.

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### Table 1 - Common Xenoestrogens and Environmental Sources

<table>
<thead>
<tr>
<th>Xenoestrogen</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polycyclic aromatic hydrocarbons</td>
<td>Formed when meat is cooked at high temperatures such as grilling or</td>
</tr>
<tr>
<td>Heterocyclic amines</td>
<td>barbecuing, and in smoked fish</td>
</tr>
<tr>
<td>Dioxins</td>
<td>Mainly found in meats and animal products, especially fish, chicken,</td>
</tr>
<tr>
<td></td>
<td>cheese and eggs</td>
</tr>
<tr>
<td>Polychlorinated biphenyl (PCB)</td>
<td>Found in paints, plastics, rubbers, dyes, and flame resistant clothes.</td>
</tr>
<tr>
<td></td>
<td>They also accumulate in farmed fish, poultry, milk and dairy products,</td>
</tr>
<tr>
<td></td>
<td>and fruits and vegetables</td>
</tr>
<tr>
<td>Dichlorodiphenyl-trichlorethane (DDT)</td>
<td>Pesticide that is now banned but still present in the water system</td>
</tr>
<tr>
<td>diethylstilbestrol (DES)</td>
<td>A drug that is now banned used to prevent miscarriages</td>
</tr>
<tr>
<td>Parabens</td>
<td>A preservative found in cosmetics such as creams and shampoos</td>
</tr>
<tr>
<td>Phthalates</td>
<td>Found in plastics, medical equipment, baby mattresses, paints and</td>
</tr>
<tr>
<td></td>
<td>personal care products</td>
</tr>
<tr>
<td>Alkylphenols and PVCs (polyvinyl</td>
<td>Found in plastics and perfumes</td>
</tr>
<tr>
<td>chlorides)</td>
<td></td>
</tr>
<tr>
<td>Metalloestrogens (Aluminium Chlorohydrate)</td>
<td>Found in anti-perspirants</td>
</tr>
<tr>
<td>Bisphenol A</td>
<td>Leaches from plastics after repeated use. Also found in the inner</td>
</tr>
<tr>
<td></td>
<td>lining of cans.</td>
</tr>
<tr>
<td>Butylated hydroxianisole (BHA)</td>
<td>Preservative found in packaged food</td>
</tr>
<tr>
<td>Dichlorobenzene</td>
<td>Potent chemical found in air fresheners and scents</td>
</tr>
<tr>
<td>Triclosan</td>
<td>An anti-microbial found in hand soap and tooth pastes</td>
</tr>
<tr>
<td>Styrene</td>
<td>Widely used plastic for food packing</td>
</tr>
<tr>
<td>Alcohol</td>
<td>Even small amounts increases estrogen levels in the body</td>
</tr>
</tbody>
</table>
Table 2: Ideas for Minimizing Your Xenoestrogen Exposure

**When Purchasing Household Products and Food**
- Choose chlorine-free products, unbleached paper products and coffee filters.
- Reduce the use of plastics whenever possible.
- Buy food grown locally and in season, organic if possible.
- Buy and use chemical free, biodegradable laundry and household cleaning products whenever possible.

**Outside the Home**
- Avoid all pesticides, herbicides, and fungicides.
- Minimize X-rays whenever possible.
- Be aware of noxious gas such as from copiers and printers, carpets, fiberboards, and at the gas pump.

**In the Kitchen**
- Use filtered water to drink and bathe in to avoid chlorine.
- Whenever possible, choose organic foods.
- Buy hormone free meats and dairy products to avoid hormones and pesticides.
- Do not microwave food in plastic containers.
- Avoid the use of plastic wrap to cover food for storing or microwaving.
- Use glass or ceramics whenever possible to store food.
- Do not leave plastic containers, especially your drinking water, in the sun.
- If a plastic water container has heated up significantly, throw it away - do not drink the water.
- Don't refill plastic water bottles.
- Avoid freezing water in plastic bottles to drink later.
- Peel non-organic fruits and vegetables.

**Personal Products**
- Avoid creams and cosmetics that have toxic chemicals and estrogenic ingredients such as parabens and stearal konium chloride.
- Minimize your exposure to nail polish and nail polish removers.
- Use naturally based fragrances, such as essential oils.
- Read the labels on condoms and diaphragm gels.
- Use chemical free soaps and toothpastes.
- Use chlorine free tampons, menstrual pads, toilet paper, paper towel etc.

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**Additional Sources**
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- [www.organicexcellence.com](http://www.organicexcellence.com)
Polycystic ovary syndrome (PCOS) is considered one of the leading endocrine disorders affecting up to 10% of all women of reproductive age. It is a complex disorder stemming from inappropriate hypothalamic-pituitary-ovarian interaction (see the article titled "An introduction to the HPG Axis"), thought to be one of the leading causes of infertility. Why and how PCOS develops is not yet understood, although accumulating evidence suggests that it may be mostly genetic.

Diagnosis, Symptoms and Risks
A PCOS diagnosis is based on menstrual irregularity, excessive production of androgens (masculinizing hormones) or excessive masculinizing traits (such as balding, excessive body and facial hair), as well as the presence of ovarian cysts. However, all other possible causes of the above mentioned traits have to be excluded for a diagnosis of PCOS to be made. There are many connections between the various factors involved in the development of PCOS but how they all fit together has not been conclusively determined.

The principal symptoms of PCOS emerge late in puberty or shortly after, stemming from two main causes: 1) a lack of ovulation, which may or may not result in irregular menstruation, and 2) excessive amounts (or due to the effects) of androgenic hormones, which cause hirsutism (excessive facial and body hair). It is not uncommon for women with PCOS to encounter other difficulties such as infertility, high risk of miscarriage, accumulation of visceral fat, obesity, various cardiovascular diseases such as diabetes, dyslipidemia, hypertension, and Metabolic Syndrome later in life. The severity of symptoms, especially hirsutism and obesity, can lead to feelings of low self-esteem, anxiety, depression and low quality of life.

Severity of symptoms and related disorders of PCOS vary greatly between individuals, yet there are some trends that have been observed with age and ethnicity. In younger women with PCOS, hyperandrogenism (excessive androgens) and chronic anovulation (lack of ovulation) are the primary disturbances, whereas, obesity, insulin resistance, and metabolic disturbances are predominant in older women with PCOS. South Asians with PCOS have a high prevalence of insulin resistance and metabolic syndrome, and are at risk for type 2 diabetes. African American and Hispanic women with PCOS are more prone to obesity and metabolic problems. Finally, there is a higher prevalence of hirsutism among women of Middle Eastern and Mediterranean origin that suffer from PCOS. PCOS is also associated with other conditions including Acanthosis nigricans (hyperpigmentation of folds in the skin), fatty liver disease, obstructive sleep apnea, carcinoma (malignant cancer cells), and potentially breast, endometrial or ovarian cancer. Interestingly, insulin resistance and obesity can further amplify the severity of the condition and its symptoms, creating a vicious cycle where the symptoms exacerbate the condition and the condition exacerbates the symptoms.

Currently, four categories of PCOS have been identified. The first is characterized by the presence of menstrual irregularities, polycystic ovaries and hyperandrogenemia (excessive masculinizing hormones), and is present in ~48% of all women with PCOS. The second is characterized by the presence of menstrual irregularities and hyperandrogenemia only, and is found in 31% of women with PCOS. The third is characterized by the presence of hyperandrogenemia and polycystic ovaries only, and is found in 10% of women with PCOS. Finally, the fourth category is characterized by the presence of menstrual irregularities and polycystic ovaries only and is
Panidis and colleagues (2012) identified the following trends: both lean and overweight/obese women in PCOS categories 1 and 2 are at a higher risk for insulin resistance than those without PCOS, while only obese/overweight women in the fourth category share the same risk. Overweight women in the first category, however, have the highest risk for insulin resistance. Serum androgen levels are highest in both lean and overweight/obese women in PCOS categories one to three compared to those in the fourth.

**Management**

Early diagnosis and preventative measures are of the utmost importance in promoting long-term health, decreasing the risk of developing other secondary illnesses, and even preventing the development of cardiovascular diseases. However, due to the individualized nature of PCOS, management must be tailored to target the displayed symptoms and to prevent the risk factors that you may have a predisposition for. It is also important to monitor progress and the development of new symptoms, and change the management routine accordingly.

**Dietary and Lifestyle Changes**

First line therapy for women with PCOS, and the only therapy incurring lifelong benefits with minimal side effects, is the reduction of central abdominal fat in all women, and weight loss in overweight and obese women. Abdominal fat is the most common fat distribution found in women with PCOS whether they're lean or overweight. Visceral fat, especially in obesity, has been found to increase some features of PCOS such as infertility, pregnancy complications and hyperandrogenism including hirsutism, and in combination with insulin resistance it can increase the risk for type 2 diabetes and cardiovascular diseases. The reduction of abdominal fat in all women with PCOS and weight loss in overweight and obese women can also help prevent long-term complications of the condition by improving quality of life, correcting hyperinsulinemia, improving fertility and improving lipid and androgen profiles. In fact, it has been found that after losing only 5% of initial body weight, obese women with PCOS had improved menstrual regularity, ovulation and pregnancy rates within weeks.

In order to best reduce insulin resistance and reduce the risk of type 2 diabetes, improve lipid profiles and reduce androgen production, diet recommendations for women with PCOS are similar to those recommended for type 2 diabetics. A high-fiber, low-glycemic-index diet with adequate protein and an emphasis on unsaturated fatty acids (especially ω-3 fatty acids) is recommended, while also maintaining a high intake of anti-inflammatory and antioxidant nutrients such as vitamin E and moderate amounts of red wine. A reduced calorie diet is recommended for obese and overweight women, while adequate calories for maintenance are more appropriate for lean women. An extreme version of a low carbohydrate diet called a ‘ketogenic diet’, in which the ratio of carbohydrates to proteins to fat is maintained at 10:30:60, was found to significantly decrease insulin resistance, free testosterone, and weight in overweight women with PCOS. However it is not recommended to maintain a ketogenic diet for a
prolonged period of time as research on long term safety is lacking; a doctor should be consulted prior to starting a ketogenic diet. Timing of caloric intake can also have an effect on PCOS symptoms in lean women; it was shown that a breakfast with more calories than dinner improved insulin sensitivity compared to a dinner with more calories than breakfast.22

Lifestyle changes can also have an impact on PCOS symptoms. It was shown that 1 hour of exercise (aerobic, resistance, or endurance) three times per week for 12-16 weeks, significantly improved insulin resistance, ovarian hormones, and reproductive function.23-26 It was also shown that the addition of aerobic or combined aerobic-resistance exercise to a calorie restricted diet significantly improved body composition in overweight and obese women with PCOS compared to those on a low calorie diet only.27 Even if healthy dietary and lifestyle options alone are not enough, a healthy lifestyle can significantly improve the success rate of other supplemental, pharmaceutical and surgical interventions. In fact, returning to a less healthy lifestyle and weight gain can easily reverse all the benefits that were obtained by exercise and healthy eating.

Supplementation
Some women with PCOS may not achieve adequate symptom relief from dietary and lifestyle changes alone, and therefore they may seek natural interventions to boost the results of healthy lifestyle modifications.

Chromium: To reduce the risk of developing type 2 diabetes, it is crucial to reduce insulin resistance. Chromium is a well-known element that has been found to reduce high insulin at doses of 200-1000 mcg/day, and the picolinate salt was found to be the most bioavailable chromium salt.28 Interestingly, circulating serum chromium has been found to be low in women with PCOS, and the differences were more pronounced in women with PCOS and insulin resistance.29

Cinnamon & Gymnema: Cinnamon was also shown to significantly reduce insulin resistance in women with PCOS compared to placebo.30 Additionally, Gymnema sylvestre, although not yet studied in women with PCOS, is a well-known herb used for lowering insulin resistance and supporting the management of diabetes.31

Vitamin D: Low vitamin D was shown to be associated with components of metabolic syndrome in women with PCOS, which include hyperlipidemia, insulin resistance, diabetes, obesity, and various other metabolic conditions.32,33 It was shown that vitamin D and calcium supplementation in overweight women with PCOS improved androgen and blood pressure profiles,34 and in infertile women it improved weight loss, follicle maturation and menstrual regularity.35,36 In another study, vitamin D supplementation in women with PCOS improved glucose metabolism and menstrual frequency.37

Folate: Folate (L-5-methyltetrahydrofolate, L-5-MTHF) is a crucial B vitamin especially for any woman looking to conceive, as it is a simple way to prevent neural tube

QUESTIONNAIRE

Should I ask my Doctor if I have PCOS?

Q1 Between the ages of 16 and 40, about how long was your average menstrual cycle (time from first day of one period to the first day of the next period)? (select ONE only)

PS: Do not include any time spent pregnant, receiving birth control pills or injections, after menopause, or after having both ovaries or the uterus surgically removed:

a) <25 days
b) 25-34 days
c) 35-60 days
d) More than 60 days
e) Totally Variable

Q2 During your Menstruating Years (Not including during pregnancy), did you have a tendency to grow dark, coarse hair on your: (Circle all that applies)
a) Upper Lip
b) Chin
c) Breasts
d) Chest Between Breasts
e) Back
f) Belly
g) Upper Arms
h) Upper Thighs

Q3 Were you ever obese or overweight between the ages of 16 and 40? (Circle one)
a) Yes
b) No

Q4 Between the ages of 16 and 40, have you ever noticed a milky discharge from your nipples (not including during pregnancy or recent childbirth)? (Circle one)
a) Yes
b) No

Key is at the end of the article.
defects in developing fetuses. However, it can also help reduce homocysteine, which is associated with recurrent pregnancy loss and an increased risk of cardiovascular disorders including dyslipidemia and blood clot formation. Folate intake was shown to significantly reduce homocysteine levels in women with PCOS at doses between 400-1000 mcg. However, many women can't even metabolize regular supplemental folate due to a common genetic mutation that makes them unable to convert the folate to its active form, L-5-MTHF. This can be overcome by directly supplementing with the bioactive folate form, L-5-MTHF.

**Inositol:** The development of insulin resistance may be linked to a deficiency in inositol, which is a messenger needed for insulin signaling. The human body contains two forms of inositol, myo-inositol (the most abundant form), and D-chiro-inositol; the ratios of each are different in each organ depending on that organ's needs. Ovaries require a high level of myo-inositol - in fact, a link between high concentrations of myo-inositol and quality, mature oocytes (egg cells) has been established. It is therefore not surprising that supplementing with myo-inositol (4g/day) during in vitro fertilization treatments have been shown to significantly improve oocyte quality, improving the chance of developing a healthy embryo by improving insulin sensitivity. However, evidence on D-chiro-inositol supplementation is controversial, with a recent study even showing worsening of oocyte quality and reduced ovarian response to fertility treatments. Melatonin: Melatonin supplementation was also found to improve oocyte quality and pregnancy rates in women undergoing in vitro fertilization. Melatonin reduces oxidative stress within the follicle. Oxidative stress increases significantly during the ovulatory process and is suspected to be a cause of poor oocyte quality. The addition of 3mg/day of melatonin to myo-inositol and folic acid supplementation significantly improves oocyte quality and pregnancy outcome in women with poor oocyte quality.

**Omega-3s:** Supplementing with omega-3 fatty acids was shown to significantly reduce liver fat content, thereby preventing or reducing fatty liver disease, in addition to improving serum adiponectin levels (a protein involved in regulating glucose levels as well as fatty acid breakdown), insulin resistance and cholesterol in women with PCOS, while another group showed that greater plasma polyunsaturated fatty acids, particularly long chain omega-3s, improve the androgenic profile in women with PCOS.

**Anti-androgenic herbs:** These can be used to lower androgen levels in women with PCOS, helping to reduce hirsutism and balding. Spearmint herbal tea was shown to have significant anti-androgen effects in polycystic women; however, because hirsutism and balding require more time to resolve in response to lowering androgen levels, the short duration of the trials did not permit them to decrease significantly. However, it is expected that longer term intake of spearmint tea would produce significant results. While other known anti-androgen herbs like saw palmetto and standardized pollen extracts have not been studied in women with PCOS, their well-known anti-androgenic properties are expected to reduce symptoms of high androgen levels in women with PCOS. Anti-androgenic supplementation or medication must not be taken during pregnancy or when trying to conceive however, as they have the potential of feminizing male fetuses.

**Soy isoflavones:** There are many options available to manage high cholesterol levels and improve the body's lipid profile. Soy isoflavones have been studied in women with PCOS, and an intake of 36 mg/day of genistein for 6 months in dyslipidemic women improved their lipid profiles.

**Other Options**
Some women may opt for prescription medication, and in severe cases, surgical intervention may be warranted. It must be noted however that lifestyle changes, including healthy diet and exercise are crucial to maintain results, no matter what other interventions are used.
For hirsutism, there are many available options. Tweezing, waxing, sugaring and shaving are the cheapest methods; however, these only provide temporary relief. More permanent relief can be provided with electrolysis or laser hair removal. Permanent hair reduction with either laser or electrolysis may take up to 2 years to significantly reduce hair growth.

Being diagnosed with PCOS may seem daunting and overwhelming, and although it is a lifelong condition with no cure, it is highly manageable. Understanding your own symptoms and working closely with your doctor are the first steps toward effective and targeted therapy. It is crucial to get diagnosed at the earliest stages of the disease in order to have the best chance at reducing the risk of, or even preventing, progression of the condition or the development of complications. A healthy lifestyle, including consistent exercise and a diet high in anti-inflammatory nutrients, antioxidants, fiber and proteins while low in carbohydrates is the first line of therapy toward managing symptoms of PCOS. In addition to a healthy lifestyle, supplements or medication may be used to target any other symptoms that do not resolve with healthy lifestyle modifications alone.

Key to “Should I Ask My Doctor if I Have PCOS?”
Award 1 point each if you:
Q1: Answered c, d or e
Q2: Circled 3 or more sites
Q3: Answered “yes”
For Q4, if you answered “yes”, then subtract 1 point, if you answered “no” then don’t change your points.
If you get ≥2 points, then you may have PCOS and should speak to your doctor.

References
25. Nybacka A et al. Randomized Comparison of The Influence of Dietary Management and/or Physical Exercise on Ovarian Function and...
Time to Remember
VEIN EASE

A New and Effective Treatment for Chronic Venous Insufficiency (CVI)