



Women's Wellness Center
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Peri-menopause and Hormone Health

An important decision every woman must make in midlife is whether or not to use hormone therapy (HT) after menopause. As a physician specializing in women's health, it concerns me that so many people today have profound misunderstandings regarding the safety and benefits of HT. If you are suffering the effects of hormone loss, you should know that relief is safe and available. If you have sailed through the menopausal transition in good health and free of any symptoms, then you may not wish to consider HT. Whether you choose to use hormones or not, your decision should be based on facts, not misconceptions or fear.

A significant number of women in my practice report that hormone therapy has been life changing for them, and they are so grateful to have their quality of life restored, but subsequently they are made to feel guilty or wrong; they receive the message that HT may be dangerous. Perhaps they read something that frightens them, a friend makes a comment, even a physician may caution against the use of HT. Women are exposed to conflicting messages, leaving them hopelessly confused.

This guide was created to clear the confusion so you can make an informed decision when the time comes in your life. I am passionate about helping women navigate the menopausal transition well, and believe each one of us can do it with grace, comfort, and optimal health.

What is menopause?

Menopause is your last period. After that you are post-menopausal for the rest of your life. Menopause is caused by a decline in ovarian hormone production. Ovarian hormones are involved in many bodily functions, not just reproduction. So, with hormone depletion, many symptoms can occur that affect both your quality of life and your long-term health.

The most common symptoms women experience during the menopausal transition are hot flashes, night sweats, depression, anxiety insomnia, fatigue, decreased libido, vaginal dryness, bladder symptoms, mental cloudiness, and memory loss. Some less common symptoms are heart palpitations, dizziness, itchy crawly skin, or a burning sensation of the mouth or tongue. Duration of symptoms can vary widely. It may be a few months, may be a few years, or may be for all remaining days on earth, not just during the transition time. The average woman will experience natural menopause between the ages of 48 and 52. Surgical menopause by removal of the ovaries results in immediate hormone loss, usually with abrupt onset of symptoms.

What is peri-menopause?

Peri-menopause includes the several years preceding menopause, and it's common for women to begin having some of the above-mentioned symptoms during this time. In addition, due to the wide fluctuations in hormone levels of peri-menopause, bleeding problems (heavy, irregular periods) are common during this phase of life. It's important to point out that all of these changes are a natural part of aging, but that doesn't mean that we shouldn't look for some relief from these life-altering symptoms.

What do our natural hormones do for us?

The current discussion involves the ovarian hormones, also called “sex hormones.” These are estradiol, testosterone, and progesterone. To enhance clarity of the topic at hand, throughout the following discussion, many questions will be answered in reference to each separate hormone.

Estradiol is the estrogen hormone that makes you look and feel female, and it controls the menstrual cycle, fertility, pregnancy, and lactation. This hormone also plays a role in the health of many bodily functions, evidenced by abundant estradiol receptors in your heart, brain, bones, joints, skin, eyes, teeth, gums, nerves, blood vessels, urinary tract, reproductive organs, and more. So, with depletion of estradiol the loss may be suffered in countless ways.

ESTROGEN: A Tale of Three Hormones

The human body makes three different estrogen hormones: estradiol, estrone, and estriol. *Estradiol* is the most potent estrogen, and by far the most active estrogen throughout a woman’s reproductive lifetime. *Estrone*, much less potent, is dominant during menopause because it is manufactured in fat cells even if ovaries are absent or non-functioning. *Estriol* is made by the placenta during pregnancy, and is present in negligible amounts otherwise. Some claim all three estrogens should be included in hormone replacement, because it’s more “natural,” and some claim that estriol is safer than other forms of estrogen. However, no scientific studies exist to support these claims, and since estradiol is the dominant estrogen of the healthy reproductive years, it makes the most sense to use estradiol for replacement therapy.

Testosterone is often considered a “male hormone” but is a vital hormone in women, eliciting physiologic effects through androgen receptors in almost all female body tissues, including breast, heart, blood vessels, intestines, lungs, brain, spinal cord, nerves, bladder, uterus, ovaries, endocrine glands, vaginal tissue, skin, bone, joints, and fatty tissue. Men produce much higher circulating levels of testosterone than women, but testosterone is still the most abundantly active sex hormone in a woman throughout her lifespan. Yes, you read that correctly – testosterone is more abundant even than estrogen in a woman’s body. Testosterone is a big deal for us women, and we should pay attention when it’s diminished.

Progesterone, during the reproductive years, is responsible for supporting and maintaining pregnancy. And, as you will see, throughout life it is important to have progesterone to balance the effects of estrogens in your body.

What are bio-identical hormones?

The term bio-identical refers to hormone formulations that exactly match the hormones of the human body. These are made in a laboratory, using soy or yams as the source. Estradiol, progesterone, testosterone, and others can be produced as bio-identical formulations – some are available commercially, some are not. Through specialized compounding pharmacies, we can provide customized prescriptions of bio-identical estradiol, progesterone, and testosterone, allowing almost infinite variation in formulations.

Bio-identical estradiol is FDA approved and commercially available under several different brand names: Vivelle Dot (patch), Estrogel, Elestrin, Evamist, Vagifem, Estring, FemRing, and others.

Bio-identical testosterone is currently not FDA approved or commercially available for women. Through compounding pharmacy technology, the product can be formulated for off-label use.

Bio-identical progesterone is FDA approved, available commercially as a capsule of micronized progesterone in peanut oil. The micronization process allows the hormone to be better absorbed, but does not change the basic molecular structure of the hormone. For those allergic to peanut oil, it is possible to formulate progesterone in olive oil through compounding pharmacy technology.

Hormones that are not bio-identical are commonly known as *synthetic* hormone formulations. Examples are conjugated equine estrogens (CEE), oral contraceptive pills, medroxyprogesterone (Provera), and methyltestosterone.

It is important to note, the general terms “estrogen” and “progestin” are often used when doctors or authors of studies discuss hormone replacement, but they do not always specify the type of estrogen or progestin, nor the route of delivery, thereby rendering their advice or data less than helpful. It does make a difference which formulation and which route is being considered, as some carry more risk than others. Unfortunately, not all studies take this crucial fact in to account, and careless statements may be made about “estrogen” being associated with certain risks (such as cardiac risk), when the fact is that non-oral, bio-identical estradiol may not be associated with the risk in question.

In this article, we refer to specific hormones estradiol and progesterone when speaking specifically of bio-identical formulations. When speaking in other contexts we may sometimes use the more general terms estrogen and progestin. For example, the discussion below remarks on conclusions of various scientific studies, some of which did not specify specific estrogen formulations in their reporting.

What Are Benefits Of Hormone Therapy After Menopause?

- **Estrogen.** The most obvious and immediate benefit is the relief of mild to severely unpleasant symptoms resulting from hormonal decline. However, when ovarian hormones decline it causes more than unpleasant symptoms. Physiologic changes occur that set the stage for chronic diseases, such as cardiovascular disease, osteoporosis, and dementia. Early replenishment of sex hormones lowers risk of these and other conditions related to aging. Below is a summary of documented benefits of estrogen therapy.

Benefits of Estrogen Therapy after Menopause

- Estrogen is the most effective treatment for symptoms of peri-menopause. These symptoms include, but are not limited to: hot flashes, night sweats, sleep disturbance, mood changes (depression, tearfulness, and irritability), anxiety, difficulty concentrating, low libido, vaginal dryness or burning, and bladder symptoms. Less common symptoms are heart palpitations, dizziness, and itchy crawly skin, dry eyes, and burning sensation of the mouth or tongue.
- Cardiovascular disease is the most common cause of death in post-menopausal women. If begun at the onset of menopause, estrogen helps prevent cardiovascular disease through a beneficial effect on cholesterol levels, decreased plaque formation in the coronary arteries, vasodilation, and anti-inflammatory properties.
- Estrogen therapy decreases risk of diabetes in postmenopausal women.
- Estrogen replacement is effective for decreasing bone loss and osteoporosis. Without estrogen replacement after menopause there is naturally a steep decline in bone density over several years. Once the bone is lost, hormones can't bring it back. Osteoporosis leads to fractures of hip or spine in postmenopausal women. The mortality rate of hip fracture after age 75 is 50%.
- Estrogen therapy has been shown to decrease incidence of Alzheimer's Dementia (if started early in menopause and continued long term).
- Estrogen therapy lowers risk of colon cancer.
- Estrogen replacement decreases risk of macular degeneration, the most common cause of vision loss and blindness in adults over 65 years of age. Estrogen also lowers incidence of cataracts.
- Estrogen therapy helps prevent degenerative arthritis.
- Estrogen therapy helps prevent tooth loss.
- Estrogen replacement can preserve or restore healthy sexual functioning, including vaginal health, maintenance of healthy sexual desire, and orgasm.
- Estrogen preserves skin tone, reducing formation of wrinkles through positive effects on collagen.

- **Testosterone.** When it comes to discussion of menopausal hormone replacement, much attention has been given to estrogen, but testosterone has been largely ignored as an essential hormone in female physiology. This is unfortunate, since women often begin to experience symptoms related to testosterone decline well before symptoms related to the fall in estrogen. In a woman's body, production of testosterone peaks in her mid 20's and begins to steadily decline, down to about 50% by age 40. This is when a woman will often present with complaints such as increased abdominal fat, hair loss, fatigue, brain fog, loss of sex drive, reduced orgasm, anxiety, irritability, depression, headaches, and general lack of well-being. We may attribute these symptoms to the inevitable decline of vigor with aging, but by recognizing them as a signal, and giving attention to hormone balance, we can improve physical health and vitality as we enter mid life.

Testosterone replacement for symptomatic women has the potential to improve mood, libido, orgasm, energy level, lean body mass, and general feeling of well-being. In addition, potential health benefits include reduced cardiac risk, improved bone density, and some studies suggest reduced breast cancer risk. Testosterone therapy can be beneficial for symptomatic individuals as early as a decade or more before onset of the menopausal transition.

- **Progesterone.** This hormone is often important to balance the effects of estrogen in the body. For example, when the uterine lining (endometrium) is exposed to estrogen, either naturally produced by the body, or as a supplement, it responds by thickening and growth. If this were to occur without the balancing effect of progesterone, the endometrium would continue to grow and thicken without limit, leading to increased risk of endometrial cancer. In addition to its uterine protective role, progesterone supplementation also helps relieve some of the menopausal symptoms, such as anxiety and sleeplessness. Some researchers have suggested that bio-identical progesterone supplementation may offer protection against breast cancer, and while this has not been firmly established, it does appear that bio-identical progesterone is quite safe with regard to breast health.

What About DHEA?

DHEA (dehydroepiandrosterone), produced mainly in adrenal glands, and a small amount in ovaries, is an important precursor molecule in the steroid hormone pathway that ultimately leads to production of testosterone and estradiol. There has been some attention given to DHEA as a possible "anti-aging" hormone supplement. It is known that DHEA levels decline as we age, similar to the sex hormones, but replacing DHEA does not seem to yield the results we might expect. With the exception of localized treatment of vaginal atrophy, and perhaps some improvement of sexual functioning, DHEA has not been shown to relieve most menopausal symptoms, nor has it been shown to produce the health benefits observed with testosterone and/or estradiol supplementation.

One theory suggests the reason DHEA does not produce expected results is that our older bodies don't convert DHEA to estradiol and/or testosterone as efficiently as in our youth. Researchers have postulated that because of the conditions of decline in testosterone plus the decline of its androgenic precursors (one of which is DHEA), combined with reduced conversion of DHEA to testosterone in target tissues, it is necessary to supplement with supra-physiologic doses of testosterone in order to overcome the compounded deficit, thereby optimizing delivery of testosterone to tissues, to fully relieve symptoms. In other words, since DHEA supplementation itself doesn't seem produce results, these investigators suggest supplementing with extra testosterone to make up for the loss of not only testosterone, but also of its precursors, accounting also for the reduced conversion of precursors to testosterone. These serum and tissue levels are easily accomplished with testosterone subcutaneous pellet therapy, which affords excellent and consistent absorption of bio-identical testosterone into the body.

Is there any safety concern with use of HT?

- **Estradiol.** When taken as a pill, any type of estrogen slightly increases the risk of blood clots, which can lead to thrombosis, stroke, or pulmonary embolism. This is because after the hormone is absorbed by the stomach, it is transported directly to the liver, where it will be handled similar to a toxin (only because the liver is not accustomed to dealing with a large amount of this hormone ingested as “food”). The extensive metabolism that ensues results in the liver increasing production of blood clotting and inflammatory factors. However, research has shown that when estradiol is absorbed slowly (by using a patch, topical cream, or subcutaneous pellet) there is not elevated risk of blood clot, because the hormone is delivered gradually into the bloodstream through capillaries, rather than first passing through the liver all at once. For the same reason, oral estrogen slightly increases the risk of gall bladder disease, which also can be avoided with use of transdermal or subcutaneous pellet therapy. Bottom line: The safe way to receive estradiol supplementation is by a non-oral route.
- **Testosterone.** Bio-identical testosterone for women has been used off-label for decades, and there is a growing body of data regarding its safety for hormone replacement. Any adverse health risk you may have seen referenced would likely be related to the synthetic pill methyltestosterone, which is subject to the first pass liver effect described above. Unfortunately, when disease risk related to hormone therapy is reported, authors commonly lump all hormones into one pile, seemingly not recognizing that synthetic formulations are often more potent, not biochemically identical to each other or to our natural hormones, and have different effects on the body than our natural hormones. Current data specifically regarding bio-identical testosterone formulations in women have not shown increased risk in cancer, cardiovascular disease, or other serious condition.
- **Progesterone.** There is no known medical or clinical risk of using bio-identical progesterone, by oral or other route of delivery. Anyone who mentions risk associated with progesterone therapy is confusing it with a synthetic progestin, such as Provera (medroxyprogesterone) or norethindrone.

Does HT increase risk of cancer?

The only cancer conclusively shown to be increased by estrogen therapy is uterine cancer, and the proper use of progesterone eliminates the increase in risk. As stated above, use of unopposed estrogen can cause over-stimulation of the cells of the uterine lining, but when properly balanced with progesterone, uterine lining growth is limited, and there is no increase in uterine cancer risk.

The cancer risk of HT that draws the most attention is the possible link to breast cancer. Many who are hesitant to use hormone therapy cite this as their main concern. Hundreds of studies have examined estrogen therapy and breast cancer, and though some show a small increase in risk, others show no increase, and still others show a decrease in breast cancer for women on estrogen therapy. Evidence does suggest that a pre-existing breast cancer will grow in response to estrogen, but it does not follow that estrogen causes breast cancer. The fact is, scientists have been studying estrogen for decades, and there still is not conclusive evidence that estrogen replacement directly causes breast cancer.

To quote a past Chairman of the British Menopause Society, *“The arguments regarding breast cancer risk could rage on for years. Whilst epidemiologists argue whether small relative risks are valid, we must not forget the main point of the argument, which is how are we going to optimize the lives of millions of women going through the menopause transition in the ever-aging population of the 21st century? If there is a risk, the risk is small, and the benefits of HRT can be life altering; it is vital that we keep this in perspective when counseling our patients.”*

Does HT increase risk of heart disease?

In 2002, it was big news and bad news when findings from the Women's Health Initiative (WHI) study (see box below) initially reported increases in cardiac risk with HT. To practicing OB/GYN's like myself, this was astonishing to hear, since observational studies for decades had shown HT to be protective of cardiovascular health, and we routinely encouraged use of HT for that very benefit. However, closer analysis of the WHI data revealed a crucial fact: the timing of HT is key, and it is most beneficial to initiate HT as early as possible during the menopause transition, before artery-clogging plaques begin to develop in the heart. Early initiation of HT also appears to be critical for optimal preservation of bone and brain health, and perhaps for protection of other systems as well.

The WHI Study: A Pivotal Point in the History of Hormone Therapy

Why the Controversy?

If HT has so many benefits, what explains the prevailing view that it's dangerous? The reason mainly stems from exaggerated reactions to a study called the Women's Health Initiative (WHI), funded by the National Institutes of Health, which literally scared women out of their hormones. When initial results of this study were reported in 2002, hormone therapy recommendations drastically changed overnight. Suddenly, doctors began advising their patients to stop HT, and people became afraid of hormones due to negative reports all over the headlines. It is tragic that this reaction was so quickly made in response to the early negative reports that were later found to be incomplete interpretations of the data. With closer analysis, flaws in the study's design became apparent, and some important lessons were learned.

Breast Cancer Consternation

Initial reports of findings stated a combined synthetic HT pill, Prempro (estrogen + progestin), increased breast cancer. Risk was reported alarmingly as a percentage rather than absolute numbers, and they reported a 26% increase in risk of breast cancer for those on Prempro compared to no HT. That sounds like a lot of extra cases of cancer, but one must understand statistics to realize what it actually means in reference to this study. The 26% increase in breast cancer represents an increase of only 8 women in 10,000 – less than one per 1000 women per year. Additionally, further analysis of the study revealed that estrogen-only therapy (no progestin) *decreased* breast cancer risk, implicating the synthetic progestin as the agent possibly responsible for the slight increase in breast cancer seen with Prempro. This was *good* news, but these findings were quietly reported two years after the initial reports had been released; by this time the general public had been convinced that hormones are dangerous, and this reassuring report received little attention.

Heart Attack Alarm

Reporting of heart disease risk was bungled in a different way. In 2002 WHI findings revealed an increase in heart attack and stroke for those on HT. However, it was only the older patients in the study, aged 60-79, who had increased cardiac disease, and they likely had pre-existing disease. Younger subjects, aged 50-59, had *less* heart attack and stroke with HT compared to no HT. Again, here was *good* news, because this is the age group typically experiencing the worst symptoms of perimenopause, and would seek HT for relief. However, this closer analysis of the data was not reported until several years after the initial negative findings had been released, and it certainly did not get the heavy media attention the negative early reports had received.

Hormone Horror

The irresponsible reporting (by study authors and the media) of the WHI study findings, particularly with respect to timing of reporting, overemphasis of negative frightening findings, neglect to prominently report positive reassuring findings, and failure to put risk into perspective, is why we have so much misunderstanding regarding risk of HT. The *hormonophobia* generated by the WHI led a whole generation of women to be robbed of the benefits of hormone therapy. It is astonishing how pervasive this fear of hormones has become, and how persistent early misconceptions can be.

Is it safe to start HT several years after menopause?

If you have symptoms from hormonal depletion, you certainly may begin using HT, even years after the menopausal transition. A common sentiment goes something like this: "I thought this menopause thing would pass in a few months and I'd ride it out, but here I am several years later, still having

horrible hot flashes, can't sleep, and have zero romantic interest." Rest assured, restoring hormone balance, even late in life can relieve these symptoms and make you feel like you again.

It is important to note here, data suggests that late starters of HT likely won't receive as many health benefits from HT as those who start within the first five or so years after menopause. Prevention of coronary artery disease, in particular, is not an advantage you will receive with delayed initiation of HT, for many will develop plaques in the coronary arteries during the first 5-10 years of estrogen/testosterone depletion. Hormones may retard or prevent these plaques from forming, but hormones do not clean them up if they have already formed. Some studies suggest initiation of estrogen replacement at that later stage could slightly increase risk of stroke. However we have to remember that studies do not always pay attention to the specific type of estrogen used, and they might include *oral* estrogens and *synthetic* progestins, which are known to increase cardiovascular risk (blood clot, stroke).

If there are studies showing no increase in breast cancer or cardiac risk with HT, why don't we hear more about them?

Stories that report increased rates of cancer are going to attract more readers. Even if we were to believe only the studies reporting increase in breast cancer risk, we still must examine the benefit side of HT. We have an abundance of data to suggest benefits of HT outweigh risks for most women.

As a way of putting risk into perspective, we can consider disease risk in terms of what's more likely to kill you. While breast cancer seems to be the number one fear of most women, it is curable, and far less likely to kill you than heart disease, osteoporotic hip fracture, or colon cancer; and we know the risk of each of these conditions is lowered with the use of HT. Centers for Disease Control and Prevention report mortality data in women, stating that 1 in 3.3 deaths (30%) was attributed to CVD whereas 1 in 31.5 deaths (3%) was attributed to breast cancer.

Moreover, studies show lower all-cause mortality for HT users who initiate early after menopause. Remember, there is risk in everything we do (or don't do): using HT, not using HT, taking drugs to treat diseases that may have been prevented with HT, driving a car, having children... It's a matter of deciding what is important to you based on your personal risk factors and quality of life. Don't let anyone tell you that HT is not an option. It is an option. You get to make the choice.

Are bio-identical hormones safer than synthetic hormones?

Clinical trials have shown that transdermal estradiol, a bio-identical product, is safer than oral estrogen, because the transdermal route avoids first-pass metabolism by the liver, thereby reducing the risk of blood clots and gall bladder disease, when compared to oral estrogen.

As for breast cancer risk, studies do not show an advantage of one type of estrogen over another. Some studies of CEE (Premarin) show no breast cancer increase and some show a small increase. The same is true for (human identical) bio-identical estradiol. Studies suggest that increased risk is observed when any estrogen is *combined with a synthetic progestin*, and that synthetic progestins may be the component of combined long-term HT that is most linked to breast cancer. Meanwhile, there is no study linking bio-identical progesterone with increase in breast cancer. Data does suggest bio-identical progesterone is safer than synthetic progestin because the latter opposes estrogen's benefits on heart health, while bio-identical progesterone does not interfere with estrogen's cardiovascular benefit.

Which hormones do I need to replace in peri- and post-menopause?

There is not a one-size-fits-all approach, and each woman should be evaluated for determination of the appropriate regimen for her individual needs. Women will vary in their requirements for estradiol, progesterone, and testosterone, and they should consult with a provider who is well informed and interested in providing hormone therapy.

What hormone delivery method is best?

Hormone therapy can be prescribed in many different formulations and delivery methods. The route chosen depends upon one's individual preferences, convenience, and cost. However, there are some clinical advantages of certain forms over others.

Transdermal (Patch, Cream, Gel)

Estradiol and testosterone are best delivered by a non-oral route, one of which is the transdermal method. This is preferable over pills to avoid the first-pass liver effect discussed above. Transdermal hormone delivery also results in steadier hormone levels throughout the day compared to pills.

Subcutaneous Hormone Pellet Therapy.

Subcutaneous hormone pellet therapy is another favorable delivery method that avoids the liver first-pass effect. This method involves a minor office procedure with insertion of 2 to 3 tiny pellets consisting of bioidentical estradiol and/or testosterone into the fatty tissue of the upper hip just beneath the skin. The pellets release hormones into the circulation gradually and consistently, and over 3-5 months are completely absorbed. This method delivers superior hormone absorption, compared to other methods, and has been used by women for decades in Europe and Australia. Pellet therapy is becoming more common in the US as a convenient and efficient way to receive HT.

Vaginal Application of Hormones

Vaginal application of estradiol can be extremely beneficial for vaginal dryness and painful intercourse, as it replenishes blood supply, moisture, tissue integrity, and elasticity. It is also beneficial for bladder health, often improving symptoms of urinary urgency or frequency. Vaginal estradiol can be supplied as a cream, a vaginal tablet, or a flexible plastic ring inserted into the vagina. These are ultra low dose vaginal treatments, meant strictly for local treatment of the vagina and bladder; they do not result in significant systemic elevation of estradiol levels.

Another option for vaginal health that provides equal benefit is DHEA supplied as a vaginal cream or suppository. As previously stated, there are no tissue receptors for DHEA, but it is converted to estradiol (or testosterone) within the cells of certain tissues, the vagina being one example, and the benefits are essentially the same as vaginal application of estradiol, providing improvement of vaginal and bladder health without increase in circulating estradiol.

Sublingual or Buccal Delivery

Hormones can be supplied as sublingual or buccal troches, which are lozenges to be dissolved under the tongue or between cheek and gum, the hormone being delivered directly into the bloodstream from the oral tissues. Some of the hormone may be swallowed and absorbed via the gut route, but this is likely negligible if troches are used correctly. This route does carry the disadvantage of short half-life (hormone levels fade before the day is done), so multiple doses per day may be required. This method does not give the steady and consistent hormone delivery of the patch or subcutaneous pellet; hormone levels will vary significantly from the time the troche dissolves and the time the next one is due.

Intramuscular (IM) Hormone Injection

IM injection of hormones is discouraged for a number of reasons. Women are less likely to have consistent symptom relief, and more likely to have side effects with IM hormone delivery. A significant drawback, besides the inconvenience of receiving a shot every 1-2 weeks, is the highly variable level of serum hormones with this method, resulting in a roller coaster pattern of hormone excess and deficiency. For relief of symptoms to last the duration of the injection, it requires a high dose be given, and still, often symptoms return before the next injection. We advocate methods that afford much more consistent hormone levels with consistent control of symptoms.

Progesterone Delivery: Oral, Vaginal, or Intrauterine Device (IUD)

As stated in discussions above, when progesterone is given with estradiol, the dose must be sufficient to ensure uterine protection. Progesterone is usually given as an oral formulation, since dosing and absorption is convenient and reliable. Other favorable methods are progesterone vaginal suppositories or a progestin containing IUD such as Mirena. Progesterone topical creams are sometimes used to treat certain symptoms, however it is important to note, the cream is not absorbed through the skin in sufficient amounts to protect the uterine lining from effects of estradiol.

Patients sometimes ask why we don't worry about the first-pass of oral progesterone through the liver, since we have said that's a drawback of oral estrogen. The fact is that while oral progesterone does undergo first-pass liver metabolism, instead of producing harmful factors in response, the liver produces metabolites that act on the brain to induce a state of calm, or even sleepiness. This is often a welcome "side effect" of using oral progesterone, and is why we recommend taking it at bedtime.

What are the side effects of HT?

- **Estradiol.** The vast majority of women using HT have relief of symptoms with no side effects. Of those who report side effects, the most common are short-term breast tenderness and uterine bleeding. Both of these are usually limited to the first few weeks after initiation of treatment, and they are due to the breast and uterine tissue being "re-exposed" to estrogen after a period of estrogen depletion. It is understandable to see such a response, since these tissues do contain estrogen receptors. If bleeding is persistent, there are several non-surgical solutions for controlling it.
- **Testosterone.** Testosterone therapy is well tolerated; the majority of women report no side effects. A small number will experience facial hair or acne, both of which can be managed by reducing the dose or another solution. Often, the women who experience these side effects prefer to manage the issue rather than reduce their dose, a fact that reveals their satisfaction with therapeutic benefits received with testosterone therapy.
- **Progesterone.** Most women who take progesterone at bedtime enjoy a good night's sleep and don't feel sleepy the next day. However, some are more sensitive than others to the side effect of sleepiness with oral progesterone. In these cases, it may be preferable to use a vaginal progesterone suppository or progestin-containing IUD as the progesterone component of their HT, to avoid the sleepiness side effect.

Will HT bring my periods back?

HT can be used in a continuous or cyclic fashion. To avoid monthly bleeding you will use estrogen and progesterone daily, continuously. Some women have nuisance breakthrough bleeding (irregular spotting or bleeding) with the continuous regimen, perhaps due to differences in uterine anatomy or fluctuations in the body's natural estrogen production. These few will be happier using cyclic HT so

that bleeding is regular and predictable. A common solution to eliminate bleeding is a progestin containing intrauterine device (IUD), such as Mirena.

Does HT cause weight gain?

Many women have weight gain at about the same time they begin HT, so they believe that HT is the reason for weight gain. In reality, statistics show that over time, women using HT after menopause have *less* weight gain than those *not* using HT. A very few women will have fluid retention with HT, but this is not common. Weight gain is part of normal physiology of aging. The menopausal transition is a time of significant change in a woman's hormones and metabolism. This includes not only ovarian hormones, but insulin, cortisol, and many other factors that control how you metabolize energy and accumulate fat. It is well known that the rate of metabolism slows down during perimenopause, so one's weight will increase if the same caloric intake and same level of exercise is maintained. One way to increase your metabolic rate is to add muscle-building to your exercise routine. Muscle tissue burns more calories than other tissues, even at rest. Some women experience improvement in muscle mass and reduction of subcutaneous fat when testosterone supplementation is included as part of their hormone replacement regimen.

Does menopause affect thyroid health?

While thyroid hormone does not sharply decline at menopause, it is natural for thyroid hormone production to decrease gradually with age. Some of the symptoms of peri-menopause can overlap with symptoms of low thyroid hormone. Fatigue, depression, sleep disturbance, low libido, brain fog, decreased mental sharpness, and difficulty losing weight are all common with deficiency in thyroid hormone. It is important to consider thyroid health during any evaluation of hormonal health related to the menopausal transition. Replacement of low, or even borderline-low thyroid hormone can make a dramatic difference in quality of life.

How long should I use hormone therapy?

When it comes to symptom control, the question is how long do you wish to feel your best? Some women will have a natural resolution of hot flashes after a few years, some won't. Even so, there are numerous bodily changes to consider: bone health, cardiovascular health, vaginal health, bladder health, skin health, sexual health, emotional health, and mental acuity, to name a few. Ongoing benefits will be lost when hormones are discontinued.

Each woman must decide, with the help of a well-informed health care provider, what is right for her, based on all of the available data. The truth is, the available data is imperfect and incomplete (and always will be), so we are taking a small amount of risk when we decide to use (or not use) hormone therapy long-term. Estradiol, testosterone, and progesterone benefit your body in countless ways during the pre-menopausal years. It is counter-intuitive to think that replacing modest amounts of these very same hormones after menopause would cause harm. Studies do suggest that benefits outweigh risk for most women.

Is it necessary to check hormone levels?

Monitoring hormone levels can be of use in specific situations, though it is not necessary in all cases. Some women ask about saliva testing of hormones, which has been advocated by certain books (often co-authored by those who have a stake in saliva-testing laboratories). Despite very convincing arguments in these books, there is no scientific validity in the practice of monitoring saliva levels of ovarian hormones. Monitoring hormone levels in the blood is scientifically based, and if hormone monitoring is indicated, serum testing is the most reliable method.

Special Cases for Consideration of HT

Family history of breast cancer. A woman who has witnessed loved ones suffering with breast cancer may be particularly wary of using any form of HT, and even dismiss it as an absolute impossibility. This view is understandable, given the media attention to HT, heavily weighted on the negative. While I certainly understand and respect that viewpoint, I do feel it is important for women to understand a family history of breast cancer is not an automatic contraindication to using HT. Having one first degree relative with breast cancer increases individual risk by a few percentage points, going from 11% baseline risk to perhaps 12-16% lifetime risk, depending on other factors. If more than one family member has had breast cancer it imposes additional risk to the individual. This and other factors are all taken into account when making the decision to use HT or not. If a woman is suffering menopausal symptoms on a daily (and nightly) basis, quality of life is worth saving. Using HT for a period of 2-5 years would be reasonable, to get through the transitional phase, which tends to be the worst of symptoms. Even long-term use would be acceptable for many, accompanied by annual mammography screening.

The exception would be an individual carrying a gene mutation that places her at extreme elevated risk of breast cancer (50 to 70% risk). The mutation is called the BRCA mutation, and is carried by only a small percentage of the population. A woman may wish to pursue genetic testing for this mutation if she has multiple first-degree relatives with breast and/or ovarian cancer.

Personal history of breast cancer. There is still controversy in this area because studies are mixed concerning use of estradiol therapy after breast cancer. Some studies report no increase in recurrence risk, some show a small increase. This issue is no more settled than the entire argument of HT and breast cancer risk. However, there may be promise in considering testosterone-alone supplementation in breast cancer survivors with menopausal symptoms. According to a 2011 study of 300 pre and postmenopausal women with perimenopausal symptoms, testosterone subcutaneous pellet therapy alone (with no estrogen or progesterone) was effective in controlling symptoms. Another study reported in 2014 followed 72 breast cancer survivors treated with subcutaneous testosterone implants, with pellets replaced every 3 months, and found relief of menopausal symptoms with no recurrence in breast cancer in up to 8 years of therapy. These study subjects also received a medication to block conversion of testosterone to estradiol. Thus, for women with concerns about estrogen risk, there is the option of testosterone therapy without estrogen.

History of blood clot. Women with a prior history of blood clot in the lung (pulmonary embolus) or any type of deep vein thrombosis (DVT) have an increased risk for blood clots in general, and even more so with use of *oral* estrogen. However, numerous studies suggest it is safe to use estradiol and/or testosterone via subcutaneous pellet therapy or the transdermal route, plus oral bio-identical (not synthetic) progesterone.

Do other treatments exist for menopause symptoms besides prescription HT?

Some symptomatic women do not wish to use hormone therapy for medical or personal reasons. While no single remedy can relieve all the symptoms of menopause as effectively as HT, various remedies and medical therapies can be effective for individual symptoms. Let's take the most common symptoms one by one.

Hot flashes. Using a small fan at your desk, or a large one in your bedroom at night can help decrease the discomfort of hot flashes. You may notice hot flashes appear with certain triggers, such as heat, or emotional anxiety. Breathing exercises for stress-reduction may be of help when you feel a hot flash coming on. Some over-the-counter remedies have been effective for short-term relief of hot flashes and night sweats. Some examples are dietary soy, very low dose progesterone creams, and

herbal remedies such as Black Cohosh. While short-term studies do not show any harm, they also do not show these remedies to be very effective.

Sleep disturbance. If you have chronic sleep disturbance, proper sleep hygiene is important. Try to maintain the same sleep schedule every day of the week and weekend, do not consume caffeine after noon, and do not let yourself get emotionally worked-up in the late evenings by watching or reading the news, or discussing stressful topics just before bedtime. Start winding down in the evenings to help your body relax and make the transition to sleep. Low dose progesterone cream (available over-the-counter) may be effective short term.

Mood changes. For depression and/or anxiety symptoms, anti-depressant medication can be effective. Serotonin enhancing drugs, such as Prozac or Zoloft, may be particularly helpful.

Decreased libido. Sex therapy or counseling with a psychologist can be helpful for working out emotional or relationship issues that contribute to sexual dysfunction. However, if there is an underlying hormone imbalance, counseling can only help you to a certain point. The genital tissues have a high concentration of hormone receptors for good reason.

Vaginal symptoms. Vaginal dryness and pain during intercourse can sometimes be relieved with a personal lubricant, such as K-Y products, Astroglide, or Replens. However, a lubricant cannot restore tissue thickness, elasticity, and pliability. Sometimes lubrication just isn't enough to keep the vagina comfortable during intercourse.

Are there other alternatives to address health concerns related to aging?

Again, no single treatment (except HT) has been identified that can positively affect all of the conditions caused by hormone deprivation. However, various treatments and positive lifestyle habits are known to be of benefit for individual factors. These positive lifestyle choices are recommended whether one is using HT or not. Let's look at specific health concerns one by one.

Prevention of cardiac disease. In many ways, this is a lifestyle-driven disease, though genetic make-up plays a role also. Weight control, exercise, and not smoking will significantly lower risk. Fish oil supplements, baby aspirin, and Vitamin D supplements can lower cardiac risk through their ability to decrease inflammation in the body. Lipid lowering medications can lower cardiac risk in certain high-risk individuals. Of course, any drug brings its own list of risks and side effects.

Prevention of osteoporosis. We know that getting plenty of calcium in the diet (and with supplements), supplemental vitamin D, and regular weight-bearing exercise will help to maintain strong bones. And we know that during the first few years after menopause women often lose a significant percentage of bone density in the absence of estrogen and/or testosterone replacement. Whether one develops osteoporosis after menopause depends on genetics, lifestyle and diet, and how much bone "reserve" is present pre-menopause. So, lifestyle choices are important way before menopause. Several non-hormonal drugs are available for treatment or prevention of bone loss. Like all medications, these are associated with risks and side effects.

Prevention of Breast Cancer. While age and genetic make-up are the strongest factors influencing breast cancer risk, lifestyle is a contributor that we can control. Studies show that maintaining a healthy weight, regular exercise, limiting alcohol intake, not smoking, and taking supplemental vitamin D can all decrease risk of breast cancer. After age 40, annual screening with mammography is recommended for all women. Early detection greatly improves survival.

Prevention of Alzheimer's Dementia. Studies have shown that keeping mentally active and intellectually challenged during your entire lifetime can help prevent Alzheimer's Dementia. Regular physical exercise and maintaining an anti-inflammatory diet have also been shown to decrease the risk. Genetics are also a factor.

What else should I be doing to stay healthy after menopause?

Correction of hormone deficiencies and making positive lifestyle choices are keys to healthy aging. Maintaining a healthy weight, good nutrition, exercise, healthy strategies for handling stress – these are all of vital importance for preventing disease. It's up to each individual to be proactive about health and wellness. This includes visiting a healthcare provider regularly. At Women's Wellness Center, these visits are designed to educate, enlighten, and motivate women, to help them make healthy choices.

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Rev. 5/30/20