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Are Bio-Identical Hormones Safer than Synthetic?
Part 1 – Progesterone and Progestins

By
Arlene Evans-De Beverly, PA-C

Yes, according to a recently published medical article*, Bio-Identical hormone therapy is safer. This opinion is based on the review of 197 medical studies. The medical journal article concludes that the Bio-Identical hormones have different effects on the human body when compared to synthetic hormones. This particularly applies to the risk for breast cancer, heart disease, heart attack and stroke. Both scientific and medical evidence demonstrate the sometimes dramatic differences between Bio-Identical and synthetic hormones as well as the safety of the Bio-Identical hormones. Certainly, more studies need to be performed to further differentiate the differences.

If you have followed the hormone debate, you have undoubtedly heard that there have been no studies on the Bio-Identical hormones. You have been told that nothing supports the concept that one form of hormone replacement therapy is better for you than another. Yet, the discussion that follows is extracted, in part, from a course of study approved for physicians to earn continuing medical education credit.

It is my purpose to highlight some of the differences in these hormones. This month, the focus is on progesterone and progestins. Next month we will look at the estrogens.

The italicized material is taken directly from the article cited.

Progesterone versus Progestins

Progesterone: There is only one progesterone. It is identical, in structure and in function, to that produced by our ovaries.

Progestins: There are many progestins. They are unique molecules, foreign to the human body. Each progestin differs one from another, molecularly and have different effects on our bodies. They are manufactured by pharmaceutical companies and primarily used in hormone replacement therapy and contraception. The most well known, widely used and studied is medroxyprogesterone acetate (MPA), otherwise known as Provera.

From the study: *"The effect of progesterone compared with MPA included a 30% reduction in sleep problems, a 50% reduction in anxiety, a 60% reduction in depression, a 30% reduction in somatic symptoms, a 25% reduction in menstrual bleeding, a 40% reduction in cognitive difficulties, and a 30% improvement in sexual function. Overall, 65% of women felt that HRT combined with progesterone was better than the HRT combined with MPA."*

Are there negative effects associated with the progestin, MPA (Provera)?

From the study: *"...negative effects included increased vaginal bleeding (P = 0.003) and increased breast tenderness (P = 0.02), with a trend for increased hot flashes with the use of MPA compared with progesterone."*

Are Bioidentical Hormones (Estradiol, Estriol, and Progesterone) Safer or More Efficacious than Commonly Used Synthetic Versions in Hormone Replacement Therapy?

Kent Holtorf, MD

Does Progesterone differ from Progestins with regard to Breast Cancer Risk?

There are many studies that have shown that progesterone and synthetic progestins have very different effects on the breast.

Progesterone: With and without estrogen has been shown to decrease breast cancer risk. There are several recognized ways that this is accomplished. Progesterone consistently blocked estrogen effects in the breast. Importantly, progesterone also converts some of the more potent forms of estrogen to less active forms, again minimizing estrogen effects on the breast tissue.

Progestins: With and without estrogen increase breast cancer risk. The generally recognized mechanisms are varied, but generally consist of the inability of progestins to minimize estrogen activity. In fact, they can stimulate estrogen activity in breast tissue. They can also stimulate conversion of less active estrogens to become estrogens that are known to have potentially cancer causing effects on the breast tissue.

From the study: *"Synthetic progestins have potential antiapoptotic effects and may significantly increase estrogen-stimulated breast cell mitotic activity and proliferation. In contrast, progesterone inhibits estrogen-stimulated breast epithelial cells."*

From the study: *"In 2007, Fournier et al reported an association between various forms of HRT and the incidence of breast cancer in more than 80 000 postmenopausal women who were followed for more than 8 postmenopausal years. Compared with women who had never used any HRT, women who used estrogen only (various preparations) had a nonsignificant increase of 1.29 times the risk for breast cancer (P = 0.73). If a synthetic progestin was used in combination with estrogen, the risk for breast cancer increased significantly to 1.69 times that for control subjects (P = 0.01). However, for women who used progesterone in combination with estrogen, the increased risk for breast cancer was eliminated with a significant reduction in breast cancer risk compared with synthetic progestin use (P = 0.001)."*

It seems as if there are those in the medical community who are willing to look at the studies that do exist and render unbiased judgment. We must remember there are well-intentioned and intelligent medical professionals on both sides of this ongoing debate. We must also remember that HRT is a billon dollar business; we will hear much more from the pharmaceutical companies before they relinquish a penny of their profits without protest.

July 1, 2009, we will post part two of the series taken from the study: The Estrogens.

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The Bioidentical Hormone Debate:

Are Bio-Identical Hormones Safer than Synthetic?
Part 2 – The Estrogens

By
Arlene Evans-De Beverly, PA-C

Yes! According to a recently published medical article in Postgraduate Medicine*, Bio-Identical hormone therapy is safer. This opinion, published in 2009, is based on the review of 197 medical studies. The medical journal article concludes that the Bio-Identical hormones have different effects on the human body when compared to synthetic hormones. This particularly applies to the risk for breast cancer, heart disease, heart attack and stroke. Both scientific and medical evidence demonstrate the sometimes dramatic differences between Bio-Identical and synthetic hormones as well as the safety of the Bio-Identical hormones. Certainly, more studies need to be performed to further clarify the differences.

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It is my purpose to highlight some of the differences in these hormones. This month we will focus on the estrogens. The italicized material is taken directly from the article cited.

Estrogens and Breast Cancer

There are 3 main estrogens in a woman's body: Estradiol, Estrone and Estriol.

Each was studied individually. Each has very different actions on your breast tissue; either stimulating or protecting you from potential breast cancers.

The effect of estrogen on breast tissues takes place through 2 main estrogen receptors: estrogen receptor-alpha and estrogen receptor-beta.

Alpha estrogen receptor-------- promotes breast cell proliferation, potentially stimulating cancer
Beta estrogen receptor --------- blocks proliferation and potentially prevents breast cancer

Estradiol - Conventional and Compounded

Estradiol is available in many different strengths and forms. The strengths can vary from very strong ones that are designed to affect the entire body to very low doses that can be used to "spot treat" tissues such as the vagina, when it is very dry.

Estradiol equally activates the alpha and beta estrogen receptors in the breast. This could stimulate breast cancer.

When estradiol is used in conventional medicine, what you are taking is100% estradiol.

WOMEN PROBLEMS. Estriol has been used in compounding for over 50 years.

------It costs upwards of 100 million dollars for a pharmaceutical company to get FDA approval. No company has been willing to spend the money to do the research on estriol since it was Proven, some decades ago, that estriol was a 'weak' estrogen when it came to protecting bones.

------Many large pharmaceutical companies, including the makers of Premarin, use estriol in the products they manufacture for women in the rest of the world.

Premarin-Conventional only

One more estrogen to discuss, the most frequently prescribed estrogen for many decades was Premarin, the equine (horse urine) estrogen. It contains many different hormone molecules that makes it bio-identical for horses, but not for women. When we consider its effects on your alpha and beta receptors, it is very clear why we don't use it in compounding. It only binds to the breast cancer stimulating alpha cells **and** makes the breast cancer protective beta cells less sensitive to the helpful protection your own body is trying to provide.

From the study: *"Estradiol equally activates ER-α and ER-β, while estrone selectively activates ER-α at a ratio of 5:1. In contrast, estriol selectively binds ER-β at a ratio of 3:1. This unique property of estriol, in contrast to the selective ER-α binding by other estrogens, imparts to estriol a potential for breast cancer prevention, while other estrogens would be expected to promote breast cancer. As well as selectively binding ER-α, CEE components are potent downregulators of ER-β receptors. Whether this activity is unique to CEE is unclear, but it could potentially increase carcinogenic properties."*

From the study: *"Conjugated equine estrogens also contains at least one particularly potent carcinogenic estrogen, 4-hydroxy-equilenin, which promotes cancer by inducing DNA damage"*
From the study: *"Because of its differing effects on ER-α and ER-β, we would expect that estriol would be less likely to induce proliferative changes in breast tissue and to be associated with a reduced risk of breast cancer. Only one in vitro study on an estrogen receptor-positive breast cancer tissue cell line demonstrated a stimulatory effect of estriol as well as for estrone and estradiol. Melamed et al demonstrated that, when administered with estradiol, estriol may have a unique ability to protect breast tissue from excessive estrogen-mediated stimulation. Acting alone, estriol is a weak estrogen, but when given with estradiol, it functions as an antiestrogen. Interestingly, estriol competitively inhibits estradiol binding and also inhibits activated receptor binding to estrogen response elements, which limits transcription."*

Estrogens and Progestins (See Part 1 of this series in Document Library For more information on Progesterone and Progestins)

And yes, there have been studies looking at what happens to breast cancer risk when synthetic progestins are used with estrogen therapy, especially with Premarin. Synthetic progestins increase the risk, albeit by a small percentage. But why not use bio-identical progesterone that has been shown to reduce breast cancer risk, especially when combined with estriol?

From the study: *"Mueck et al compared the proliferative effects of different estrogens on human breast cancer cells when combined with progesterone or synthetic progestins. They found that progesterone inhibited breast cancer cell proliferation at higher estrogen levels, but that synthetic progestins had the potential to stimulate breast cancer cell proliferation when combined with the synthetic estrogens equilin or 17-alpha-dihydroequilin, which are major components of CEE."*

Most of us who prescribe compounded hormones Bio-identical hormones use a very low percentage of estradiol mixed with an estrogen, called estriol to the estrogen receptors in a much different fashion.

Estrone - Conventional and Compounded

Estrone is available in many different strengths and forms. Conventional medicine generally uses it in an oral table form.

Estrone activates the alpha receptor (cancer stimulating) 5 times more than it stimulates the cancer protective beta receptor. In other words, it is 5 times more like to stimulate potential breast cancer than it is to protect you from breast cancer.

When estrone is used in conventional medicine, what you are taking is usually 100% estrone.

Estriol-Compounded only

Estriol attaches itself to the beta receptors, the protective receptors, 3 times more than it attaches to the alpha receptors. This makes estriol a desirable form of estrogen allowing for the potential to protect you from breast cancer.

When we use estriol in compounding Bio-identical hormones, we usually use it at 80% and pair it with 20% estradiol.

Why do we even add estradiol to the compound mix? There are many good reasons including the fact that estradiol can do more to keep your bones strong than can estriol, when used alone. Also, some studies show that when these two estrogens are used together, there may be even more breast cancer protection.

For women who are at high risk for breast cancer we can certainly use an even high percentage of the potentially protective estriol. In fact, some of my patients taking only estriol as the estrogen in their therapy.

More on ESTRIOL

When a woman is pregnant, her body produces as much as 15 times more progesterone and 1000 times more estriol than when she is normally cycling. After a woman has had a baby, she continues to make more estriol than a woman who has never been pregnant. Many studies suggest that it is these higher levels of our natural hormones that grant us lower risk of developing some of the more common forms of breast cancer. Many studies have shown that even in the menopause, lower levels of estriol are associated with an increased incidence of breast cancer.

ESTRIOL IS NOT FDA APPROVED.

Many large pharmaceutical companies, the FDA and many uniformed health care providers emphasize that estriol has not been approved by the FDA. Let's make sure that fact is in our headlines. BUT, let's talk about the significance of estriol's non-FDA approval.

------The FDA clearly acknowledges that they have NO REPORTS OF ESTRIOL CAUSING

Hot Flashes?

Arlene Evans-De Beverly, PA-C

Hot flashes are often the first symptom that women recognize as the approach of perimenopause and menopause. If you are having a few hot flashes and want to do what you can without prescription medicine to treat them, read on.

What you put in your mouth can help heat you up or cool you down!

Heating you up?

Some foods seem to trigger hot flashes. Perhaps as important as which foods women should eat to prevent hot flashes are those foods they should avoid. Many foods are thought to contribute to or worsen discomfort from hot flashes. Alcohol, caffeine, excess sugar, dairy products, meat products and spicy foods rank among the top aggravators of severe hot flashes as well as mood swings. Also, eating or drinking foods that are hot in temperature may trigger yet another hot flash that you might have avoided.

Foods that are obviously hot and spicy trigger the temperature regulation mechanism. If they bother you, skip them. Though we may not think of garlic as being "hot" in flavor, many women are sensitive and may want to eliminate or decrease garlic intake.

Let's cool down!

Phytoestrogens - Diet can have a lot to do with hot flashes. However, common foods in the Japanese diet may be useful in preventing hot flashes. These foods are high in phytoestrogens. Phytoestrogens are naturally-occurring plant chemicals that can act like the female hormone, estrogen. When naturally occurring, they are much weaker than the estrogen produced by your body.

Using soy to treat hot flashes is controversial. Though only a few medical studies support the use of soy, many women tell me that it helps them.

Small amounts of soy based foods are all that many women seem to need. Getting just 2 ounces of tofu or tempeh (a cake made from soybeans) a day can help prevent hot flashes from coming back. Or you could have a bowl of miso soup, which is flavored with a salty condiment made from soybeans and salt. Soy based shakes are another alternative and are easy to find premixed or you may want to mix your own.

Beans, especially soybeans, contain the compounds genistein and daidzein, which are estrogenic and may help control hot flashes. Only 7 percent of menopausal Japanese women suffer from hot flashes, as compared to 55 percent of women living in the United States. In fact, there is no Japanese word for "hot flashes". The Japanese diet is also low in fat and high in soy products such as tofu. For some women, especially those who have elected to avoid estrogen therapy, adding two to three teaspoons of soy protein to their daily diet can ease the discomfort and debilitating feelings of hot flashes. Soy protein (found at the health food store) can be added to breakfast cereal or mixed with beverages. Soy nuts are also readily available. Most women seem to like them. Soy may provide relief for those who aren't ready to start estrogen replacement therapy or replacement therapy with "natural" hormone compounds.

Black beans, can be added to soups or sprinkled into salads. They contain about the same amount of phytoestrogens as soybeans. Ground flaxseed, which can be baked into bread and muffins, is also a good source.

Calcium, magnesium and foods high in vitamin E -- like cold-pressed oils, green leafy vegetables, nuts and almonds also seem to help keep the heat at bay.

But with any supplement, you need a quality product. If you are a great supplement label reader, go shopping for your products, relying on your own knowledge. However, you may want someone whose medical knowledge or supplement label reading skill you can trust. Let them make a brand recommendation.

Vitamin B6, 100 milligrams, may prevent hot flashes and reduce Premenstrual Syndrome (PMS)

Lifestyle changes can also help ease hot flashes. These changes are the changes that seem to help about everything you can think of..... regular exercise and quitting smoking.

If these simple measures are not helpful, you need contact your health care provider for other suggestions, including prescription medications. My patients are often ready to consider hormone replacement therapy. The overwhelming majority of them are very happy with the Bio-identical hormones.

To learn more about perimenopause and menopause management, the CD, Prepare and Defend, is available from this website or from Richardson's Custom Rx; contact information is listed under 'Related Links" on the home page.

Other Benefit and Risk Comparisons

Though we have covered a great deal in this series, there is much more information that is available. It seems as if there are those in the medical community who are willing to look at the studies that do exist and render unbiased judgment. We must remember there are well-intentioned and intelligent medical professionals on both sides of this ongoing debate. We must also remember that HRT is a billon dollar business; we will hear much more from the pharmaceutical companies before they relinquish a penny of their profits without protest.

We have learned much about hormone therapy, both about the characteristics of the individual components and how best to administer them. As I write this, knowing that you are reading, learning, questioning and teaching, I celebrate each of you and your quest to be at your very best.

For Part 1: Progesterone and Progestins (See Document Library)

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Kent Holtorf, MD

Why Use a Troche?

Arlene Evans-De Beverly, PA-C

You have decided to replace your decreasing hormones with natural hormones instead of the synthetic alternatives. That is a good choice! But what is the best way to get the hormones into your body?

If we are going to the effort to replace your hormones with the bio-identical hormones, let's take that a step further and consider how your body was designed to receive the hormones...and the answer is not through your stomach!

A capsule or tablet may be the quick and easy answer, but many of the benefits of natural hormones will be lost as the hormones go through the process of digestion.

Your glands secrete hormones into the local blood supply where they eventually move into the main blood supply that travels throughout your body. This is the way your body is designed to receive hormones; it is the physiologically natural pathway.

When hormones are swallowed, they are exposed to digestive acids and enzymes as they are broken down and are absorbed through the gut wall. Then, like virtually everything absorbed by the digestive process, they are transported directly to the liver in what is called liver first-pass metabolism.

The synthetic hormones generally have a full day's amount of hormone in each tablet or capsule. Swallowing the tablet (or capsule) causes a full twenty four hours worth of hormones to flood the liver. The liver is expecting very small amounts of hormone to be delivered to it over a full 24 hours, not in just a few minutes! Such a large influx of hormone is hard on the liver. Other medications add to the liver's burden and increase the risk of liver toxicity, injury to the liver and gall bladder disease.

No message can be delivered to the liver to tell it that this rapid rise in hormone concentration is short term. The liver seeks to protect you from this hormonal assault. It responds to the fact that your hormone levels are far too high, out of control and potentially damaging to you. The liver begins to make changes to protect you from this danger. The net result is that it affects the way your body has access to the hormones. It certainly affects the estrogen and progesterone you might be taking, but also has undesirable effects on other circulating hormones and chemicals as well. This includes, but is not limited to, thyroid hormone, cortisol, antithrombin III, blood sugar (glucose) interactions with the pancreas and increasing a substance called C-reactive protein. These changes can increase your blood pressure and cholesterol, affect your mood, lower your thyroid and cortisol potential and increases your risk for a stroke, heart attack and development of diabetes.

Today, there are many ways hormones can be delivered to your body; all avoiding the liver first pass that can cause so many problems. These include injections, transdermal (across the skin) and transmucosal (through a mucous membrane) delivery.

Injections have various drawbacks including discomfort, the extra cost of sterile supplies and widely varying hormone levels that do not reflect "natural" levels.

Transdermal delivery of medications has gained rapid popularity during the last 10 or 15 years. Hormones, nitroglycerin and drugs for blood pressure and pain are just some of the different medications in a patch form that are applied to the skin for absorption. However, some women are very sensitive to the adhesives that are used in the patches; other women have trouble getting the patches to adhere to their skin. Add to this that there are no patches that contain natural progesterone; only synthetic progestins.

Creams , suppositories and troches are other forms of transdermal or transmucosal absorption, all of which bypass the digestive system and first-pass metabolism. This is good.

Creams can be very effective, but because of the extreme variation in skin type (thickness, fat content, water content, difficulties in exact measurements), their absorption is erratic and unpredictable from one patient to the next and often require different creams for the different hormones. So not only is the absorption less than ideal, it can be more costly.

Rectal suppositories can be effective and dependable for drug delivery, but lack convenience and may not be in the rectum long enough to be absorbed (you may need to have a bowel movement).

Troches, however, offer the best of all worlds. Troches have regained tremendous popularity for the absorption of medications, especially hormones. They are effective because the lining of the mouth is thin and rich in blood supply.

Troches are small lozenges that dissolve between the cheek and gum or even in the vagina. A well made "Base A" troche provides the best absorption; it dissolves slowly over a period of about 20 to 40 minutes. As it dissolves, the hormones are gradually absorbed into the blood stream, resulting in physiologically natural hormone blood levels. Also, because these are bio-identical to the hormones your body has produced, they are efficiently recognized, utilized, metabolized and excreted by the body. Since your own hormones only last about 10 to 14 hours, your natural hormone replacement should be dosed twice a day to give adequate and sustained blood levels. A word of caution – if you are going to use the troches in the vagina – be certain that they are not flavored with mint! Mint causes a burning sensation in the vagina that you will want to avoid!

Because of the tremendous advantages in consistency, effectiveness and the ability to avoid the digestive process, I strongly recommend troches as the primary dosage form for hormone replacement therapy for both men and women.

And remember, if you are trying to "make it easier" by taking your troches only once a day, in stead of the recommended twice a day, you are depriving your body of what it was designed to receive 24 hours a day!