Charles Cannata, RN, MDX, ©January 2013

ONE PERSON'S OPINION:

The Debate between Traditional (synthetic) Hormone Therapy and "Bioidentical" Hormone Therapy

There exists an on-going debate with regard to Traditional Hormone Replacement Therapy (THRT) and "bio-identical" Hormone Replacement Therapy (BHRT). Some physicians and regulatory agencies believe the risks and side effects of BHRT are the same as those for THRT. I hope the following narrative will serve to shed light on the origin of this debate.

There was a time in the 80's and early 90's that HRT was considered by many (including The Mayo Clinic – *see excerpt below*) to be a viable method of treatment for post menopausal symptoms. Not only was HRT considered effective in addressing hot flashes and night sweats it was also thought to be cardiovascular protective and may have protective properties with regard to dementia. These thoughts comprised much of mainstream medicine until 2002.

"Hormone replacement therapy — medications containing female hormones to replace the ones the body no longer makes after menopause — used to be a standard treatment for women with hot flashes and other menopause symptoms. Hormone therapy (as it's now called) was also thought to have the long-term benefits of preventing heart disease and possibly dementia.

Use of hormone therapy changed abruptly when a large clinical trial found that the treatment actually posed more health risks than benefits for one type of hormone therapy, particularly when given to older postmenopausal women. As the concern about health hazards attributed to hormone therapy grew, doctors became less likely to prescribe it" [1]

The "large clinical trial" that occurred during the mid to latter 90's, which was abruptly halted in 2002 was the Women's Health Initiative (WHI). The WHI was a large scale study funded by the National Institute of Health (NIH) and was commissioned to study the long-term effects of hormones on post-menopausal women and their symptoms.

There has been much controversy in the years following the abrupt cessation of the WHI in 2002 with regard to the benefits of HRT as compared to the risks. Because the WHI was represented as testing hormones on the symptoms of menopause, the negative outcomes that were noted as a result of the study left many in the medical profession believing the risks of HRT outweighed the benefits. This conclusion was based solely on the results of the WHI. However, in the years since 2002 we have learned a great deal.

First and foremost, we've learned that the substances used in the WHI were not human hormones at all but chemically altered drugs that were represented to be hormones by the drug manufacturers. Please, let me say that again. The WHI did not test human hormones. The oral substances used in the WHI were Conjugated Equine Estrogen, CEE or brand name Premarin - a series of estrogens, some derived from the urine of pregnant mares. CEE consisted of >50% estrone, which is a human hormone and considered to be a weak estrogen referred to as "the estrogen of menopause" combined with equilin,

15%-25%, and equilenin – the latter two being derived from the urine of pregnant mares – hence Premarin…a contraction of pregnant/mares/urine…clever, and, medroxyprogesterone acetate, a synthetic progestin or brand name Provera. A combination of the two was brand named Prempro. Obviously, equine estrogen is processed differently in the body than human estrogen. The human body does not contain horse enzymes.

While it was hoped that these synthetic drugs would mimic the effects of human hormones in the relief of menopausal symptoms, instead, these substances were deemed responsible for unwanted outcomes such as heart attack, stroke and increased risk of breast cancers. The study was abruptly halted.

In numerous studies conducted using human "bio-identical" hormones, it is clear that natural hormones (those manufactured or compounded to be chemically identical to human hormones) often have the opposite effect of the synthetic counterparts and benefit the patient in areas of cardiovascular health. In addition, it was found that natural progesterone may be protective against breast cancer whereas synthetic progestins have been associated with an increase in breast cancer risk.

In a landmark 2009 paper by Kent Holtorf, MD he writes,
"Background: The use of bioidentical hormones, including progesterone, estradiol, and estriol, in hormone replacement therapy (HRT) has sparked intense debate. Of special concern is their relative safety compared with traditional synthetic and animal-derived versions, such as conjugated equine estrogens (CEE), medroxyprogesterone acetate (MPA), and other synthetic progestins. Proponents for bioidentical hormones claim that they are safer than comparable synthetic and nonhuman versions of HRT. Yet according to the US Food and Drug Administration and The Endocrine Society, there is little or no evidence to support claims that bioidentical hormones are safer or more effective.
Objective: This paper aimed to evaluate the evidence comparing bioidentical hormones, including progesterone, estradiol, and estriol, with the commonly used nonbioidentical versions of HRT for clinical efficacy, physiologic actions on breast tissue, and risks for breast cancer and cardiovascular disease.
Conclusion: Physiological data and clinical outcomes demonstrate that bioidentical hormones are associated with lower risks, including the risk of breast cancer and cardiovascular disease, and are more efficacious than their synthetic and animal derived counterparts. Until evidence is found to the contrary, bioidentical hormones remain the preferred method of HRT." [2]

This work is but one of many, many others that sought to study the same subject and arrived at similar conclusions.[3] In addition, a clear distinction between 'drugs' and 'hormones' was made,

" 'Drug think' is responsible for much of the current confusion about hormone supplementation. The public and physicians think about pharmacology rather than physiology. From a physiology textbook one would never get the impression that hormones are anything other than chemical messengers necessary for health. Without hormones, we cannot live. Why then do we speak as though hormones are dangerous substances? And why do we assume that the harmful effects of non-hormones [synthetic drugs] will be like those of our endogenous hormones? The answer is suggested by the fact that medical students and doctors in training have minimal exposure to physiology and massive

exposure to pharmacology. Exogenous chemicals, different from the actual hormone they are meant to replace, are used interchangeably in clinical practice, the popular press, and in prestigious medical journals, producing much of the controversy that surrounds hormone replacement."[4]

In spite of the literature and these findings, many medical professionals believed then and still believe now that the WHI remains the benchmark study on the effects of hormones on post-menopausal women. This is why we have the continuing debate from some doctors and regulatory agencies that THRT is the same as BHRT and that BHRT carries the same risks and side effects as THRT.

I've heard people ask "What specific training does one have for hormone treatments with bio identical hormones?" It is curious that I never heard that same question posed to those who used the synthetic versions such as Premarin, Provera and Prempro.

While most medical professionals would agree more large scale studies are indicated, one should not completely dismiss the current literature that supports bio-identical hormones are potentially safer/more effective and carry lower risk than the synthetic drugs used in the WHI.

But why then have there been no large scale, double blind studies of BHRT in the U.S.? In an article by Jeffrey Dach, MD he writes ***"[Because] U.S. patent law which prevents patenting a bioidentical hormone, the drug industry created chemically altered hormones which could be patented and sold at higher profit margins."*** [5]

It takes millions of dollars to conduct the large scale double-blind studies upon which many FDA–approved drugs make it to market. The ability to patent these synthetic drugs provides market exclusivity to the drug manufacturer and billions of dollars in revenue without competition. In 2001 Premarin was the best-selling drug in the U.S. generating $2 Billion annually for Wyeth.[6] Since bioidentical hormones cannot be patented, and are much cheaper to produce than market exclusive synthetics, no one seems to have yet come forward with the ability to fund *the* definitive study. So, is the science of medicine being hindered by a lack of funding or potential for profits?

In Europe, however, one such study is noted by Dr. Dach as well as another published in the New England Journal of Medicine, ***"The following two studies show that bio-identical hormones are safe: One is the French Cohort Study which showed that Bio-identical hormone therapy does not cause increased risk of breast cancer. The second is the June 2007 NEJM Calcium Score study which showed no increase in heart disease risk with estrogen."*** [5]

Perhaps more randomized trials could further support the conclusions noted above, but sources to fund such studies are still elusive.

The differences in the synthetic versus the bio identical substances are in the chemical structure.

So What Possible Difference Can One Molecule Make?

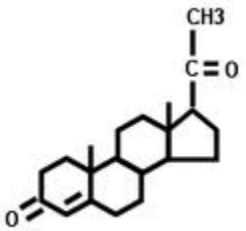
Bio identical hormones are referred to as such because they are chemically identical to the human hormones made in the body, by the body; a complete molecular match. Bio identical hormones cannot be patented for market exclusivity.

Synthetic hormones, in order to be patentable to provide market exclusivity for the manufacturer, must be chemically altered so as to be different from the natural hormone they intend to represent. To chemically alter the structure of the hormone, an extra oxygen or hydrogen (for example) is placed here or there within the chemical structure.
So, what possible difference can one molecule make?

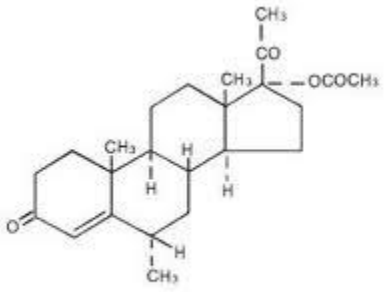
Let me offer this analogy:
Imagine you have two 8 ounce glasses of clear liquid in front of you.
One is H_2O – Water. The other is H_2O_2 – Hydrogen Peroxide. The difference? One oxygen.
If you drink the 8 ounce glass of H_2O (water), you'll be well hydrated. If you drink the 8 ounce glass of H_2O_2 (hydrogen peroxide), you could begin vomiting violently and may require hospitalization.

That's the difference that one molecule can make.

Below are the chemical structures for the natural progesterone molecule and the synthetic progestin, medroxyprogesterone acetate (MPA) marketed as Provera.



Progesterone molecule



medroxyprogesterone acetate

The controversy regarding synthetics versus bioidentical hormones continues. A thoughtful person, seeking relief from symptoms of hormone loss, must educate themselves and make an informed decision based on the current literature. Often this will mean presenting such supporting documents to your PCP, who may be one that still relies on the WHI as the benchmark for hormone replacement therapy.

While some of the studies noted above report that bioidentical hormones are "safe", one should consider that in medicine and human physiology nothing is ever completely certain and risks and side effects are possible. While it *can* be said that "bioidentical" hormones have *fewer* risks than synthetic drugs, self-education as to potential side effects and risks is paramount. Bella Vita Medical can help you sort through the literature so you can make an informed decision as to benefits versus risks.

It is this writer's hope that you may now understand the origin of the debate a little better when physicians or regulatory agencies "warn" of risks and side effects of BHRT as being consistent with THRT. Take time to read the literature and arrive at your own conclusion.

While some may say this controversy revolves more around Big Pharma's interests in promoting patented synthetics over non patentable bio identical alternatives; I will remain mum on that subject….for now.

Let me leave you with a few last questions. If synthetic progestins are "just like" natural progesterone, why is it that fertility specialists use natural progesterone to support pregnancy, while synthetic progestins are used in "the morning-after pill" to abort pregnancy? And...(this is for the medical folk) why is it that while synthetic Premarin can raise serum estrogen levels, it seem to have little if any effect on FSH, whereas natural estradiol will not only raise serum levels, the FSH will drop accordingly. It appears the pituitary does not recognize synthetic. And finally, we know, through the WHI, that within 5 years of launch the study was abruptly halted because of the unwanted (and unanticipated) outcomes from the use of Premarin, Provera and Prempro. But consider that Bioidentical hormone pellets have been in use since 1939 in both the U.S. and Europe. Would you think that if there were significant unwanted outcomes from the specific use of bioidentical hormones we would have heard or read something about it by now?

You can choose to put both THRT and BHRT into the same category due to a perceived lack of specific studies focused exclusively on the bioidenticals, but I would submit there is enough anecdotal evidence (even if not "evidence based medicine") to suggest strongly that there is indeed a difference. But that's just one person's opinion.

Educate yourself, read the literature. Nothing is totally without risk, not even the water from our taps. Weigh the potential risks against the possible benefits and decide for yourself.

All literature referenced above is available in entirety on our web site or through the links provided, for your review. www.bellavitamedicalcenter.com

REFERENCES:

1. SOURCE: http://www.mayoclinic.com/health/hormone-therapy/WO00046
2. Kent Holtorf, MD published in Postgraduate Medicine, Volume 121, Issue 1, January 2009, entitled The Bioidentical Hormone Debate
3. Hormones in Wellness and Disease Prevention: Common Practices, Current State of the Evidence, and Questions for the Future by Erika Schwartz, MD and Kent Holtorf, MD published in Prim Care Clin Office Pract 35 (2008) 669–705
4. Point/Counterpoint: The Case for Bioidentical Hormones by Steven F. Hotze, M.D. and Donald P. Ellsworth, M.D., published in Journal of American Physicians and Surgeons Volume 13 Number 2 Summer 2008

5. Jeffrey Dach, MD on January 11, 2008, and published on his blog: (http://jeffreydach.com/2008/01/11/fda-declares-war-on-bioidentical-hormones-by-jeffrey-dach-md.aspx
6. Source: Wall Street Journal, March 16, 2009 The Truth About Hormone Therapy by Erika Schwartz, MD, Kent Holtorf, MD and David Brownstein, MD