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Hormone Therapy: It's Time for a Second Opinion

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Loyd V. Allen, Jr., PhD, RPh
IJPC Editor-in-Chief

It is an honor to have the paper published by such a highly respected professional journal as the *International Journal of Pharmaceutical Compounding* (IJPC). I can think of no better means through which concerns about societal rights to obtain bioidentical hormone replacement therapy can be voiced and shared. I am grateful to Dr. Allen and IJPC for allowing me this limited license to redistribute the Feature Article titled "Hormone Therapy: It's Time for a Second Opinion".
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In natural hormone replacement therapy, a type of practitioner called a compounding pharmacist has made some of the most significant advances over the past decade. Compounding pharmacists are specially trained pharmacists who prepare customized medications, such as natural hormones, that are designed to the unique needs of each woman.

Joseph J Collins, RN, ND – © 2000 - "Discover Your Menopause Type"

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HORMONE THERAPY

IT'S TIME FOR A SECOND OPINION

ABSTRACT: The opinion paper titled "Compounded Bioidentical Hormones," published by the American College of Obstetricians and Gynecologists in November 2005, appears to be aimed at influencing how some clinicians care for their patients. The paper may not accurately report the findings of authors listed in its own references in regard to safety and efficacy of bioidentical hormones, nor does it address the fact that a number of mass-produced preparations on the market include bioidentical estradiol, progesterone, and/or testosterone. The authors of the paper take the point of view that hormone therapy does not belong to a class of drugs with an indication for individualized dosing, but this position is not congruent with the fact that manufacturers of mass-produced hormones have U.S. Food and Drug Administration approval when they discuss flexible dosing of bioidentical hormones. The opinion paper openly opposes compounded bioidentical hormones, yet fails to mention the legal precedence and regulatory oversights that support the use of compounded prescriptions to dispense hormone replacement therapies, a practice that has since been upheld by a federal court. Also, the opinion paper fails to recognize correlations between plasma and salivary hormone levels reported by researchers listed in its own references. While it is always wise for clinicians to review the opinions of medical organizations, it is sometimes appropriate to ask for a second opinion.

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The American College of Obstetricians and Gynecologists (ACOG) committee opinion paper titled "Compounded Bioidentical Hormones," which was published in the November 2005 issue of *Obstetrics and Gynecology*, continues to raise questions. While this paper does not present itself as peer-reviewed research, or a scientific review paper, or a meta-analysis, the fact that it was issued by ACOG apparently has resulted in the misperception that the case made in the paper is scientifically valid. Despite ACOG's disclaimer that the information in its opinion paper should not be construed as dictating an exclusive course of treatment or procedure that should be followed,[1] it appears that some clinicians are allowing this opinion paper to influence patient care. While it is always wise for clinicians to review the opinions of medical organizations, it is sometimes appropriate to ask for a second opinion.

ACOG's disclaimer in the paper states that "This document reflects emerging clinical and scientific advances as of the date issued and is subject to change."[1] With that point in mind, clinicians reading the opinion paper should ask themselves if the paper accurately reflects the clinical and scientific advances that have transformed how hormone replacement is currently practiced.

In 2007, approximately 50 million women in America were affected by menopause, and with the growing trend to move away from synthetic hormones to bioidentical hormones, we would hope that when ACOG opined on compounded bioidentical hormones, that opinion would demonstrate an unbiased and exhaustive review of the medical and scientific literature. Furthermore, we would hope that the criteria for forming an opinion about compounded human hormone replacement therapy (HRT) also would be applied to mass-produced HRT, and, likewise, that the criteria for forming an opinion about salivary hormone testing also would be applied to serum testing.

EFFICACY AND SAFETY OF BIOIDENTICAL HORMONES

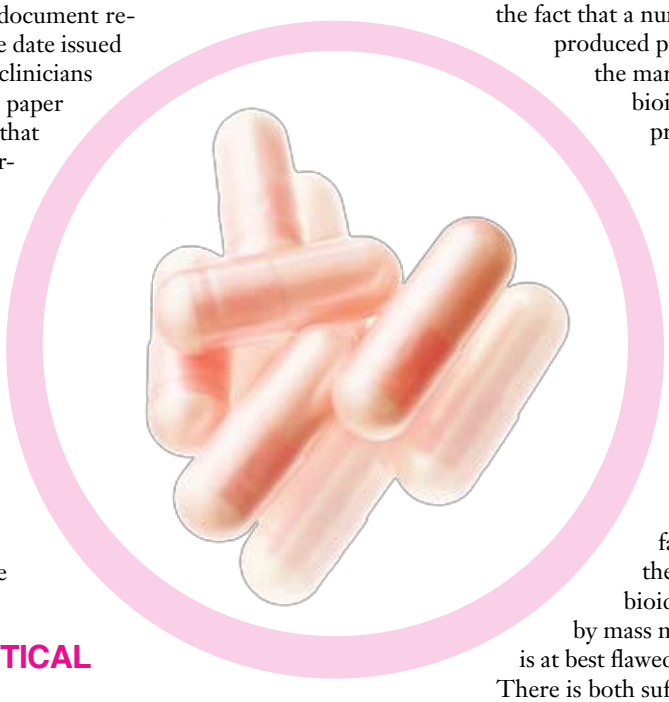
Bioidentical hormones are exactly what the name implies; they are hormones that are biochemically identical to the same molecule occurring naturally in the human body. By definition, estradiol from any source is biochemically identical (bioidentical) to the estradiol that occurs naturally in the human body.

ACOG's opinion committee apparently reviewed a 2004 paper from the journal *Menopause* which reviewed some of the bioidentical hormone literature.[2] The opinion committee failed, however, to recognize or point out the science that supports the use of bioidentical hormones. The *Menopause* review presents findings first published by Ryan and Rosner which demonstrated that micronized progesterone and medroxyprogesterone acetate (MPA) both elicit improvement in climacteric symptoms and quality of life.[3] Only micronized progesterone, however, produced specific improvements in menstrual problems and cognitive function.[3] The review paper also noted that micronized progesterone and MPA elicit similar improvements in endothelium-dependent vasodilator responsiveness and effects on markers of inflammation, hemostasis, and fibrinolysis inhibition in healthy postmenopausal women.[4] Furthermore, the review paper stated the following:

> The Postmenopausal Estrogen/Progestin Interventions trial did not detect differences in efficacy or adverse effect profiles but it had a better effect on the lipid profile, including endometrial histology, when micronized progesterone was used in place of MPA.[2]

Neither the *Menopause* review nor the ACOG opinion paper mentions that, according to The National Center for Biotechnology Information, over 500 published research papers that address the use of bioidentical hormones have been published,[5] nor do they suggest that the amount of research on bioidentical hormones warrants an extensive meta-analysis.

It should be noted that the opinion paper does not address the fact that a number of mass-produced preparations on the market contain bioidentical estradiol, progesterone, and/or testosterone, products that have U.S. Food and Drug Administration (FDA) approval and are recognized as safe and effective. An opinion against bioidentical hormones that fails to address the growing use of bioidentical hormones by mass marketers of HRT is at best flawed and inappropriate. There is both sufficient scientific evidence and FDA approval of bioidentical hormones to support their current use in clinical practice.



INDIVIDUALIZED DOSING

While the ACOG opinion paper states that "hormone therapy does not belong to a class of drugs with an indication for individualized dosing,"[1] the review reveals "commercial products" that include various dosages of micronized estradiol as a hormone that is monitored and adjusted on the basis of well-defined endpoints. The measurements can be used to guide the clinician to adjust the administered dose such that the benefit-to-risk ratio is greatly increased.[2] With growing concerns about the benefit-to-risk ratio of HRT, hormones are definitely a class of drugs with an indication for individualized dosing. As a side note, prednisone, a widely prescribed steroid, is routinely dosed on a mg/kg/day basis. Moreover, liothyronine (T4) dosing is recommended at 1.7 mcg/kg/day.[6]

The benefits of "individualized dosing" have not been ignored or discounted by the FDA or by manufacturers of mass-produced

hormones. Medscape reports that on June 21, 2007, the FDA announced its approval of a 0.1% estradiol gel (Divigel), which is available in individual-use packets with corresponding strengths of 0.25, 0.5, and 1.0 mg of estradiol "for dosing flexibility."[7] On August 9, 2007, the FDA announced its approval of a "metered-dose" estradiol transdermal spray (EvaMist), which contains 1.53 mg of estradiol per spray, and noted that, "based on clinical response, the dose may be increased to 2 to 3 sprays per day."[8]

The recently released Divigel and EvaMist are just some of the latest examples of how manufacturers of mass-produced hormones (and the FDA) recognize that flexible dosing of bioidentical hormones is appropriate, safe, and efficacious for hormone replacement.

The opinion paper does not address the fact that a number of mass-produced preparations on the market promote individualized dosing of HRT and tout dosing flexibility or dosage modification based on the individual needs of the patient. It may be concluded that an opinion against individualized dosing of HRT that fails to address the growing use of individualized dosing of HRT by mass marketers of HRT is at best a flawed and inappropriate opinion. There is both sufficient scientific evidence and FDA approval to support the current clinical practice of flexible dosing of bioidentical hormones.

COMPOUNDING PHARMACISTS

The FDA report cited by ACOG titled, "Report: Limited FDA Survey of Compounding Drug Products," is a survey that by the FDA's own admission lacks scientific credibility.[9] The survey makes no valid statement regarding compounded prescriptions or compounded bioidentical hormones. It was very limited in its scope: only eight compounded hormone samples were tested from only five different pharmacies. The data on all three progesterone capsules and one of the progesterone injectables were compromised when no storage information was found and no storage information was requested by the FDA, even though the testing of specimens may have been delayed by as much as 95 days.[9]

The actual conclusion of the "Limited FDA Survey" states the following:

> The survey had several limitations including a small sample size, the inability to collect and complete original and repeat analyses on all product samples originally identified for the survey, and the fact that the compounding pharmacies selected for the survey were limited to those permitting Internet purchase of the drug products chosen for sampling.[9]

It is fair to say that if any research or review paper with such limitations was submitted to a peer-reviewed journal, it would be immediately rejected for publication.

Even the FDA denies the scientific validity of the survey. The following quotes are excerpted from a dialogue between FDA's Dr. Steven Galson, Director of the Center for Drug Evaluation and Research, and Senator John Ensign (Republican-Nevada) on October 23, 2003.[10]

> **Dr. Galson:** I want to emphasize that this was not a comprehensive scientific survey. It was a small sample size.
>
> **Senator Ensign:** I normally don't take witnesses to task, Dr. Galson, but I do want to take you to task on something. You're a scientist, and to present nonscientific data studies--and I'm glad you mentioned that it wasn't--is problematic. You have to remember, you're not talking to scientists up here. You can influence public policy. We look at you as an expert, and you presented that in a fashion that is misleading. Senators look at that as a scientific study. That's irresponsible and you really shouldn't do that, especially as a representative of a governmental body.
>
> **Dr. Galson:** I wasn't trying to present these as scientific data.

The fact that ACOG would publish an opinion paper citing a survey that is not scientifically valid is unsettling. Moreover, clinicians reading the FDA survey or the ACOG opinion should keep in mind that neither document is scientifically valid. The reader also should keep in mind that pharmacists and physicians are licensed and regulated with the same scrutiny by state and federal laws. The National Association of the Boards of Pharmacy and the United States Pharmacopeial Convention, Inc. (the national standard setting organization for pharmacy and pharmaceutical manufacturers), have established standards for compounding that are enforced by many states. The materials that make up the compounded prescriptions are all sourced from licensed FDA-registered manufacturers. In many cases, they are the same sources used by large pharmaceutical manufacturers. The FDA, the Supreme Court, Congress, and virtually every major health professional organization recognize the value of compounding.[11]

Despite the attempts of large pharmaceutical manufacturers to deny patients the right to have access to compounded prescriptions, the legal precedence that allows pharmacists to compound pharmaceutical agents and dispense compounded prescriptions was upheld by a Federal District Court Judge in Midland, Texas, on May 25, 2006.[12] The court's ruling confirmed that compounded preparations are not illegal, not unapproved, nor are they new drugs subject to FDA's new drug approval process for new manufactured products. In other words, there is sufficient legal precedence, regulatory oversight, and federal ruling to support the practice of using compounded prescriptions to dispense HRT.

SALIVARY/HORMONE TESTING

The aforementioned *Menopause* review paper by Boothby et al, titled "Bioidentical hormone therapy: A review," presents some conclusions about salivary hormone testing that appear contrary to those of the works reviewed.[2] Those conclusions appear to be parroted by the ACOG opinion paper. Despite the opinions expressed in both the ACOG opinion and the *Menopause* review, there is substantial evidence that hormonal levels in saliva are biologically meaningful.

The statement "Whereas saliva is an ultrafiltrate of the blood and in theory should be amenable to testing for 'free' (unbound) concentrations of hormones, this has not proved to be the case" is credited to a 1979 paper by Marder et al.[13] In that one-page paper, the authors reveal that salivary and plasma fluctuations of estradiol correlated well, even though the saliva levels represented less than 10% of plasma levels. The researchers observed that the plasma-saliva ratio is different for each steroid hormone. The variation in plasma-saliva ratio for each hormone has been noted by other researchers, including Klee et al, who stated "When measurement techniques are compared, the numbers correlate with each other but certainly do not represent the same value."[14] The opinion paper fails to recognize the correlation reported by these researchers or their observation that plasma-saliva ratio is different for each hormone.

The ACOG opinion fails to recognize the correlation reported by other researchers that are actually referenced in the ACOG opinion, such as:

- "Salivary and serum E2 correlated significantly with each other and with the number of mature follicles."[15]
- "Salivary cortisol closely paralleled plasma free cortisol both within and between the groups."[16]
- "Serum and salivary progesterone peaked simultaneously and there was a significant correlation between the concentrations measured concurrently...thus supporting the current concept of a relatively rapid diffusion of steroids from plasma to saliva."[17]

The ACOG opinion points out that salivary hormone levels vary by time of day and cites a paper by Raff et al demonstrating this fact.[18] The opinion paper fails to point out either these researchers' recognition of the circadian rhythm of salivary cortisol or their conclusion that alterations in the circadian rhythm of salivary cortisol are associated with increased risk factors. There appears to be no effort to point out that by July 1, 2005, over 250 published peer-reviewed research articles supported the clinical value of circadian rhythm salivary cortisol analysis, or that over 80 additional peer-reviewed research articles were published between July 1, 2005, and July 1, 2007, according to The National Center for Biotechnology Information (PubMed).[5] In total, over 2,000 published research papers address the use of salivary hormone tests.[5]

Although the ACOG opinion appears to correctly interpret research by Lewis et al[19] and Wren et al,[20] whose findings point out that salivary progesterone levels are variable following application of progesterone in a cream, they fail to note the February 2005 *Menopause* paper by Stanczyk which revealed that when progesterone was applied in a cream, the time to peak serum level varied in all subjects.[21] Interestingly, when progesterone is also taken orally, the time to peak serum level varies by as much as a factor of 40 from woman to woman.[22,23] Variability in time to peak serum level has been observed in commercially produced oral progesterone (Prometrium) as well.[24]

If the topic of variable absorption were to be discussed in a credible fashion, then it should include the following observations:

- Commercially available testosterone gels exhibit peaks at variable times.[25]
- With orally administered MPA, there is a significant trend toward higher MPA concentration and bioavailability with increasing age.[26]
- Ethinylestradiol has a high interindividual variability in systemic availability.[27]
- As noted previously, when micronized progesterone was administered orally, serum and salivary progesterone peaked simultaneously, and there was a significant correlation between the serum and salivary progesterone concentrations measured concurrently.[17]

The observation that steroid hormones have variable rates of absorption, and the observation that this pharmacokinetic property can be observed and monitored by salivary hormone tests, together provide a strong argument in favor of routine salivary testing of hormones, so that the clinical practice of flexible dosing of both mass-produced and compounded bioidentical hormones can be carried out with safety and efficacy.

Concerning the observation that salivary hormone levels are affected by diet, the ACOG opinion paper failed to point out that foods can change serum hormone levels as well.[28] A 2003 paper pointed out that grapefruit juice may increase bioavailability of both orally administered estradiol valerate and micronized progesterone, as noted on serum tests.[29] The effects of foods on hormone levels have nothing to do with the ability of either serum or salivary hormone tests to accurately monitor those changes.

Hormone levels in saliva are biologically meaningful and can be used to assess endogenous hormone levels and to assess the safety and efficacy of hormone therapies.

CONCLUSION

Bioidentical hormones, individualized dosing, compounded prescriptions, and salivary hormone testing have all played a significant role in transforming the practice of HRT. Bioidentical hormones and individualized dosing are modalities utilized by large pharmaceutical manufacturers and recognized as valid by the FDA. Compounded prescriptions are legally dispensed by compounding pharmacists who are regulated by state and federal laws. Salivary hormone testing provides a means to monitor flexible dosing of bioidentical hormones.

With these points in mind, clinicians reading the opinion paper should ask themselves if the paper accurately reflects the clinical and scientific advances which have transformed how HRT is currently practiced. More importantly, clinicians who have read the opinion should familiarize themselves with original published research, with the scientists and pharmacists responsible for presenting these modalities to clinical practice, and with the clinicians who use these modalities to provide efficacious individualized care. Then, the reader will have no doubt that it is time for a second opinion.

REFERENCES

1. ACOG Committee on Gynecologic Practice. ACOG Committee Opinion #322: Compounded bioidentical hormones. *Obstet Gynecol* 2005; 106(5 Pt 1): 1139–1140.
2. Boothby LA, Doering PL, Kipersztok S. Bioidentical hormone therapy: A review. *Menopause* 2004; 11(3): 356–367.
3. Ryan N, Rosner A. Quality of life and costs associated with micronized progesterone and medroxyprogesterone acetate in hormone replacement therapy for nonhysterectomized, postmenopausal women. *Clin Ther* 2001; 23(7): 1099–1115.

4. Koh KK, Jin DK, Yang SH et al. Vascular effects of synthetic or natural progestagen combined with conjugated equine estrogen in healthy postmenopausal women. *Circulation* 2001; 103(15): 1961–1966.
5. The National Center for Biotechnology Information (PubMed). All databases. [National Center for Biotechnology Information Website.] Available at:www.ncbi.nlm.nih.gov. Accessed August 20, 2007.
6. Merck & Co., Inc. Levothyroxine. *Merck Manual Professional.* [Merck Website.] Available at: www.merck.com/mmpe/lexicomp/levothyroxine.html. Accessed August 15, 2007.
7. [No author listed.] Medscape. FDA Approvals: Divigel, Norditropin, Zyflo CR. *Medscape Medical News.* [Medscape Website.] Available at: www.medscape.com/viewarticle/558654. Accessed August 15th, 2007.
8. [No author listed.] Medscape. FDA Approvals: EvaMist and Privigen. *Medscape Medical News.* [Medscape Website.] Available at: www.medscape.com/viewarticle/561167. Accessed August 15th, 2007.
9. [No author listed.] Center for Drug Evaluation and Research. *Report: Limited FDA Survey of Compounded Drug Products.* [U.S. Department of Health and Human Services. U.S. Food and Drug Administration Website.] Available at: www.fda.gov/cder/pharmcomp/survey.htm. Accessed August 15, 2007.
10. U.S. Senate Health, Education, Labor and Pensions Committee Hearing on Pharmacy Compounding. October 23, 2003. Available at: http://frwebgate.access.gpo.gov/cgibin/getdoc.cgi?dbname=108_senate_hearings&docid=90-129. Accessed August 20, 2007.
11. [No author listed.] International Academy of Compounding Pharmacists. *Frequently Asked Questions.* [International Academy of Compounding Pharmacists Website.] Available at: www.iacprx.org/site/PageServer?pagename=FAQs. Accessed August 20, 2007.
12. [No author listed.] National Community Pharmacists Association. 2006 Press Releases. *Federal Court Upholds Pharmacists' Ability to Compound Drugs.* [National Community Pharmacists Association Website.] Available at: www.ncpanet.org/media/releases/2006/federal_court_upholds_pharmacists_ability_to_06-02-2006.php. Accessed August 20, 2007.
13. Marder MZ, Joshi U, Mandel ID. Estrogen concentration in human parotid and submaxillary saliva. *J Dent Res* 1979; 58(12): 2370.
14. Klee GG, Heser DW. Techniques to measure testosterone in the elderly. *Mayo Clin Proc* 2000; 75 Suppl: S19–S25.
15. Hardiman P, Thomas M, Osgood V et al. Are estrogen assays essential for monitoring gonadotropin stimulant therapy? *Gynecol Endocrinol* 1990; 4(4): 261–269.
16. Meulenberg PM, Ross HA, Swinkels LM et al. The effect of oral contraceptives on plasma free and salivary cortisol and cortisone. *Clin Chim Acta* 1987; 165(2–3): 379–385.
17. Bolaji II, Tallon DF, O'Dwyer E et al. Assessment of bioavailability of oral micronized progesterone using a salivary progesterone enzyme immunoassay. *Gynecol Endocrinol* 1993; 7(2): 101–110.
18. Raff H, Raff JL, Duthie EH et al. Elevated salivary cortisol in the evening in healthy elderly men and women: Correlation with bone mineral density. *J Gerontol A Biol Sci Med Sci* 1999; 54(9): M479–M483.
19. Lewis JG, McGill H, Patton VM et al. Caution on the use of saliva measurements to monitor absorption of progesterone from transdermal creams in postmenopausal women. *Maturitas* 2002; 41(1): 1–6.
20. Wren BG, McFarland K, Edwards L et al. Effect of sequential transdermal progesterone cream on endometrium, bleeding pattern, and plasma progesterone and salivary progesterone levels in postmenopausal women. *Climacteric* 2000; 3(3): 153–154.
21. Stanczyk FZ, Paulson RJ, Roy S. Percutaneous administration of progesterone: Blood levels and endometrial protection. *Menopause* 2005; 12(2): 232–237.
22. McAuley JW, Kroboth FJ, Kroboth PD. Oral administration of micronized progesterone: A review and more experience. *Pharmacotherapy* 1996; 16(3): 453–457.
23. Freeman EW, Weinstock L, Rickels K et al. A placebo-controlled study of effects of oral progesterone on performance and mood. *Br J Clin Pharmacol* 1992; 33(3): 293–298.
24. Levine H, Watson N. Comparison of the pharmacokinetics of Crinone 8% administered vaginally versus Prometrium administered orally in postmenopausal women. *Fertil Steril* 2000; 73(3): 516–521.
25. Mazer N, Bell D, Wu J et al. Comparison of the steady-state pharmacokinetics, metabolism, and variability of a transdermal testosterone patch versus a transdermal testosterone gel in hypogonadal men. *J Sex Med* 2005; 2(2): 213–226.
26. Järvinen A, Kainulainen P, Nissilä M et al. Pharmacokinetics of estradiol valerate and medroxyprogesterone acetate in different age groups of postmenopausal women. *Maturitas* 2004; 47(3): 209–217.
27. Baumann A, Fuhrmeister A, Brudny-Klöppel M et al. Comparative pharmacokinetics of two new steroidal estrogens and ethinylestradiol in postmenopausal women. *Contraception* 1996; 54(4): 235–242.
28. Dillingham BL, McVeigh BL, Lampe JW et al. Soy protein isolates of varying isoflavone content exert minor effects on serum reproductive hormones in healthy young men. *J Nutr* 2005; 135(3): 584–591.
29. Fingerová H, Oborná I, Petrová P et al. Does grapefruit juice increase the bioavailability of orally administered sex steroids? *Ceska Gynekol* 2003; 68(2): 117-121.

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