GENDER BIAS IN THE TREATMENT OF MENOPAUSAL WOMEN:

I am Hot as Hell and Not Going to Take It Anymore, Part 1

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Abstract

Gender bias within hormone replacement therapy has been prevalent for decades, and the circumstances surrounding this bias continue to worsen. A billion-dollar industry has been built on dozens of testosterone replacement therapies and medications to treat andropause and erectile dysfunction for men; women have been less fortunate. This article discusses this bias and the well-orchestrated attempt by the pharmaceutical industry to eliminate bioidentical hormones, as well as to downplay the important role of compounding pharmacies in fulfilling the needs of women in this longstanding gender gap.

"Something is rotten in the state of Denmark." (Shakespeare W.; *Hamlet*.) A blatant case of gender bias is keeping women from receiving the same treatment options for mid- and later-life loss of sex drive as their male counterparts; as well as other important menopausal-related symptoms and subsequent chronic diseases that develop from loss of important reproductive hormones. This gender bias has been prevalent for decades, and the circumstances continue to worsen with existing guidelines, "expert" consensus statements and a "newly released report" from the National Academies of Sciences, Engineering, and Medicine (NASEM).

There appears to be a well-orchestrated attempt by the pharmaceutical industry to eliminate bioidentical hormones as well as the compounding pharmacies that fill the longstanding hormone gender gap – which will cause women to needlessly suffer.

A billion-dollar industry has been built on dozens of testosterone replacement therapies and medications to treat andropause and erectile dysfunction for men; women have not been as fortunate. There is a paucity of options for women, even though they experience the loss of sex drive at the same rate as men and have more prevalent symptoms due to loss of reproductive hormones estradiol *and* testosterone.

This would make one think there are no good solutions for women. This belief could not be further from the truth. There are numerous evidence-based medical solutions to treat women. The U.S. Food and Drug Administration (FDA), the medical community, and supporting medical organizations, however, have turned a dismissive, patronizing blind eye to women.

Nothing exemplifies this point so perfectly as the need for testosterone therapies in women. There is a common misperception that women's bodies do not produce much testosterone or none at all. This is just not true. Testosterone is the most abundant and biologically active hormone throughout a woman's lifespan. Testosterone levels drop in the years prior to and during menopause. This decrease causes similar symptoms of deficiency in women as it does in men, and it occurs earlier in a woman's life compared to men. This can lead to:

- New onset mood disorder or worsening of existing ones
- Apathy
- Impaired glucose metabolism which leads to weight gain, insulin resistance/diabetes
- Fatigue
- Muscle wasting
- Bone loss
- Cognitive impairment
- Migraine headaches
- Low libido and other sexual function disorders

Despite these potentially life-changing symptoms, there are *zero* FDA-approved testosterone products for women. One consequence of this is that women who have symptoms resulting from low testosterone are largely prescribed antidepressants and other drugs that don't address the root cause of their trouble...*men get the products they need and women get psychotropic drugs*.

Thankfully, women have been able to turn to hormonal specialists who can prescribe compounded testosterone. These therapies can take the form of:

- transdermal creams and gels,
- fast-burst sublingual tablets,
- injections,
- troches, and
- pellets that are implanted under the skin.

Given all the benefits and importance of bioidentical testosterone therapies in women, why have their treatments been stalled, delayed, or not even considered? There are a multitude of reasons, but the most prevalent reasons may be:

1. Pharmaceutical companies protecting their bottom line and utilizing medical organizations and "clinical guidelines" as their Trojan horse;
2. Pharmaceutical companies are not going to take bioidentical hormones to market if they cannot patent protect their investment;
3. Exclusion of women in medical research; and
4. Use of fear tactics and retribution to prevent providers from prescribing non-FDA approved hormone therapies for women.

In this two-part series, these reasons will be explored in detail allowing the reader to better understand the basis of these reasons, as well as the long-term consequences as it relates to women's health and the gender gap as a whole in medicine.

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Part one of the series specifically addresses reasons one and two: **Protecting the Bottom Line** and **Lack of Patent Protection.**

Part two of this series, will conclude with reasons three and four: **Exclusion of Women in Medical Research** and **Fear and Retribution.**

After exploring the information in both series, I hope that you will be "mad as hell" and won't take it anymore either. The mission is too great, and our female patients depend upon us to do right by them.

Protecting the Bottom Line

Despite the popularity of compounded hormone products, particularly testosterone, they are often a regular target of some in medicine who cite research while attacking them. This research is often affiliated with medical organizations, societies, and pharmaceutical companies that seem to have an interest in preserving the status quo of limited and clinically-obsolete FDA-approved treatment options for women.

Commercial conflicts of interest that preserve this status quo are highly problematic. This is especially so when "experts" of clinical guidelines or the organizations that publish them have substantial conflicts themselves. In addition, when scientific evidence is suppressed, or valid arguments or deemed controversies are completely ignored, it contaminates the intellectual integrity of the process and recommendations. Nowhere in medicine is this contamination so clear as the guidelines that address women's hormonal needs for both estradiol and testosterone.

One of the most significant activities that professional medical associations have is to formulate practice guidelines and devise performance and outcome measures. These activities not only guide diagnostic and treatment decisions they actually inform the standard of care that practitioners use. These organizations carry considerable weight with third-party payers, and impact malpractice litigation and punitive board actions. Clearly, pharmaceutical and medical device companies have a stake in all these activities.[1-3]

For this reason, the establishment of guidelines and recommendations should be independent of all industry influence – actual or perceived. Under no circumstances should these organizations accept funding from industry stakeholders to develop guidelines or outcome measures. The lion's share of the data, guidelines, and input of many articles and reviews like the NASEM report are provided by The North American Menopause Society (NAMS) and The Endocrine Society.

Both of these "industry-sponsored" organizations openly share that they accept considerable funding from the pharmaceutical industry, and the authors and expert opinions are "paid-for" industry key opinion leaders (KOL). For example, NAMS has an official corporate liaison council that includes generous contributions, and their annual report lists many grants with murky details.

To make matters worse, many of the recommendations of their guidelines are based solely on "*expert opinion*" and not supported by evidence. In the case of the NASEM report, very few of these KOL's have the needed experience in treating patients with compounded bioidentical hormone replacement therapy (cBHRT) and testosterone supplementation in women.

The use of inflexible medical guidelines from two highly conflicted medical societies create a de facto regulatory scheme fraught with economic, legal, and patient-care consequences, depriving both doctors and patients of the right to the treatment choices that lie at the heart of autonomy. Despite the potential for clinical guidelines to restrict patient care, promote the interest of commercial third parties, and be misused by medical societies against their competitors, guidelines have remained largely unregulated.

Traditionally, there has been no legal remedy for flawed guideline development processes. However, in 2006, a landmark case led successfully by the Attorney General of Connecticut launched an anti-trust investigation into the development of Lyme disease treatment guidelines by the Infectious Diseases Society of America, one of the largest medical societies in the U.S. The investigation showed the pitfalls and conflicts of interest related to medical societies' unilateral recommendations; this established precedent that all medical societies should heed.[4]

When one reads the list of the authors, in particular, on the "Global Consensus Position Statement of the Use of Testosterone Therapy for Women," provided in the author list in Table 1 of that Statement, (of which NASEM and recent journal articles draws the conclusion that there is no medical need for testosterone use in women), it is a "who's who" of big pharma players.[5] The listed authors only address their own recent pharmaceutical-sponsored randomized control trial as being valid; totally ignoring any other data, implying the data itself doesn't exist.

The "consensus" was formatted to appear as "guidelines," but there was no peer review process. The paper itself is both biased and flawed, as are the Endocrine Society's guidelines on androgen therapy in women. They have no evidence to recommend against compounded hormones, and, in fact, proclaim that many of their recommendations are based on "expert opinion," which in itself is problematic. This panel of so-called "experts" do not routinely treat women using testosterone, so how can they make properly informed recommendations?

In 2019, the publication "Testosterone Insufficiency and Treatment in Women: International Expert Consensus" was released by a group of established experts in the field of cBHRT. This group of experts[6] had over 100,000 patient "YEARS"" experience with testosterone supplementation in women. This real-world experience coupled with the roughly 100 references/studies (versus the one meta-analysis/14 references in the above-mentioned testosterone consensus

by the International Menopause Society publication and the paltry "expert opinion" by authors who don't routinely treat women with testosterone therapy) guided their recommendations which included:

These therapies should be highly regarded in promoting hormonal wellness and managing the signs and symptoms of menopause while likely simultaneously lowering patients' breast-cancer risk in most cases.

- Testosterone is NOT a male-exclusive hormone. It is the most abundant gonadal hormone throughout a woman's life.
- Serum testosterone levels do not correlate with symptoms of testosterone deficiency in women. Optimal ranges of serum testosterone levels in women have not been established.
- Female testosterone insufficiency is a clinical syndrome that may occur during any decade of adult life.
- Testosterone therapy may be breast protective.
- Testosterone insufficiency in women negatively affects sexuality, general health, and quality of life. Supplementation may positively influence sexuality, general health, and quality of life.
- Testosterone insufficiency may be associated with an increased risk of cardiovascular disease in women.
- Testosterone optimization may be brain protective and may enhance cognitive function.
- Testosterone optimization may be a key component for improved bone health.
- Testosterone therapy in women has no adverse effects on lipids and/or cardiovascular risk.
- Studies of testosterone supplementation show benefits exceed the risk and that consistent purity and potency can be achieved.

This report by true expert front-line physicians with substantial experience and minimal conflict of interest should be given considerable weight by organizations crafting guidelines or authors of articles addressing female hormone replacement. At the very least, the publications should recognize the counter arguments to provide substantive balance to them.

Furthermore, the NASEM report and published guidelines do not take into consideration the magnitude of research done by Dr. Rebecca Glaser in regard to the breast cancer protection testosterone pellets confer in women.[7,8]

The dogmatic propagation about the harms of hormones initiated by the improper handling and reporting of the Women's Health Initiative (WHI) data continue to promote fear that hormones cause breast cancer. This is despite the fact that the majority of the breast cancer risk in the research is suggestive of the role of non-bioidentical highly inflammatory (FDA approved) progestogen Provera.[9]

Dr. Glaser's research on testosterone pellets and much of the WHI data on estrogens promote protective effects of hormones when prescribed appropriately. Even the initial Premarin arm in the WHI showed a significant reduction in breast-cancer risk, and, when statistics were corrected, the Prempro arm went from a significant increase to an insignificant increase for breast-cancer risk.[10] These therapies should be highly regarded in promoting hormonal wellness and managing the signs and symptoms of menopause while likely simultaneously lowering patients' breast-cancer risk in most cases. However, where is the media and the medical profession/guidelines shouting this from the rooftops?

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Lack of Patent Protection

A common question that is asked by not only patients but other medical providers is, "why don't compounded-product makers obtain FDA approval for the most commonly made products?" This shows a lack of understanding of the approval process and the ability for the companies that go through this very intense process to be able to patent protect their investment in bringing a drug to market.

To have a solid, patented product, a drug must have a unique chemical structure or unique delivery mechanism. Most cBHRT would not meet that definition, making it impossible for a company to protect its patent. Companies are not going to invest the millions of dollars to bring to market a "drug" it can't protect. Therefore, limiting a patient access to only FDA-approved hormones would limit their ability to obtain a majority of true "bioidentical" hormones that are found to be better tailored for the body, given the body recognizes it as its own.

One of the most recent FDA-approved bioidentical hormone products, Bijuva, did an equivalence study to other FDA-approved products and claimed it was a unique patentable product, (oil-filled gel cap with bioidentical hormones). This would have been a good product for women had it avoided the first-pass liver effect of oral medications (which increases clotting factors and complications that arise from this). Also, this limits the therapy to a one-dose combination and doesn't provide the other needed female hormone... testosterone. Once again, another FDA product was approved, but it doesn't meet the needs of our female patients. Compounding fills this gap, and options are the key.

In addition, there is a false perception that compounders are "creating new indications or a clinical need" for hormones based on a list of symptoms. This shows a lack of understanding of the difference between symptoms and syndromes. Symptoms (which they are claiming are indications) are what make up syndromes. If one treats the menopausal syndrome, they will treat the majority of the symptoms that make up that syndrome. A huge challenge in the current medical profession is the disjointed look at symptoms and signs where, most often, getting to the root cause of all the symptoms is the answer. The traditional untrained specialist may treat symptoms individually, but a trained hormone expert will often take the big-picture approach and identify that the lion's share of the symptoms makes up the larger hormonal syndrome and treat the syndrome accordingly with hormones as opposed to a cocktail of individual drugs to treat the symptoms.

The sad truth is that the failure to approve a female testosterone product began over two decades ago, and we still do not have any FDA-approved testosterone products for women. This failure is not only alarming but embarrassing to the medical profession as a whole in our inability to provide equal access to essential hormones that have been made available for men, but not to women.

Summary

This part 1 of a 2-part article discusses the gender bias within hormone replacement therapy as it relates to two of the multitude of reasons for this bias. Specifically, this article discusses "Protecting the Bottom Line" and "Lack of Patent Protection." Part 2 of this article will discuss two more reasons for this bias, specifically "Exclusion of Women in Medical Research" and "Fear and Retribution." This 2-part article covers the bias and the well-orchestrated attempt by the pharmaceutical industry to eliminate bioidentical hormones, as well as to downplay the important role of compounding pharmacies in fulfilling the needs of women in this longstanding gender gap.

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