

Now More Than Ever

The Vital Role of Hormone Therapy in Managing Disease

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The U.S. healthcare system is facing unprecedented challenges with the recent pandemic of coronavirus and ensuing SARS Cov2, or COVID-19, and it is vital healthcare providers keep their patients active and healthy so as to not over burden a vulnerable system.

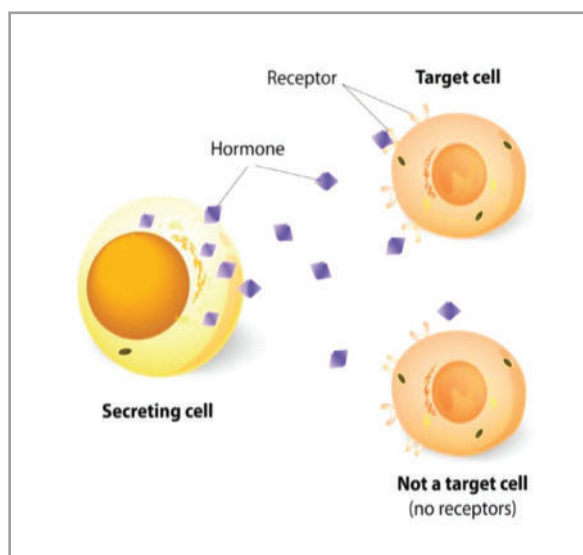
As an Acute Care Nurse Practitioner researching and practicing advanced endocrinology concepts over the past 12 years, I have recognized an overarching theme: hormones are active and play a vital role in every single body system. The far-reaching impact of restoring hormone homeostasis on health related quality of life is an often misunderstood phenomenon in both the healthcare and lay communities. With the additional burden of stress these uncertain times adds to an already encumbered psyche, classifying hormone therapies as inessential will have dire consequences.

This paper will outline the vital role hormone homeostasis plays in several common acute and chronic health conditions, **dispelling any misconception that hormone maintenance is elective and unnecessary.**

Hormones aren't just for hot flashes and ED

A myth our healthcare providers must often unravel is the concept that hormone therapy (HT) for women is used simply to abate hot flashes, vaginal dryness, and other nasty symptoms of hormone fluctuations; and testosterone replacement therapy (TRT) in men is primarily to assist in sexual function. Nothing could be further from the truth. In fact, these "side effects" of HT and TRT are what we call a bonus.

Hormones play a vital role in all body systems. Androgen receptors are found in virtually every tissue in both women and men from the brain, breast, heart and bones, indicating the role they play in normal tissue homeostasis as well as pathologies such as breast cancer, osteoporosis, neuropsychological and neurocognitive decline as well as cardiovascular and a plethora of other disease processes ¹.



In addition to improving overall sense of well-being, energy levels, libido and quality of life (QOL), HT has been shown to prevent osteoporosis, reduce cardiovascular disease risk, reduce hypertension, increase muscle mass, increase muscle strength, increase bone density, reduce visceral fat, reduce total cholesterol levels, induce glucose homeostasis, increase metabolism, manage PMS, reduce severity and

frequency of migraine headaches, improve cognition, improve memory, prevent Alzheimer's disease, and improve Parkinson's symptoms, thus having a positive impact on health related QOL ².

1. Aminorroaya, et. al., 2005; Amory, et. al., 2004; Araujo, et. al., 2011; Bachmann, 1999; Beauchet, 2006; Bialek, et. al., 2004; Boyanov, et. al., 2003; Cherrier, et. al., 2001; Davis, 1999; Davis & Tran, 2001; Davison, et. al., 2011; Glaser, et. al., 2012; Hammond, et. al., 2001; Isidori, et. al., 2005; Okun, 2006; Pike, et. al., 2009; Vanderschueren, et. al., 2004; van Geel, 2009
2. Bachmann, 1999; Conner, et. al., 2008; Carnahan & Perry, 2004; Davis, et. al., 2001; Davis & Tran, 1999; Dokovic, et.al., 2015; Ebinger, et. al., 2008; Frye, et.al., 2009; Glaser, et.al., 2011; Glaser, et.al., 2013; Glaser & Dimitrikakis, 2013; Hodosy, et.al., 2012; McHenry, et.al., 2014; Miller, et.al., 2007; Miller, et.al., 2009; Nappi & Lachowsky, 2009; Osborne, et.al., 2009; Panay & Fenton, 2009; Sands & Studd, 1995; Schutter, et.al., 2005; Studd & Panay, 2004; Zarrouf, et.al, 2009

Psychological androgen and estrogen replacement have been shown to improve mood, lift anxiety and depression, and improve sleep patterns. The hippocampus and amygdala, critical regions in the brain owing to incidence of depression, are rich with androgen receptors, a key explanation of clinical response with androgen therapy ³. Sleep deprivation has the most significant compounding effect and exacerbates the depression, anxiety, moodiness and impaired cognitive function a person may be experiencing with absent or sub optimal hormones.

The presence of depression, anxiety and altered mood states is a widespread, worldwide phenomenon, crossing cultural and ethnic lines ⁴. Depression and anxiety are twice as likely to occur in women as in men, are a leading cause of dysfunction and disability in women and noted in several studies to be a key component of decreased QOL and sense of well-being ⁵.



The differences between men and women in depression rates have also been observed worldwide, and these documented sex differences have led to the scholarly observation that hormone fluctuations are a major contributor ⁶. Depression in men is an often overlooked diagnosis, and men with suboptimal testosterone are more than twice as likely to suffer mental health issues than their optimized counterparts ⁷.

Cardiovascular Disease

Cardiovascular disease is of utmost concern with regards to an overburdened healthcare system. Heart disease rates and heart attacks have soared in recent years, despite the judicious use of statins. Hundreds of studies reveal the essential role sex hormones play in cardiovascular disease prevention and stabilization. Further, many recent studies have demonstrated **the detrimental effects of discontinuing hormone therapy** in women.

A landmark study reviewed the number of excess deaths from avoidance of HT, namely estrogen. This study came on the heels of HT avoidance post publication of the Women’s Health Initiative (WHI) trial when the media portrayed “hormones” as bad for women. Providers stopped prescribing based on misinterpretation of the WHI data by the media, and the results revealed a staggering **91,610 excess, avoidable, deaths** in women who had had a hysterectomy and not been given HT to manage the deficiencies ⁸. The number did NOT include women globally with hormone decline who had not had a hysterectomy.

3. Ebinger, et.al., 2008
4. Ebinger, et.al., 2008; Gyllstrom, et.al., 2007
5. Davis & Tran, 2001; Gyllstrom, et.al., 2007; McHenry, et.al., 2014; Rohr, 2002
6. Gyllstrom, et.al., 2007; Bromberger, et.al., 2007;
7. Freeman, et.al., 2004; Maartens, et.al., 2002; Panay & Fenton, 2009; Soares, et.al., 2003; 6. Studd & Panay, 2004
8. Jung & Shin, 2016;
9. Gagliano, et.al., 2018; Sarrel, et.al., 2013

Other studies revealed discontinuing estrogen in women was associated with increased risk of cardiac and stroke death in the first post treatment year. Rapid withdrawal of estrogen and discontinuation of HT may result in vasoconstriction and potentially adverse arterial changes and cardiovascular events, as the vasodilatory effects of estrogen suddenly cease.

Declining estrogen may also modulate cardiac rhythm, perhaps via calcium ion channels or by preventing long QT interval. Acute withdrawal of estrogen may predispose patients to fatal arrhythmias.

Increased cardiovascular death risks question the safety of HT discontinuation practice to evaluate whether a woman could manage without HT. Further, women who stayed on their HT had a vastly reduced mortality rate compared with women who stopped treatment ⁹.

Low serum testosterone is associated with several cardiovascular risk factors including dyslipidemia, adverse clotting profiles, obesity, and insulin resistance. Testosterone has been reported to improve symptoms of angina and delay time to ischemic threshold in unselected men with coronary disease. In men, endogenous testosterone concentrations are inversely related to mortality due to cardiovascular disease and all causes. Low testosterone may be a predictive marker for those at high risk of cardiovascular disease, and Low testosterone is an independent predictor of severity of CAD ¹⁰.



Androgenic hormones are beneficial for endothelial cells (ECs) because these hormones induce nitric oxide production, proliferation, motility, and growth of ECs; inhibit inflammatory activation and induction of procoagulant, and adhesive properties in ECs. Further, androgens show antithrombotic properties, thereby

possessing cardioprotective function ¹¹. One study showed a strong and independent association between low serum (blood) concentrations of testosterone and heart attacks in men with type 2 diabetes ¹².

Low testosterone is associated with hypertension in several studies. Molecular mechanisms linking androgen dysregulation to hypertension seem to be related to increased visceral fat, promoting a chronic inflammatory state through different mechanisms. One proposed mechanism may involve the recruitment and over-activation of NF- κ B where it may cause the production of inflammatory cytokines and other immune factors. Chronic inflammation and adipocyte dysfunction may alter endothelial function leading to hypertension. Both in men and in women, particularly in the postmenopausal period, low testosterone seems to be a major determinant of the increased prevalence of hypertension ¹³.

10. Venetkoski, et.al., 2018; Salpeter, et.al., 2009; Sarrel, et.al., 2013; Mikkola, et.al., 2015; Hodis & Mack, 2018; Venetkoski, et.al., 2018
11. Gururani, et.al., 2016; Malkin, et.al., 2004; Khaw, et.al., 2007
12. Chistiakov, et.al., 2018
13. Daka, et.al., 2015
14. Moretti, et.al., 2017

The role of androgens in women as it relates to heart disease cannot be understated. Studies show a positive association between low testosterone levels and severe atherosclerosis (heart disease) in postmenopausal women. Further, higher levels of androgens in postmenopausal women have a protective role in the development of atherosclerosis, and women in the ELITE trial who were on and stayed on estrogen had a 50 percent reduction in the progression rate of heart disease compared to women who were NOT on estrogen ¹⁴.



Estrogen protects the heart from ischemic injury, and postmenopausal HT use is accompanied with reduced mortality risk after primary acute coronary syndrome. Authors concluded estrogen should be considered as a preventive strategy for reduction of bone loss, bone fractures, new onset diabetes mellitus, CHD and all-cause mortality ¹⁵.

Neurological Disease

Hormone therapy, both estrogen and testosterone, plays an efficacious role in preventing neurodegenerative conditions.

Estrogen can reduce the risk for Alzheimer's disease and minimize cognitive decline by protecting against B-amyloid induced degeneration ¹⁶.

Estrogen is an immunomodulator and protects the brain from ischemic injury during and after stroke by activating several neuroprotective pathways in the brain. Following brain injury or ischemia, there is a rapid local production of estrogen, indicating that the hormone may be involved in an immediate physiological response to limit tissue damage ¹⁷.

Chronic Pain and Fibromyalgia

Chronic pain is a debilitating condition that is prevalent in society. Healthcare providers who utilize hormone optimization as a part of managing their chronic pain patients are forward thinking and understand opioid induced androgen deficiency, as well as the role suboptimal hormones play in the pain signaling threshold and pain transmission.

Testosterone deficiency in chronic pain patients has now been recognized by many observers. Due to its critical biologic functions in pain control, testosterone testing and replacement is now recommended to be a mandatory component in the treatment of chronic pain. Numerous studies on both animals and human subjects have also demonstrated the potential effects of gonadal hormones, such as estrogens, on pain transmission. These effects most likely involve multiple neuroanatomical circuits as well as diverse neurochemical systems¹⁸.

15. Debing, et.al., 2007; Hodis, et.al., 2014

16. Mikkicola, et.al., 2015

17. Henderson, 2014

18. de Tassigny, 2017; Petrone, et.al., 2014; Petrone, et.al., 2015

19. Meganne, et.al., 2016; Tennant, F., & Lichota, 2010; Amandusson, & Blomqvist, 2013; Ghorbanpoor, et.al., 2014; White & Robinson, 2015

Given the plethora of data showing both estrogen and testosterone to downregulate pain signaling and be a mandatory component of pain management, estrogen and testosterone optimization in these patients is a vital aspect of their care.

Final Thoughts

Treating thousands of patients—healthy and chronically ill alike—for over a decade with hormone optimization has afforded me a view many healthcare providers do not have. Countless healthcare providers, medical and nursing board appointees and lawmakers are still under the uneducated notion that hormone replacement is simply to curb symptoms of menopause transition in women, and sexual dysfunction in men. These notions could not be further from the truth, as partially demonstrated in this monograph.

This writing is by no means an exhaustive list of the studies surrounding the importance of hormone homeostasis. There are literally thousands of studies that point to the crucial need for patients to remain on, or even start, a hormone therapy program, especially during times of extreme and excessive stress.

For hormone therapy patients reading this who have been told your treatments are “not medically necessary” at this time, it is time to you to respectfully disagree with your healthcare provider and seek a second opinion.

For medical providers reading this work, may you be enlightened and find your passion reignited for providing the highest level of care for your patients.

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