Hidden in Plain Sight:

A Real Solution to the Diseases of Aging and the Imploding Medicare System

By Dr Mark Richards

INTRODUCTION:

Our nation is facing a health delivery crisis that has significant potential to bankrupt us. "Baby boomers" are rapidly developing the "diseases of aging" including heart disease, diabetes, and osteoporosis at the very time they are decreasing their productivity through retirement or disability. The expected result is that a huge demographic block of our population will soon be sucking resources out of our economy much faster than wealth can be generated.

Plastic surgeons bring a unique perspective to health problems due to our intensive and broad scientific training ranging from tissue transplantation and its biochemistry to physiologic and physical restoration of form and function. As physicians and scientists, we have a moral and ethical obligation to provide only therapies shown to be beneficial through the practice of evidence based medicine. Furthermore, we have a responsibility to raise public awareness of beneficial therapies and to expose treatments with no proven benefits or disproportionate risks.

What is evidence based medicine? As Kent Holtorf MD succinctly stated: "Physicians must translate both basic science results and clinical outcomes to decide on the safest, most efficacious treatment for patients. Evidence-based medicine involves the synthesis of all available data when comparing therapeutic options for patients. Evidence-based medicine does not mean that data should be ignored until a randomized control trial of a particular size and duration is completed. Rather, it demands an assessment of the current available data to decide which therapies are likely to carry the greatest benefits and the lowest risks for patients." [1]

Many of us have practices that rejuvenate appearance, but provide little to rejuvenate the human being behind the facade. There are thousands of "anti-aging" companies, organizations, and physicians that ignore evidence based medicine standards and offer the latest in unproven ideas and products for sale. I would even speculate that more than a few plastic surgeons are currently selling some type of supplemental anti-aging "cures" to their patients. The demand from our patients is huge. The pressures on the practicing physician are great. But we should not ignore the strong scientific backbone of our training and embrace hyped and unproven therapies. There is a treatment with a *seventy year history* of restoring health, vitality, and happiness to many, that is currently being offered to only a few. I hope this article stimulates your interest in learning more concerning the science of bio-identical time release testosterone supplementation for women and men in the treatment of what is best termed "relative androgen deficiency", or RAD.

BACKGROUND:

Historically, the independent partial synthesis of testosterone from a cholesterol base earned Butenandt and Ruzicka the 1939 Nobel Prize for Chemistry. Testosterone has been administered in the United States since 1938, and was available in compressed pellet form before 1940. Much non-scientific "confusion" has surrounded this compound, in large part because it is not patentable. Its poor commercial viability negatively impacts research funding and limits our medical education on its uses.

The term "bio-identical" incites unnecessary prejudices. A bio-identical hormone is simply one that is molecularly identical to the hormone the human body makes, *regardless* of its synthetic derivation. In other words, it has the exact same three dimensional molecular shape and atomic composition as our "in vivo" produced hormone. As such, a "bio-identical" hormone functions at various receptor sites and inside cellular chemical pathways exactly like the in vivo produced hormone[2].

THE EVIDENCE BASED MEDICINE and SCIENCE:

RAD occurs when the serum testosterone levels are insufficient for an individual's needs. This can be due to an absolute deficiency, a relative insufficiency (e.g. in high stress situations), or a decreased sensitivity to testosterone (along the lines of insulin resistance). It is a common disease of both women and men that usually starts in their 40s and 50s, but can occur at younger or older ages. [3-12]

RAD is outwardly manifested by a decline in one's general health and well-being (often termed "menopause" or "andropause"), and is accompanied by various physical, cognitive, and emotional disease states.[13-19] Epidemiological studies have clearly shown a strong correlation between low testosterone levels in men and women and their respective mortality rates.[20-25] In particular, documented correlations exist between low testosterone and heart disease[25-30], diabetes/metabolic syndrome[31-34], breast and prostate cancer[35-47], atherosclerosis[48-51], osteopenia[52-54], depression[13-19,55-57], fatigue[13-19,52,53], loss of muscle mass[11-17,56,57], increase in visceral fat[58], cognitive failures including spatial orientation, balance, and mobility,[56,59-61] loss of libido[13-19], hormone related insomnia[13-19], vaginal dryness[13,17-19], erectile dysfunction,[14,15,56,57,62,63] and thermodysregulation[13-19](hot flashes). This is especially troubling as several epidemiologic studies have shown a significant drop (~20%) in male testosterone levels since the 1980s[64-65]. Unfortunately, no statistically significant data was obtained on women's testosterone levels over the past decades since the critical importance of testosterone in women's health was not researched until recently. It makes logical sense that whatever environmental disruptor is affecting testosterone synthesis and sensitivity in one sex is likely affecting the other.

The important question follows: Given the strong association of RAD with the above diseases, how beneficial is testosterone supplementation for those already suffering from RAD associated symptoms and diseases? The answer is clear. Many of the above listed diseases have been shown to be prevented, improved, or cured with bioidentical testosterone supplementation.[48,57,61,66-106] For example, a 2005 article in the American Journal of Cardiovascular Drugs[48] reviewing just the cardiovascular benefits finds testosterone supplementation to "reduce serum levels of the pro-inflammatory cytokines interleukin (IL)-1beta and tumor necrosis factor (TNF)-alpha, and to increase levels of the anti-inflammatory cytokine IL-10; to reduce vascular cell adhesion molecule (VCAM)-1 expression in aortic endothelial cells; to promote vascular smooth muscle and endothelial cell proliferation; to induce vasodilatation and to improve vascular reactivity, to reduce serum levels of the pro-thrombotic factors plasminogen activator

inhibitor (PAI)-1 and fibrinogen; to reduce low-density lipoprotein-cholesterol (LDL-C); to improve insulin sensitivity; and to reduce body mass index and visceral fat mass." They conclude: "These actions of testosterone may confer cardiovascular benefit since testosterone therapy reduces atheroma formation in cholesterol-fed animal models, and reduces myocardial ischemia in men with CHD." Conversely, when multiple researchers looked for any significant ill effects of bio-identical testosterone supplementation, they have found none after 70 years of experience and investigations[107-111].

Why do both sexes suffer due to RAD? To state the obvious (and allowing for individual genetic differences): men and women are of the same species, and therefore cellularly and biochemically nearly identical. Intracellular estrogen is critical in both sexes for survival. Evan Simpson and colleagues were among the first to report that in women "the estrogen which is responsible for breast development, for the maintenance of bone mineralization and for the maintenance of cognitive function is not circulating estrogen but rather that which is produced locally at these specific sites within the breast, bone and brain." There is a convincing body of evidence showing that all cells requiring estrogen for proper functioning create their own estrogen intracellularly through the aromatase enzyme conversion of testosterone to estrogen[112-117]. To cling to the idea taught to us in medical school that a high circulating level of estrogen, *which occurs only in one sex for a small percentage of its lifetime*, is necessary for optimal health, makes no logical, biochemical, or evolutionary sense. The unavoidable facts are that we are the same species, and both sexes produce the necessary intracellular estrogen required for health locally from testosterone. This explains why the symptoms of male and female RAD ("andropause and menopause") *are nearly identical* as seen in the international menopause and andropause rating scales[15-19]. Furthermore, our new understanding of estrogen synthesis explains why menopause (like andropause) seems most successfully treated with only steady state time release bioidentical testosterone and no estrogen[76.]

The ramifications of tissue estrogen production through testosterone conversion are huge. Each cell can regulate its internal estrogen concentration through a feedback loop adjustment of aromatase concentrations, provided there is sufficient testosterone available. Supplementing humans with estrogen is not optimally effective at treating menopause or andropause symptoms as it fails to replace the deficient testosterone levels and does not provide the critical substrate the body needs to produce and regulate intracellular estrogen. Furthermore, when estrogen is *unopposed* by testosterone, it causes cellular proliferation leading to several problems including increased cancer risks - even when supplementing only with bio-identical estrogens[118-121]. Testosterone is a non-proliferative hormone[36,38,42,43,47,70,76,122-125,129]. As an exclamation point to this last statement: Contrary to what we were taught in medical school, men with low testosterone are at highest risk for prostate cancer, and more likely to have an aggressive grade prostate cancer[39-45].

Humans are designed to fully breakdown oral ingestion of bio-identical testosterone and estrogen in their liver via the portal system before these hormones can reach systemic circulation. While evolutionarily sound, this has encouraged the pharmaceutical industry to create molecularly altered (but patentable and profitable) mimics of these hormones that bypass hepatic degradation. Unfortunately, these mimics seem to uniformly have negative health effects. For example, the only oral version of chemically altered testosterone approved for use in the US is methyl-testosterone which is known to cause irreversible liver damage and is converted to 17-α methyl-estradiol by aromatase. [126,127] (Aromatase is present in large quantities in the fat tissues.) 17-α methyl-estradiol is highly stimulatory to the breast tissue because it binds many times more strongly to estrogen receptor alpha than naturally occurring estradiol. Additionally, 17-α methyl-estradiol may serve as an endocrine disruptor by blocking cells' androgen receptors. These combined properties suggest an explanation for the further increase in the incidence of breast cancer in women using oral methyl-testosterone (e.g. as in Estratest™) compared to the increased levels noted

from Premarin™ alone[119,128]. Methyl-testosterone's metabolites also explain the poor efficacy of this compound when compared to parenteral bio-identical testosterone. This example serves as a reminder that careful reading of the scientific literature is always necessary to determine whether bio-identical hormone or mimics of testosterone were used in the study, as the effects are very different and require a different interpretation of the results[119].

Embracing the importance of evidence based medicine and the mountain of scientific evidence as to the benefits of testosterone supplementation in men and women with RAD, leaves one remaining important question. How do we optimally provide appropriate and consistent levels of testosterone to the cells that need it? The only reliable means of obtaining consistent steady state levels is through insertion of a highly compressed bio-identical testosterone pellets designed for steady state release[130,131]. The rapid swings or variability in serum testosterone levels that occur when using depo-injections or transdermal gels are well documented in pharmacodynamics studies[127,131,132].

CONCLUSION:

In my practice, women receive pellet reinsertion every 3 months and men every 4 months. (The female testosterone supplementation dosage is far below the masculinization dose.) The "in-office" process is quick and done under local anesthesia through a 3 millimeter skin puncture which is taped closed. The process is easily teachable to physicians who wish to learn and invest time in understanding the science.

Despite having treated hundreds of patients and countless hours of study, I am still awed by the cost effectiveness, safety, and efficacy of bio-identical testosterone pellets for men and women with relative androgen deficiency *– the most common debilitating disease of aging*. At a time when our nation's Medicare health expenditures are leading us toward insolvency, a therapy that significantly increases the healthy functioning and productivity of its aging citizens should be our highest priority. *The answer to our patients' and nation's problem has been hiding in the science literature in plain sight for 70 years!*

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Competing Interests Disclaimer: In addition to providing bioidentical hormone pellet therapy to his patients, Dr. Richards provides paid instructional training to physicians on the science and clinical practice of bioidentical pellet therapy through his association with Medinars, LLC. He also lectures (without pay) to physicians on the science behind the evidence based medical treatment of RAD with testosterone.

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