



COMPOUNDING WITHOUT
COMPROMISE SINCE 1962

ANDROPAUSE

THE MALE MENOPAUSE

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When it comes to hormones and aging, it has been said women fall off a cliff while men roll down the hill. Either way, the result is the same.

Knowledge and attitudes regarding the existence and treatments for andropause – the “male menopause” – have recently undergone revolutionary change. Growing public and professional awareness of common symptoms associated with male aging has resulted in open discussions of these problems, which are now viewed like other medical conditions.

Andropause may consist of a variety of signs and symptoms, including:

- Weakness
- Fatigue
- Disturbed sleep
- Reduced libido
- Osteoporosis
- Heart Disease
- Artherosclerosis
- Irritability
- Insomnia
- Erectile Dysfunction
- Slow wound healing
- Prostate Problems
- Low sperm counts
- Depression, anxiety
- Reduced muscle mass
- Memory impairment
- Impaired blood cell formation
- Reduced cognitive function
- Apathy
- Hyperlipidemia
- Immune system impairment

Testosterone is classified as an androgen, and is typically thought of as the male hormone. However, it is also normally produced in lower levels in the female body as well, where it plays a vital role in sexual function, bone health, mental status and many other areas of health.

Please do not confuse natural testosterone with synthetic derivatives or “anabolic steroids,” used by some athletes and body builders resulting in disastrous effects like heart and liver problems and cancer. This is a common mistake made by many experts, and even in

medical literature. The term “testosterone” is often used incorrectly as a generic term when referring to numerous synthetic derivatives, as well as natural testosterone. Studies must be reviewed carefully to determine the form of testosterone that was used. For example, administration of synthetic androgens, like stanozolol or methyl-testosterone, causes profound decreases in HDL-C (“good cholesterol”) and significant increases in LDL-C (“bad cholesterol”). Yet, hormone replacement with natural testosterone results in *lower total cholesterol and LDL cholesterol levels* while having little to no impact on serum HDL cholesterol levels.

On the average, a man’s testosterone levels begin to decline at a rate of 1% per year after age 40. It is estimated that 20% of men aged 60-80 years have levels below the lower limit of normal. Blood testing may be used to determine an individual’s testosterone levels and to establish the need for testosterone replacement therapy.

In an exam, patients are frequently told their blood levels are “normal.” These levels may be considered normal for a given age, but may still represent up to an 80% reduction from youthful peak testosterone levels.

Symptoms of testosterone deficiency are often attributed to other problems. The symptoms are also often denied by the patient or unrecognized by the physician.

Testosterone is necessary for spontaneous erections, normal libido, and ejaculation. The Massachusetts Male Aging Study reported that hypogonadism is the sole cause of erectile dysfunction (ED, formerly termed impotence) in 10% of cases. Unfortunately, many of these men and their physicians will not be aware of the cause and the option of treatment using natural testosterone, as ED is often still erroneously considered a psychological problem. They may instead resort to other forms of therapy with the potential for side effects, rather than experience the many benefits of natural hormone replacement.

Several factors cause the decline of testosterone and in total can have a profound effect:

- Testosterone-producing leydig cells begin to die off.
- SHBG (sex hormone binding globulin) increases with age, binding more hormone and decreasing the availability of **active** testosterone.
- There is more estradiol but less LH (luteinizing hormone) reaching the testes, so less testosterone is produced.

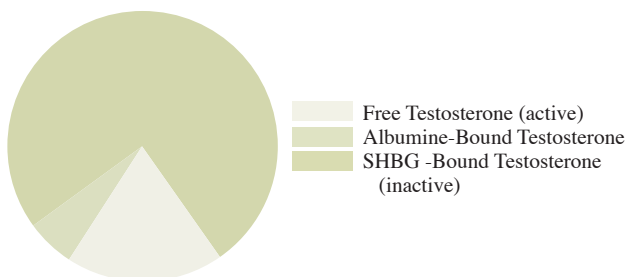
Because serum levels of SHBG increase with aging, the decline in active testosterone is often much greater than the decline in **total** testosterone levels. With aging, there is also a loss of circadian rhythm (24 hour cycle) of testosterone secretion.

In addition, for numerous reasons, most men's estrogen levels rise. This, combined with lower testosterone levels, continues to worsen the already unfavorable ratio of testosterone to estrogen.

FREE TESTOSTERONE (ACTIVE) VS. TOTAL TESTOSTERONE

A man may be considered hypogonadal at any age if **total testosterone** is less than 200ng/dl. Hypogonadism is defined as **active testosterone** less than 60ng/dl. If only total testosterone is studied, about 5% of men are hypogonadal. If active testosterone is used as the determining assay, as many as 50% of men aged 60 or older could be testosterone deficient. Basaria and Dobs of Johns Hopkins University recommend that elderly men with symptoms of hypogonadism and a total testosterone level <300ng/dl should be started on hormone replacement.

Some men may actually go through a rather sudden change in testosterone levels similar to hormonal changes that women experience at menopause, but most men have a more slow and subtle hormonal decline. When hormones are replaced or restored back to physiologic levels considered normal for younger males, men may



experience a dramatic reversal of many of the changes caused by aging.

The diagnosis of hypogonadism is made based on the presence of signs or symptoms and confirmed by laboratory testing, which should include:

- Total testosterone
- Estradiol
- Bioavailable testosterone (Free plus Albumin Bound)
- Lipid Profile
- CBC
- PSA

Proper monitoring of laboratory values and clinical response are essential when prescribing testosterone replacement therapy.

Goals of Testosterone Replacement Therapy in Adult Hypogonadal Men (≥ 50 yrs)

- *Improvement in psychological well-being and mood*
- *Improvement in erectile dysfunction*
- *Improvement in libido*
- *Increased muscle mass*
- *Increased strength and stature*
- *Preservation of bone mass*
- *Decrease in cardiovascular risk*

Information from the medical literature regarding the benefits of testosterone therapy includes:

Osteoporosis – Gradual loss of testosterone is one of the major causes of osteoporosis in elderly men. In one study, 59% of men with hip fracture had low testosterone, compared with 18% of controls. Fracture occurs at a later age in men than women because men's bones are more dense at baseline. Several studies have reported beneficial effects of testosterone therapy on bone in older men, showing an increase in BMD (bone mineral density) and slowing of bone degeneration.

Cardiovascular disease – Risk is decreased with higher serum total testosterone levels, according to most reports. A number of studies have demonstrated that testosterone minimizes several important risk factors for heart attack, including:

- *Reducing cholesterol and triglycerides*
- *Reducing blood glucose levels*
- *Decreasing visceral fat mass*
- *Normalizing blood clotting*

The degree of atherosclerotic disease, as measured by the mean percent coronary artery occlusion, increased significantly with declining levels of testosterone. Visceral fat accumulation is connected with increased

vascular risk, and studies have shown that androgen administration can decrease this fat accumulation.

Depression – Standardized measurements of depression are worse when levels of active testosterone are low; perhaps because an associated decrease in sexual function results in depression, irritability, and mood swings. In the Rancho Bernardo Study, which examined the association between levels of sex hormones and depressed mood in 856 men ages 50-89, active testosterone levels were 17% lower for depressed men. The results suggested that testosterone treatment might improve depressed mood in older men who have lower levels of active testosterone.

BPH and Prostate Cancer – “Although it is known that the clinical course of prostate cancer is accelerated by testosterone, its incidence is not increased by [testosterone] administration... There is even no clear evidence that testosterone replacement accelerates the development of BPH.”

Drugs & Aging 1999 Aug; 15(2):131-42

What is the Optimal Form of Testosterone?

Testosterone USP is the official natural testosterone of the United States Pharmacopoeia, meeting all compendia requirements. Upon a prescription order, we use Testosterone USP to compound numerous dosage forms. The information that follows should be considered as prescriber, patient, and pharmacist work together to meet the specific needs of each patient.

Perhaps the greatest advantage is the ability of the compounding pharmacist and physician to tailor the dose to exactly fit the individual, avoiding the “one size fits all” mentality. As an added bonus, it is typically a fraction of the cost of the commercially-made testosterone that come in limited doses and dosage forms. Compounding pharmacists are also able to add other hormones to the dose like DHEA, pregnenolone, androstenedione and progesterone as the physician sees fit, for a more balanced approach.

Transdermal (Topical) – Testosterone is well absorbed from creams and gels which avoid first pass liver metabolism. A satisfactory response can be achieved with twice daily dosing. Compounded preparations can be very advantageous. There is no need to shave the area of application, the medication can be administered as a

single dose (rather than multiple patches), and there is no skin irritation from patch adhesive (used in commercially manufactured products). The cream or gel can be applied two or three times daily to simulate the normal circadian rhythm.

Buccal – Troches are small, soft lozenges that dissolve between the cheek and gum in about 20 minutes, gradually releasing testosterone into the general circulation. Dosed two to three times daily and absorbed through the oral mucosa, troches also avoid first-pass liver metabolism. This offers an excellent alternative to oral Testosterone USP tablets, because testosterone that is absorbed through the gastrointestinal tract passes directly into the blood vessels supplying the liver, where the drug is significantly inactivated and converted to estrogen.

Intramuscular – In the form known as Testosterone Cypionate, testosterone can be dosed every 1-3 weeks. However, blood levels will vary widely between injections, resulting in unpredictable serum testosterone levels. Polycythemia, a serious blood disorder, is more common with 10-14 day regimens.

Methyltestosterone Toxicity – In the doses needed for male hormone replacement, methyltestosterone causes a rise in liver enzymes and cholesterol, peliosis of the liver, and liver toxicity. Its use is **not** recommended.

HEALTHY LIFESTYLE

A healthy lifestyle has been shown to be associated with higher hormone levels, and higher hormone levels seem to induce a more active, healthier lifestyle, according to Andropause expert Eugene Shippen, M.D. When hormone levels decline, we become less active and gain weight. As we gain weight, more of the already-declining testosterone is converted to estrogen. Lack of exercise, excessive alcohol use, and many diseases can reduce active hormone levels. For optimal results, it is vital that hormone replacement therapy be combined with adequate exercise, proper nutrition, and appropriate use of natural supplements.

In *Maximize Your Vitality and Potency – For Men Over 40*, authors Jonathan V. Wright M.D. and Lane Lenard, PH.D. recommend the following (pages 250-251):

- “Vitamin-mineral supplements. Minimum vitamin-mineral supplementation should include **vitamin C**, which has been found to promote men’s longevity (1 gram twice

daily); **vitamin E**, which is known to prevent a significant number of heart attacks (400 I.U. daily of mixed tocopherols); and a high-potency multiple vitamin-mineral combination... Men 'of an age' to think about testosterone replacement should also take **ginkgo biloba**, which has been shown in several studies to help preserve mental function in aging in both sexes... Ginkgo may also help preserve men's sexual function.

- "Special-purpose supplementation. If sexual function isn't all it should be, **L-arginine, yohimbine, ginseng, muira puama, and ginkgo biloba** have all been shown to be helpful... If the prostate is causing problems, extra **zinc, essential fatty acids (EFA)**, the botanicals saw palmetto (*serenoa repens*), *Pygeum africanum*, *urtica dioica*, and Cernilton® will all help greatly to reduce or eliminate symptoms of benign prostate enlargement."

Testosterone is converted into dihydrotestosterone (DHT) by 5-alpha reductase or into estradiol by aromatase. Significant obesity can result in high serum estrogen levels, as estrogen stores are greater in fat. Aromatase activity is higher in overweight individuals, resulting in increased conversion of testosterone to estradiol. It may be possible to maintain sufficient testosterone levels if the conversion to estradiol and dihydrotestosterone can be slowed by inhibiting the enzymes aromatase and 5-alpha reductase. Supplementation with vitamin C may reduce aromatase activity and decrease estradiol production.

There is good reason to believe that what is important to a man's health is not necessarily the absolute amount of each hormone but rather testosterone to estradiol ratio. Maintaining a proper body weight may produce a more desirable hormonal balance.

There are many issues related to the appropriate use of testosterone and related therapies that are beyond the scope of this newsletter. Considerations in Andropause treatment should include:

- the role of dihydrotestosterone (DHT) and its relationship with benign prostate hypertrophy (BPH), levels of DHT, and even DHT supplementation.
- The use of 5-alpha reductase inhibitors and aromatase inhibitors to modify the amount of metabolites DHT and estradiol that are produced when testosterone is broken down by the body.
- DHEA (dehydroepiandrosterone) and its role as an "anti-aging" supplement and in the treatment of symptoms of Andropause.

Our compounding pharmacists welcome the opportunity to discuss these subjects with patients and physicians. Patients may wish to schedule a consultation to discuss these topics in detail.

We recommend the following books about Andropause and testosterone therapy:

Maximize Your Vitality and Potency – For Men Over 40
By Jonathan V. Wright, M.D. and Lane Lenard, Ph.D.

The Testosterone Syndrome
By Eugene Shippen, M.D.

These books and supplements are available at O'Brien Pharmacy..

References from the medical literature:
Drugs & Aging 1999 Aug;15(2):131-42

Endocrinology and Metabolism Clinics of North America 1998 Dec;27(4): 969-87 authored by J.L. Tenover, M.D. of Emory University School of Medicine

What are Natural or "Bio-Identical" Hormones?

The recent surge in public interest regarding natural products and integrative medicine has left many people confused about the benefit/risk ratios of various manufactured versus "natural" preparations. This is an area that we must clarify. When referring to hormones, the term "natural" can be more clearly defined as "bio-identical." For example, conjugated estrogens (often prescribed for menopausal women) are derived from horses, so many people mistakenly consider conjugated estrogens to be "natural". However, these hormones are not natural, not bio-identical, and do not occur in humans. Administration of hormones from other animals and synthetic derivatives has been linked to numerous health problems, including cancer. Furthermore, only bio-identical hormones can follow the normal metabolic pathways and be broken down into other hormones and derivatives which are needed by the body. This is one reason that synthetic and animal hormones can cause so many side-effects in both men and women.

