Chapter 11

PUTTING IT ALL TOGETHER

In the previous chapters I discussed numerous aspects to taking control of your male health, but where does one begin? In this chapter I will lay out step by step what you need to follow if you believe you may be suffering from low testosterone and what you can share with your physician to help you achieve an accurate diagnosis and more importantly the right therapy for you. Let’s begin.

STEP ONE: TAKE THE QUIZ

Taking inventory of your symptoms is a great place to start to understand what your body may be telling you.

Adam Questionnaire
Androgen Deficiency in the Aging Male (ADAM) Questionnaire

1. Do you have a decrease in sex drive?
2. Do you have a lack of energy?
3. Do you have a decrease in strength and/or endurance?
4. Have you lost height?
5. Have you noticed a decreased enjoyment in life?
6. Are you sad and/or grumpy?
7. Are your erections not as strong?
8. Has it been more difficult to maintain your erection throughout sexual intercourse?
9. Are you falling asleep after dinner?
10. Has your work performance deteriorated recently?

If you answered yes to number 1 or 7 or if you answer yes to more than 3 questions, you may have low testosterone. The next steps would be to make an appointment with your physician, share the questionnaire with him, and then get the labs so you can begin to evaluate your personal course of action.
STEP TWO: GO TO THE DOCTOR AND GET YOUR PHYSICAL

Crucial to the process of getting the correct diagnosis, you need to have a face-to-face consultation with your physician which includes a physical exam. During this consultation your doctor should take note of your questionnaire and perform a thorough physical examination, which includes a testicular examination and a digital rectal examination of the prostate. I know no one really wants to have it done, however it is an important part of the physical exam and prostate cancer is the fifth leading cause of cancer death in men. Prostate cancer occurs in a little over 1 million men per year with an estimated number of deaths just over 300,000 per year. The prostate exam procedure is quick, painless, and you’re done.

You may also want to share with your physician the nutritional questionnaires from chapter 8. These questionnaires offer a window into your body’s current state of functioning and how well you may or may not be treating the only home you will ever really know – your own uniquely divine body. These questionnaires will help you gain insight into the degree of stress in your life and if you may be heading down the pathway to adrenal fatigue and dysfunction. You will also discover your personal allostatic load, which is the "wear and tear on the body" that heightens over time when you are exposed to repeated chronic stress, whether it is physical or emotional.

Stress hormones such as cortisol and epinephrine are the main hormonal mediators in the stress response and they can have both protective and damaging effects upon your body. When they are functioning appropriately they are essential for survival, however, if they are in constant demand due to ever-present chronic stress they can negatively affect the neuroendocrine system, immune system, digestive system, cardiovascular system, and central nervous system, disrupting your body’s natural homeostasis.

The questionnaires will help you learn about your current state of digestion. This is critical to the absorption of nutrients, the status of your immune system, if your thyroid is functioning appropriately, if you consuming enough healthy fat, if your vitamin D levels up to par, if your sex hormones are in balance, and more.
**STEP THREE: GET THE LABS**

So you’ve taken the quiz and answered yes to 3 or more of the questions indicating you may have low testosterone. Your body has been talking to you and you notice that you have low energy and don’t have the get up and go to use to have, your libido has taken a vacation and that your erections are not as strong. You may also see you are gaining fat around the middle, your muscles are shrinking, and you’re feeling like a grumpy old man. Your doctor has performed the physical exam and now it’s time to get the right labs to make the diagnosis. When you have your laboratory performed what we’re doing is gathering your personal biomarkers, which allows us to understand your current state of health. This health baseline will help not only to make the diagnosis but also to guide your therapy. I personally love looking at biomarkers as we are getting an intimate view of what is occurring inside your body. This information is invaluable, providing much more accuracy for a proper diagnosis. The following table below is the initial screening labs that should be ordered.

### Initial Screening Labs

- Total Testosterone
- Testosterone Bioavailable or Weekly Bound
- Testosterone Free
- Cortisol AM
- SHBG
- HgA1c
- Thyroid Panel
- (TSH, FT4, FT3, rT3)
- LH/FSH
- DHT
- DHEA-Sulfate
- Sensitive Estradiol
- Liver panel
- Serum Chemistries
- CBC
- Insulin Immunoassay
- Lipid Panel or Lipoprotein panel
- Prolactin
- Vitamin D
- Cardiac CRP
- Homocysteine
- Iron
- TIBC
- Ferritin
- IGF-1
- IGF-BP3
- PSA
- Lyme titer if relevant by history
- Uric Acid
- Urinalysis
Biomarkers to Strongly Consider:

- IgG Food Sensitivity Testing
- Micronutrient Testing
- Lp-PLA2
- MPO
- NMR lipid, VAP, Berkley Heart Lab, or Cleveland Heart Lab
- MTHFR
- APO E

If you have a family history of an inherited blood clotting disorder or are not sure then you should consider these labs as well.

- Factor V Leiden mutation
- Factor VIII
- Factor XI
- Factor II (Prothrombin Gene)
- Fibrinogen
- Homocysteine

Labs to consider after initiation or follow up of testosterone replacement therapy

These follow-up labs should be run at 3-4 weeks after starting therapy, changing therapy, or the delivery method. The same labs should also be performed at 3-month intervals during the first year and after the first year every 6 months or as necessary to monitor for unwanted side effects.

- Total Testosterone
- Sensitive Estradiol
- SHBG
- DHEA-S
- DHT
- Bioavailable Testosterone or “Free and Loosely Bound”
- Free Testosterone if Bioavailable T is unavailable
STEP FOUR: UNDERSTANDING SOME OF YOUR LABS

In my opinion this is the difficult part. Even after 19 years of providing testosterone replacement therapy and literally looking at thousands of lab results no two men are ever alike. The variations of lab results are seemingly endless and all their individual health goals are different, which is one reason as to why there will never be an acceptable “cookbook methodology” to the delivery of hormone replacement or for truly personalized care. This is why working with a skilled, experienced physician in testosterone replacement therapy who can deliver individualized personalized health care will pay off tenfold.

Now on to understanding some of the crucial labs, since the majority of individuals will be having serum blood levels tested I will discuss the following tests from that perspective.

SEXUAL HORMONE BINDING GLOBULIN

Sex hormone binding globulin, or SHBG, does exactly what it says - it binds sex hormones. Without knowing your sex hormone binding globulin level you cannot understand the levels of your sex hormones. Elevated SHBG issues can be somewhat more problematic and challenging causes of low bio available testosterone. Your SHBG is produced by the liver and bind both male and female hormones. Once these hormones are bound to sex hormone binding globulin they are unavailable for use because now they cannot bind to their appropriate hormone receptor.

So, higher sex hormone binding globulin lowers the bio available testosterone. The lower the sex hormone binding globulin level the greater the amount of free testosterone. Interestingly there is an order to which sex hormone binding globulin binds.

SHBG binds DHT > Testosterone > Androstenediol > Estradiol > Estrone

This demonstrates that sex hormone binding globulin has an affinity for the more androgenic hormones first. This means is that if both testosterone and estrogen are at equivalent levels, sex hormone binding globulin will bind more testosterone then estrogen making the level of bio available estrogen higher.
Unfortunately as we age the sex hormone binding globulin level and estrogen levels increase, while free testosterone levels and total testosterone levels decline. There is no real way to manipulate sex hormone binding globulin levels, though I have had some success with using Nettle Root 300 mg 3 times daily.

Factors that lower SHBG:

- Testosterone
- Growth hormone
- Prolactin
- Insulin
- Transcortin

**TOTAL TESTOSTERONE**

Total testosterone is a fairly simple test that tells us the total testosterone concentration in the bloodstream at a given time. Ideally you like to have this lab drawn between 8 AM and 10 AM as the concentration of total testosterone will be at its highest. However this is just an isolated level of the total testosterone. Serum testosterone levels change throughout the day, and there is actually quite a bit of variability in the serum testosterone levels especially in younger men; but as we age that variability starts to decline. Variability of testosterone levels is actually a sign of good health. I like to see this level between 800-1200 pg/dL.

A total testosterone less than 350 ng/dL is considered low, however symptoms can be felt at higher total testosterone levels. It is important to note that it is not the exact number but rather your clinical symptoms correlated with your numbers.

Now here is where sex hormone binding globulin comes into play. High levels of sex hormone binding globulin will bind testosterone making your free testosterone low and unavailable for use by the tissues. You can have a normal total testosterone level with high sex hormone binding globulin levels that then make free testosterone levels low and you suffer from the symptoms of low testosterone. While total testosterone is important for making dosage adjustments, it does not give us the complete clinical picture.
**BIOAVAILABLE TESTOSTERONE**

This is the actual amount of testosterone that is available for use in the body that can bind to the androgen receptors and cause the positive effects of this powerful hormone. Bioavailable testosterone is the sum of the free testosterone plus the loosely bound to albumin testosterone. Normal range for bio available testosterone is 40-250 ng/dL.

**FREE TESTOSTERONE**

This is a measure of testosterone that is available to be used by the body. Free testosterone represents the actual amount of testosterone in the blood stream and ready to bind to receptor sites. I generally follow this value and like to see it in the range of 150-200 pg/dL

**ANDROGEN METABOLISM**

Testosterone is made in the testis and the adrenal glands. 5α-DHT is the most potent androgen, about three times more than testosterone, but it is primarily made within the liver and target cells and not by the testes. 5α-DHT is deactivated to 5α-androstanediol within target tissues and then conjugated for excretion. The corresponding beta metabolites, 5β-DHT and 5β-androstanediol are substantially less androgenic.

**5Α-REDUCTASE ACTIVITY**

The two enzymes 5α and 5β-reductase act on the androgen androstenedione which creates androsterone and etiocholanolone and testosterone that creates 5α-DHT and 5β-DHT. They also metabolize progesterone and cortisol. The alpha metabolites of androstenedione and testosterone are far more androgenic than their beta counterparts. An individual with increased 5α-reductase activity may have issues with excess facial hair growth, alopecia or hair loss, acne, oily skin and potential prostate issues.
DIHYDROTESTOSTERONE-DHT/PROSTATE SPECIFIC ANTIGEN-PSA

DHT or dihydrotestosterone is one of the breakdown products of testosterone caused by the 5 alpha reductase enzyme reactions. DHT further breaks down into 2 metabolites: $5\beta$-DHT, which is the less androgenic form, and $5\alpha$-DHT, which is the more androgenic form responsible for oily skin, acne, prostate issues and male pattern baldness. If you happen to be a man who makes more $5\alpha$-DHT, saw palmetto can help reduce this more potent androgen. If you happen to be a man who makes more $5\alpha$-DHT and 4 hydroxyestrone, the genotoxic estrogen, this may possibly have negative prostate implications.

It is vitally important to measure DHT levels because higher levels of DHT can elevate your PSA. This level generally remains below 4 ng/mL. If however the PSA starts to rise it is usually do to infection of the prostate or benign prostatic hyperplasia, which is an enlarged prostate or potentially prostate cancer.

It is advisable to have a baseline PSA and digital rectal examination at initiation of testosterone replacement therapy and then to repeat the PSA lab at 3 months after initiation of therapy and annually thereafter. If there are changes to the digital rectal exam or if there is a rise of greater than 0.35 ng/mL per year of the PSA velocity then a urologic consultation would be appropriate. If you are a man over 60 years of age with a rise of greater than 0.75 ng/mL per year of the PSA velocity, this would be an indication for urologic referral.

ESTROGEN

The other breakdown product of testosterone is estradiol or E2, which is a type of estrogen. As men age there is an increase in the conversion of testosterone to estrogen by the enzyme aromatase. The increase in estrogen many times leads to a simultaneous increase in SHBG, exacerbating the issue by binding more of the testosterone making it unavailable. What further complicates the issue is as men gain weight around their mid-section and fat accumulates their levels of aromatase increase causing further conversion of testosterone to estrogen.

Now estrogen has both “beneficial” and “unwanted” side effects on the alpha and beta-receptors within the cell affecting health, growth, and function of estrogen responsive tissues in the breasts, testes, prostate, brain, and bone.
ESTROGEN METABOLISM

In regards to estrogen in men the primary concern is if they are making too much and which hydroxylation pathway their body prefers. Estrogens in men are produced from testosterone and androstenedione via aromatase activity.

The majority of estrogen is hydroxylated down a protective pathway creating 2-hydroxyestrone (2-OH-E1). This estrogen metabolite is considered protective in both women and men and is the preferred pathway leading to methylation and subsequent excretion of metabolites. However, phase 1 hydroxylation can take two other pathways: one towards 16-hydroxyestrone (16-OH-E1), the bad, or 4-hydroxyestrone (4-OH-E1), the ugly. Neither of these estrogen metabolites is desirable, with 16-OH-E1 exerting negative effects on the alpha and beta receptors triggering expression of target genes within the cell affecting the growth and function of estrogen responsive tissue in the prostate, breast, and testes. 4-OH-E1 is considered carcinogenic and its methylation to 4-methoxyestrone (4-MeO) leading to excretion is the most desirable protective pathway for this potentially genotoxic metabolite.

In the example on the next page you can see that this man makes a large amount of the beneficial 2-OH-E1 (bottom of the report, center), but also makes a large amount of 4-OH-E1 (left of the 2nd pie chart) as well. Fortunately he has strong methylation activity (bottom center left), however some nutrition adjustment and judicious use of aromatase inhibitors can improve his profile even further. Remember chapter 7, heal your gut and detox your liver? This is why healthy liver function of phase 1 hydroxylation and phase 2 methylation is so important in the clearing of estrogen and its metabolites.
By now you have probably noticed that the lab I like to follow is the sensitive estradiol. This is an important point because the standard estradiol test will overestimate the amount of estrogen in the man’s system, leading to possible inappropriate aromatase inhibitor usage. Over the years I have performed both standard and sensitive estradiol tests on clients and the results are always different. Below is a patient’s standard and sensitive estradiol assays and at the time he was having headaches and some joint aches, both symptoms of low estrogen. Stopping the aromatase inhibitor did the trick.

PROLACTIN

Prolactin is a hormone release from the pituitary gland and when prolactin is too high it can cause hypogonadism. The most common cause being a pituitary tumor that is called an adenoma and it is not cancerous but it is a cause of low testosterone. Such things as eating and having sex can also elevate prolactin. There are also common medications, which can elevate prolactin such as antidepressants, opioids, calcium channel blockers, and other medications.

LEUTEINIZING HORMONE-LH

Luteinizing hormone is produced by the pituitary gland and makes way to the testicles where it stimulates the Leydig cells to produce testosterone. If the hypothalamic-pituitary-testicular axis is intact and LH levels surge, more testosterone is produced when LH levels decrease less testosterone is produced. The release of luteinizing hormone is pulsatile in nature and as we age frequency and strength of the pulsatile release decreases contributing to andropause.
The initial picture we usually see in the late 30s and early 40s is one of hypogonadotropic hypogonadism. This is a low GnRH (gonadotrophic releasing hormone) released from the hypothalamus with a low LH released from the pituitary and low testosterone released from the testicles. This is where natural therapies such as lifestyle modification, exercise, and strategic supplementation can optimize the natural production of testosterone, delaying the need for direct hormone replacement and where HCG therapy is a most valuable player. Inevitably at some future date the system will start to fail and that is when we have an andropause, or what the media likes to call “manopause”. The clinical picture generally now is one of low testosterone with high LH and high GnRH or hypergonadotropic hypogonadism, which is a mouthful that means you are on the downhill slope to no longer feeling like the man you used to be. Sometimes the changes are rapid and noticeable and other times the changes are so slow you do not notice until one day you wake up looking in the mirror wondering when the former you disappeared.

FOLLICLE STIMULATING HORMONE-FSH

Follicle-stimulating hormone is another gonadotropic hormone that is less pulsatile than LH and has a longer half-life. FSH can be valuable in evaluating the hypothalamic pituitary testicular axis.

DHEA-S

In the blood we monitor DHEA-S. DHEA is an important player in the overall health and wellness of both men and women with strong benefits related to neurocognitive function, cardiovascular health, sex drive, muscle development, and immune health. DHEA is metabolized into both estrogen and testosterone and adding it to the treatment regime should not be taken lightly as the downstream metabolites could cause issues if dosed incorrectly and not monitored. There are multiple delivery methods that include gels, creams, capsule, sublingual spray, and troche.
CBC/CHEMISTRIES

At the initial evaluation and all follow ups a CBC is necessary for baseline evaluation of the hemoglobin and hematocrit. One of the potential side effects of testosterone replacement therapy in particular injectable testosterone is that it can stimulate bone marrow production of red blood cells by enhancing production of erythropoietin stimulating factor. In approximately 5-7% of patients this increased production is enough to cause erythrocytosis (increased red blood cells), necessitating the cessation of testosterone replacement therapy or therapeutic phlebotomy. If your hemoglobin and hematocrit exceed 18.0 and 55.0 then therapy needs to be withheld and or blood donation considered.

At the initial evaluation serum chemistries should be drawn as well to identify any abnormalities and to have a baseline to refer as necessary. In my experience it is not unusual to discover abnormalities in the serum chemistries such as having a low magnesium level that contribute to low testosterone.

HOMOCYSTEINE

Many of you have probably never heard of this amino acid injury and are wondering what this has to do with low testosterone. High homocysteine levels are a marker for inflammation. This nasty little amino acid damages the endothelial lining of the artery and contributes significantly the incidence of heart disease, stroke and Alzheimer's disease. If your body has difficulty absorbing B vitamins or you have a lifestyle with poor diet and excessive alcohol that contributes to decreased absorption of nutrients, then high levels of homocysteine are contributing to your disease burden. Remember if the blood doesn't flow the sex is a no go!
HgbA1c

HgbA1c levels indicate how well your blood sugars have been controlled over the last 3-4 months. Imagine for a minute that your red blood cells are like a doughnut. Healthy red blood cells are like a plain doughnut; however unhealthy red blood cells are like a doughnut with sprinkles. High levels indicate risk for the development of diabetes. Numerous studies have demonstrated the serious effects of consistently elevated HgbA1c levels on the oxidation of LDL cholesterol. Epidemiologic studies have shown that higher levels are associated with substantially higher risks for congestive heart failure, heart disease, heart attacks, strokes, brain atrophy, cancer, vascular endothelial dysfunction, increased blood clotting, high blood pressure, diabetes, and thyroid disorders. It is strongly recommended to identify and treat impaired fasting glucose early as its progression into diabetes and coronary artery disease is silent and progressive until a catastrophic event occurs. Ideally you want a hemoglobin A1c level of 5 percent or lower.

CARDIAC CRP or hs-CRP

Cardiac CRP or high sensitivity CRP which stands for C-reactive protein is a direct measure of inflammation of the endothelial lining inside the blood vessels. Increased inflammation of the endothelial lining attributes to the buildup of plaque and increases your risk of heart attack or stroke. Back to that blood flow again!

IRON/TIBC/FERRITIN

At the initial evaluation it is essential to screen for excessive iron, total iron binding capacity, and elevated ferritin levels which can contribute to low testosterone. Hemochromatosis, which is an inherited disease that causes an enhanced gastrointestinal absorption of iron, leads to iron accumulation in numerous organs to include the skin, joints, pancreas, heart and the testicles, which can cause hypogonadism and low testosterone. Also non-intentional excessive iron intake whether it is from supplements or from a contaminated water supply can also lead to decreased testosterone production.
**LIVER PANEL**

The liver is a vitally important organ where glucose is converted into energy. The liver also manages the storage of glucose in muscle and plays a role in the creation of fat. One of the main jobs is to process or detox whatever you eat or drink, medications or supplements that you take, or toxins that enter your body. The liver function tests are AST, ALT and GGT.

**VITAMIN D**

Vitamin D is present in numerous cells throughout the body and plays a role in the immune system, brain function, mood stability, bone health and cardiovascular health. It is one of the most common nutritional deficiencies that I see on a daily basis. Excessive alcohol consumption, not enough time spent outdoors or poor nutrition habits all lead to this deficiency. If vitamin D were exclusive to one pharmaceutical company, I would be their biggest prescriber! Here in Midwest Ohio everyone is deficient. In general I like my patients to have vitamin D levels that reach 60-80 international units.

Generally, I use vitamin D3 ranging from 1000 international units - 10,000 international units per day depending on the patient and their individual needs. If you have trouble absorbing vitamin D3 a prescription for vitamin D2 (ergocalciferol) may be in order. If you suffer from a mood disorder correcting a vitamin D deficiency may be beneficial, I have personally seen numerous individuals’ lives change drastically with simple vitamin D supplementation.

**LYME TITER**

If you are an outdoorsman and you have a history of a tick bite, I highly recommend having a Lyme titer. Lyme disease is due to a spirochete, borrelia burgdorferi and is a disease resulting in body wide inflammation. I have seen several cases of undiagnosed Lyme disease presented to my office with complaints of low testosterone. The most dramatic was a man with a Bell’s palsy (facial drooping on one side) who came into the office complaining of low testosterone only to discover he had Lyme disease he contracted during a fishing trip in upper New York State.
FACTOR V LEIDEN MUTATION/FACTOR VIII/FACTOR XI/FIBRINOGEN

If you have a family history of an inherited blood clotting disorder, a personal history of blood clots or are not sure then you should consider these labs as well:

THE DYNAMIC DOU: Adrenal & Thyroid Function

Free T3 & T4, TSH

The thyroid gland is responsible for how quickly the body uses energy and makes proteins. The two hormones that it makes are free T3 and free T4 and they are responsible for regulating metabolism as well as the rate of function of other systems in the body. TSH or thyroid-stimulating hormone, which is released from the anterior pituitary, stimulates the thyroid gland to release free T3 and free T4. Measuring all 3 hormones is necessary to evaluate the functioning of the thyroid gland.

CORTISOL

Cortisol is a hormone secreted by the adrenal glands released under emotional or physical stress that directly affects your blood sugar. When your body is under stress, either physical or psychological, your HPA-axis (hypothalamic-pituitary-adrenal axis) is encouraged to produce ACTH (adrenocorticotropic hormone) which stimulates the adrenal glands to make the stress hormone cortisol and to a some extent DHEA-S. The majority of cortisol is then metabolized to "metabolized cortisol". One needs to examine the levels of both "free" and "metabolized" cortisol to correctly assess adrenal function.

In healthy adrenal function, the daily free cortisol levels are expected to rise in the morning and fall throughout the day, reaching the lowest point right after going to sleep.

Any event that raises your cortisol to high can have detrimental effects upon your blood sugar metabolism, which causes you to store energy as fat. This is one piece of the puzzle as to why you get fat deposits around your midsection as you age.
STEP FIVE: CONSIDER THESE POWERFUL DIAGNOSTIC TESTS

VO2 ASSESSMENT

A VO2 Max test involves a graded exercise test on a treadmill or on a bike. The test begins at a very light intensity and gets slightly harder each minute until maximum exertion. The subject wears a mask and we measure the volume of air expired along with the percentages of oxygen and carbon dioxide in the expired air. From this data, we can determine the following:

Aerobic Threshold:

Aerobic threshold is the optimal intensity (wattage, running speed and/or heart-rate) for developing endurance. At aerobic threshold intensity, the body is recruiting almost all of the slow-twitch muscle fibers, but not yet recruiting any of the fast twitch fibers. Most individuals, without the benefit of physiological testing, overestimate this intensity. Using optimal intensity for basic endurance training maximizes fat burning and minimizes recovery time and injury risk. Most individuals perform basic endurance workouts at an intensity that is too high. Conducting basic endurance workouts at optimal intensity is much more efficient, enabling increased training volume as well as greater frequency and better quality workouts.

Lactate Threshold:

Known as the red-line to endurance athletes, this threshold is the highest intensity at which the body can recycle lactic acid as quickly as it is produced. Just below lactate threshold (LT), an athlete is working hard and acid levels are moderately high, but it does not accumulate. Speeding up just a little will cause lactic acid accumulation. Knowing this precise threshold enables an individual to work out most efficiently. Lactic acid is a byproduct of exercise, which makes the muscles burn, and may contribute to fatigue. During exercise, even at low intensity, we are always producing lactic acid. Individuals’ muscles are also constantly burning lactic acid and using it as a fuel. At low intensity the muscles easily recycle as much acid as is produced. The higher the intensity is, the more acid the muscles produce. At lactate threshold intensity, the muscle is able to recycle the acid as quickly as it is produced. If the individual speeds up just slightly, the muscles produce more acid than it can recycle and acid accumulates, causing fatigue and damaging the muscles.
VO2 Max:

VO2 Max is the volume of oxygen the body uses during one minute of maximal exercise. This data tells your potential for endurance. While aerobic and lactate thresholds are the best predictors of current endurance performance, VO2 Max is one indicator of an individual’s potential.

CAROTID ULTRASOUND & CAROTID INTIMA-MEDIA THICKNESS (CIMT)

CIMT is a noninvasive ultrasound test that is being recommended by the American Heart Association and the American College of Cardiology to screen for heart disease in apparently healthy individuals ages 45 or greater. The carotid arteries provide a "window" to the coronary arteries. Not only do they have similar risk factors - more importantly, the relationship between the atherosclerotic burden in a carotid artery and a coronary artery is the same as between any two coronary arteries. Therefore carotid atherosclerosis provides a window into the amount of coronary atherosclerosis in an individual. CIMT is an independent predictor of future cardiovascular events, including heart attacks, cardiac death, and stroke.

NEUROCOGNITIVE ASSESSMENT

Neurocognitive testing is a method clinicians use to assess a patient's memory, mental speed and other cognitive functions. Individuals with hormone deficiencies, elevated inflammatory markers, and genetic mutations such as MTHFR are at greater risk for dementia and neurocognitive assessment gives us an ability to detect early decline.
DEXA SCAN

DEXA stands for dual energy X-Ray absorptiometry. It is a totally safe, painless, noninvasive way to measure bone density and determine total body fat. The amount of x-ray exposure from DEXA is less than 1/10th of the dose you would get from an ordinary chest x-ray. Men and women with endocrine disorders, such as low growth hormone, low testosterone, high thyroid hormone (Grave's Disease), high cortisol hormone (Cushing's Syndrome), and hyperparathyroidism can also experience bone loss leading to osteoporosis.

Osteoporosis can lead to hip fractures and spontaneous vertebral fractures, which lead to loss of height. Both of these are easily prevented if the diagnosis is made early. There are various therapies available to treat osteoporosis. The earlier that therapy is initiated the less likely the patient is to develop fractures.

ARTERIAL OCCLUSION TESTING

Arterial occlusion testing is a noninvasive diagnostic device used to measure vascular reactivity for early detection of cardiovascular disease and monitoring response to therapy. The test begins with an automated blood pressure measurement, followed by cuff occlusion of the right arm. During the cuff occlusion (2 to 5 minutes), fingertip temperature in the right hand falls because of the absence of warm circulating blood. Once the cuff is released, blood flow rushes into the forearm and hand, causing a temperature rebound in the fingertip, which is directly proportional to the vascular reactivity. Vascular dysfunction is considered to be the earliest clinically detectable stage of subclinical atherosclerosis.
STEP SIX: THE NATURAL OPTIONS

If you're a man in your 30s and 40s and your laboratory panel discloses a hypogonadotropic hypogonadism, in other words a low GnRH, low LH, and low testosterone then natural therapies such as lifestyle modification, exercise, strategic nutrition and supplementation can optimize the natural production of testosterone delaying the need for direct hormone replacement. This approach can help your body’s natural ability to maintain hormonal homeostasis for an indefinite period of time until the time arrives that you enter andropause. The hypothalamic-pituitary-testicular axis has an amazing ability to regain its plasticity if nurtured in the correct environment.

This is where you should begin. The hypothalamic-pituitary-testicular axis is an amazing, delicate and intricate dance of multiple hormones and you should take every step possible to maintain this balance until the very end when it becomes necessary to exert outside control. As a man and as a physician skilled in the arts and science of hormone replacement my preference always is and always will be to attempt to maintain this delicate balance. It is helpful to be strategic and this is where intracellular nutrient testing, food sensitivity testing and advanced hormone tests can make a monumental difference. Refer to chapter five for the necessary steps to take to regain control.

I know you are wondering, “Why can’t you just tell me what to take?” Good question and that is because there is no cookbook for this approach. Every man is different and every man we see at the Alpha Male Medical Institute is built a personalized plan to help him reach his natural hormonal best. No two men ever present with the same intracellular nutrient deficiencies, food sensitivities, preexisting disease states and severity of disease, mental status, hormone status, or functional status of their multiple axes.

Each man is unto himself a unique composite of his current time and place in his personal health continuum, which requires a personalized, precise, and ever adapting approach to achieve constant health and vitality.
STEP SEVEN: THE HCG OPTION – HUMAN CHORIONIC GONADOTROPIN

When purely natural options fail to regain control of your testosterone levels, under the correct circumstance hCG is a powerful stimulator of the testicles to help them manufacture testosterone. The administration of hCG will stimulate the production of endogenous testosterone. This is because the alpha subunit of hCG and lutenizing hormone are identical, which means that it acts as an LH analog. Additional benefits of the use of hCG is that it preserves testicular size and sperm count. HCG is a purified natural hormone from the urine of pregnant women. HCG is simple to use with a low side effect profile and often amazing results. A simple injection into the abdomen with a small insulin needle twice each week is all you need. Dosages can range anywhere from 500 international units to 5000 international units twice each week.

Your physician needs to follow your laboratory 4 weeks after initiation of therapy and at intervals of 3 months. You and your physician should discuss your results along with how you are feeling overall because what is important is not what the lab values show but how you are responding and feeling with treatment. The overall goal is to achieve hormonal balance and enhance your vitality and health. Combined hCG therapy along with healthful nutrition, stimulating exercise, appropriate supplementation and hydration, adequate rest and the increase in testosterone will go to work producing lean muscle and a healthier functioning metabolism. HCG is a great way to enhance the production of testosterone until the testicles stop responding to this analog hormone. What happens at this point is that testosterone levels begin to decline again and the man slides into andropause. This is when I usually change men over to testosterone or combination therapy.
STEP EIGHT: TESTOSTERONE REPLACEMENT THERAPY

My step wise approach to improving a man’s level of testosterone starts with natural therapies that involve the use of specific nutritional plans, strategic personalized supplementation, meaningful exercise, sleep hygiene and advanced testing. When this approach is either on a downslope or failing, I make the move to hCG or testosterone. If hCG was my first choice, I will continue with hCG until it no longer can deliver which at that time I then add testosterone to the treatment regime.

Testosterone has several potential delivery methods and any doctor can make any of these modalities work. All are completely acceptable delivery methods but they all have their own technical advantages and disadvantages, however my personal preference is that of injection. It is simple; it can be done at home, it is reliable, consistent, predictable, and it is easy to measure.

Listed below are the many delivery options for testosterone replacement therapy. I have placed them in the order from my lowest preference to highest.

The Subcutaneous Implant

Small pellets no larger than a grain of rice are implanted under the skin through a small incision in either the buttocks or the abdomen. I implanted pellets for a few years and after monitoring hundreds of lab values and patients and the numerous side effects and complications, I ceased this procedure. In my opinion pellet therapy is barbaric and far from physiologic. It results in huge variations in testosterone levels that are not in balance with the body. There is no way to make appropriate adjustments to therapy at any given time; you have to wait 3-6 months for pellet degradation. Over the years I have seen numerous unwanted side effects from pellet therapy to include; supraphysiologic testosterone levels, anxiety, extreme agitation, expulsion of pellets, infection, adrenal exhaustion, scarring, fibrosis, ilioinguinal neuropathy and more. I realize there are those physicians and patients that prefer this method, but they are no longer used for my clients or myself and I recommend you not use them either.
Buccal Patch

A small tablet is placed between the cheek and gum a couple times a day to deliver the testosterone; the benefit is that it is supposed to avoid entering the stomach and potential liver toxicity. I would not recommend.

Transdermal Patch

A skin patch that is coated with medicine that can be applied to the scrotum or upper arm, which supplies a steady stream of testosterone to the patient. Inevitably the patch causes skin irritation not to mention usually high levels of DHT, which can lead to unwanted complications. I would not recommend.

Topical Gel and Cream

These transdermal delivery systems are available in pumps, packets, topi-CLICK® measured-dose applicators and other delivery systems. The gel and cream can be applied to the upper arms and shoulders or to the inner forearms, which are then rubbed against the sides of the body, which is the method I teach to my patients. It is best to allow time for the gel or cream to dry on the skin completely. You can either do once or twice daily dosing and both preparations create a nice variability in serum androgen levels. Some will argue that gel is better than cream however I have had excellent results with both preparations, so it is a matter of preference. Care needs to be taken not to accidentally transfer to women and children. The downside to these preparations is that they can lead to higher levels of both estrogen and DHT because their respective converting enzymes reside in high concentration in the skin. This can be problematic for those who make larger concentrations of either 5α-DHT or 4-OH-E1 or 16-OH-E1 and who have poor methylation activity. For the needle phobic individual these are definitely the way to go and I highly recommend them as a delivery system.

Intramuscular or Subcutaneous Injection

Delivery of testosterone via either intramuscular or subcutaneous injection is my preferred route of administration. Injection of testosterone into either the upper outer quadrant of the buttock can be subcutaneous or intramuscular depending on the individual. One could also use the lower anterior abdomen for subcutaneous administration or injection into the upper outer vastus lateralis muscle in the thigh for
intramuscular injection; both are simply accomplished with minimal discomfort. There is nice variability in testosterone levels from day to day which mimics the body’s natural state and serum blood levels are easily followed.

In general I use testosterone cypionate suspended in either cottonseed oil or grape seed oil and occasionally utilize testosterone enanthate suspended in sesame oil for those individuals that have sensitivities to testosterone cypionate.

I educate my patients on self-injection techniques to eliminate the need for frequent office visits, as this is substantially more convenient, especially if the patient is on a micro dose schedule of injections. I utilize a one-piece tuberculin syringe with a 25 gauge 5/8-inch needle for subcutaneous injection or a 25 gauge 1 inch for intramuscular injections.

The benefits of injection therapy are significant. Ease of administration, low cost, can do at home, produces reliable blood levels, dosage amounts and dosing regimen can be easily adjusted, can mimic natural variability, low side effect profile that is predictable, predictable onset of action and time course to benefits, and the list goes on which makes testosterone delivered by injection whether subcutaneous or intramuscular the winner in my book.

Whichever therapy you chose to utilize you must be monitored by your physician for potential side effects from therapy. Upon initiation of therapy or changes in dosing regimen at 4 weeks and then every 3 months thereafter for the first year of therapy. After the first year of therapy the monitoring interval can be broadened at the discretion of the physician.

The most common unwanted side effects from testosterone therapy are:

- Testicular shrinkage
- Decrease in HDL (good) cholesterol
- Polycythemia or increased red blood cells
- Gynecomastia or Breast enlargement
- Decrease in sperm count
- Acne
- Worsening sleep Apnea
- Edema (swelling)
Your physician can easily address all of these potential side effects. Now after many years of delivering testosterone to hypogonadal men the most common side effect to be addressed in my experience is testicular shrinkage, which is easily managed with hCG. There is potential for a nominal decrease in HDL, I have never seen any dramatic decrease. Polycythemia occurs in about 5% of men and is easily managed by stopping therapy, adjusting therapy, or blood donation. Decrease in sperm count for the majority of men is a non-issue, if the desire for pregnancy arises, switching to hCG can help. I have NEVER seen a case of gynecomastia caused by appropriate testosterone replacement therapy; I have however seen dozens of individuals with gynecomastia caused by the illegal use of steroids in multiple forms by young men, and quite dramatic.

**Potential Medication Interactions**

Beta Blockers: testosterone therapy often increases clearance of the medication requiring an increase in dosage

Oxyphenbutazone: testosterone therapy decreases the clearance of the medication requiring lowering of the dosage

Medications for Diabetes: testosterone therapy often times decreases the amount of medication needed.

**Contraindications to Testosterone Replacement Therapy**

- Cancer of the Breast
- Cancer of the Prostate, which now may be only in specific patient cases
- Untreated Pituitary Tumors

It is important to remember that every man’s body is different in numerous ways that go beyond the explanation of current science. That being said, what works well for one man may be completely ineffective for another man - which is why it is always best to take a personalized approach to your health and wellness. My dear friend and colleague Dr. Florence Comite, author of the bestselling book “Keep It Up” refers to this approach as precision medicine, and I could not agree more.
STEP NINE: DEALING WITH EXCESS ESTROGEN

One of the potential issues in testosterone replacement therapy is excess estrogen. Elevated estrogen can lead to several issues such as:

- Nipple sensitivity
- Elevation of SHBG
- Decreased libido
- Infertility
- Mood Instability
- Vasospasm
- Increased Clotting
- Swelling
- Cancers-questionable
- Prostate swelling
- Accumulation of fat
- Breast growth

It is best to wait until after the 4 week follow up labs to evaluate how your body is metabolizing your testosterone therapy before the initiation of an aromatase inhibitor such as Arimidex. It is not possible to predict which way a man’s body will preferentially metabolize the testosterone, and in many an instance I have seen a man’s estrogen stay mid-range and in balance with therapy. Driving the estrogen too low can have detrimental effects as well such as headaches, mood instability, loss of libido, cardiovascular effects, changes in lipid metabolism, vascular endothelial effects, bone health, joint aches and pains.

Decreasing the dosage of testosterone or adjusting the dose of other hormones such as DHEA can also effectively reduce levels of estrogen. If an aromatase inhibitor is needed it is best to start low and slow as the saying goes.
STEP TEN: DEALING WITH EXCESS DHT

Dihydrotestosterone the other downstream by-product of testosterone metabolism must also be monitored closely as levels may increase with testosterone replacement therapy. DHT is a very potent androgen that drives libido. 5α-DHT is the more androgenic form responsible for oily skin, acne, benign prostatic hypertrophy, and male pattern baldness. If there are no adverse symptoms with a higher DHT level then it is generally recommend withholding therapy with a 5 alpha reductase inhibitor. There are other safer approaches to lowering DHT levels, such as changing the delivery system from a gel or cream to injectable, or reduction of the dosage. Also, supplementation with saw palmetto works as well. 5 alpha reductase inhibitors have the potential to quite negatively affect a man’s libido so every caution should be made to avoid these unless absolutely necessary.

THE BAD HAT TRICK: HYPOGONADISM, ADRENAL DYSFUNCTION, AND LOW FUNCTIONING THYROID

The hat trick in sports circles signifies 3 positive events in a row; unfortunately what I call the bad hat trick is something entirely different and a health state where you never want to find yourself. Over the past few years I have noticed a common thread of 3 glandular dysfunctions occurring in some men with severe fatigue, no sex drive, muscle wasting, weight loss and or weight gain, and overall poor health. More often than not the man has been diagnosed with low testosterone and has been treated in the past or is currently being treated for low testosterone with no perceived benefit.

Often I find that these individuals are suffering from low testosterone, low adrenal function, and a low functioning thyroid and the severity of their symptoms can be quite dramatic. These men are often very difficult to treat because of their overlapping low functioning adrenal glands, thyroid gland, and low testosterone. It is crucial to understand the relationship between the adrenal glands and the thyroid gland. The adrenal gland relies on the thyroid gland to function adequately. Most every cell in your body has receptors for both thyroid and cortisol hormones. Cortisol is produced in the adrenal cortex and thyroid is produced in the thyroid gland. If you have low thyroid function you will have low adrenal function, which means a low production of cortisol and aldosterone. Which means you will often have difficulty with sodium and potassium retention, which can lead to weakness, fatigue, low blood
pressure, weak pulse, dizziness, and even difficulty standing. Because you have low cortisol levels your thyroid will not function as well and the conversion of T4 to the active T3 will be decreased. Cortisol assists the thyroid gland in working more efficiently. Thyroid hormones are crucial for appropriate adrenal function and optimal cortisol levels. As you can see there is a critical relationship between your thyroid gland and your adrenal glands.

The thyroid gland, located at the base of the front of the neck, is the engine that drives metabolism in that it helps process food and energy. When your metabolism isn't working correctly everything in your body slows down, and that means that every gland, organ, and every cell is affected. As your thyroid function slows down so do your adrenal glands, creating stress in your body; thus causing an increase in your adrenaline output and further creating more stress on the adrenal glands. Low thyroid function also leads to an increase in cortisol binding globulin, which further binds cortisol making it unavailable for use to every cell in the body. Low thyroid function even slows down the detoxification process in the liver, which can prevent the breakdown products of cortisol and estrogen from being cleared from your body.

Cortisol is a glucocorticoid that affects the metabolism of carbohydrates, fats and protein. Cortisol promotes the breakdown of protein to amino acids, opposes insulin by inhibiting cellular glucose uptake and oxidation, decreases calcium levels, suppresses the immune system, promotes the breakdown of triacylglycerol in adipose tissue to glycerol and fatty acids, and supports the action of growth hormone and glucagon. Cortisol helps keep the body's reaction to stress in perfect balance and also has a function in increasing blood sugar levels by the breakdown of the macronutrients, proteins, carbohydrates, and fats to help make energy that reaches every cell in the body.

If you are man who has low testosterone, adrenal dysfunction, and low thyroid there is a specific order in which treatment must be started. I have observed that you must first heal the adrenal glands before healing the thyroid gland and treating the low testosterone. If you increase the metabolic rate from the addition of thyroid hormone and/or testosterone before healing the adrenal glands you will often make the adrenal dysfunction worse. It is best to recover the adrenal glands first then treat the low functioning thyroid and then the low testosterone.
Tips to heal the Adrenals

- No coffee or alcohol
- No nicotine
- No sugar
- No processed foods
- Drink plenty of water
- Strategic exercise that limits heart rate, best determined by VO2 testing, in general do not exceed a heart rate of 120 beats per minute during exercise for a period of 30-90 days depending on severity of symptoms

Supplement with

- Vitamin D3
- Vitamin C
- N-acetylcystiene
- Digestive enzymes (lipase, amylase, protease, pepsin, betaine)
- Vitamin B5 (pyridoxine)
- Vitamin B6 (pantothenic acid)
- Citrus bioflavonoids
- Warm water with sea salt
- Porcine or bovine glandular support
- Licorice

Tips to heal the Thyroid

- No coffee or alcohol
- No nicotine
- No sugar
- No processed foods
- Drink plenty of water
- Eat small frequent meals
- Bedtime 10:00-10:30
- Practice Sleep hygiene
- Sublingual Iodine drops under the guidance of a physician
CONCLUSION

In bringing this chapter and the book to a close I wanted to make commentary about the field of age management medicine, hormone therapy and lifestyle intervention. Before embarking on a journey that includes hormone replacement therapy it would be best to ensure that you have a complete and thorough history and physical, laboratory, and all necessary ancillary testing completed to gather as many biomarkers as possible for your physician before starting any kind of hormone replacement therapy.

In my opinion there is an overabundance of readily available “testosterone clinics” who will be more than happy to inappropriately place you on hormone therapy with only doing the bare minimum of testing to make a “lone diagnosis” of low testosterone for the sole purpose of revenue generation with no regard to the impact of unnecessary hormones on your overall health and wellness. This is not good medicine and hormones do not function in isolation. Quite the opposite is true, for every adjustment you make there will be a downstream reaction and effect to the addition or deletion of a hormone.

There are dozens of reasons that cause an individual to have low testosterone from environmental influences, viruses, chronic illness, heavy metal toxicity, tumors, excess binding hormones, poor nutrition habits, lifestyle habits, excessive exercise and many more. Choosing the path of not investigating the cause of the hormone deficiency or excess and merely moving straight ahead to treatment with the “biggest tool in the tool box”, testosterone is not in your best interest. The unwanted side effects of inappropriate testosterone usage can have permanent lifelong implications.

Many times I am able to recover an individual’s hypothalamic-pituitary-testicular-axis with strategic changes in nutrition, lifestyle, and supplementation to completely rebuild this intricate and delicate process. It is always best to keep the body in balance and let it do what it likes to do naturally. No human intervention can ever hope to replicate this incredibly complex dance of hormones that has been divinely orchestrated. It would be with great hubris to ever think that man could ever come close to replicating what nature does so well.

One only has to look to the world of bodybuilding to see such egotism and flagrant disregard for the miracle of human life and all its complexities. Steroid abuse abounds
in every gym, community, and athletic event across our country and around the world. All the while quietly in the background many of the current and one time illegal steroid users suffer from numerous unwanted side effects such as tendon ruptures, infections, abscesses, Hepatitis B and C, liver tumors and cancer, gynecomastia, heart arrhythmias, derangement of cholesterol profiles leading to atherosclerosis, heart attacks, strokes and more.

If you are a young man contemplating the use of illegal steroids and you are reading this book, take heed. Over the years I have seen numerous men come through my doors having abused illegal steroids. These were some of the biggest, burliest men weeping like babies over the permanent side effects caused by their abuse. I have seen marriages destroyed and lives ruined by the inappropriate and illegal use of steroids. Be stronger than them. It takes a weak man to say yes to the temptation and a strong man to say no. Be a strong man and stay clean, eat healthy, exercise strategically, get adequate rest and use supplements wisely and sparingly. When the time comes as you age and andropause affects you and it becomes necessary to make the decision as to whether or not to pursue testosterone replacement therapy, it will deliver the medical results you need.

Early in my medical career I took a strong interest in the functioning of the brain, and part of that process is how the brain manufactures and releases hormones to communicate with every organ, tissue, and cell in the body. I was truly amazed that such small glands like the hypothalamus, the pituitary, thyroid, adrenals, ovaries, and testicles could exert such incredible control and function throughout the human body. Unfortunately, through medical school, internship, and residency very little education and time is spent discussing these intricate processes and what to do when things go wrong. We really had very little training in hormone physiology and our teaching physicians were not really familiar with the use of testosterone. So I took upon myself to learn everything I could that had to do with male health and wellness. It really seemed like a good fit, being athletically inclined and always being drawn to pushing my body as far as it would go, especially with triathlons.

For many years there has always been a negative light shown around testosterone replacement therapy because of an incorrect assumption that somehow testosterone caused prostate cancer. This assumption is incorrect and not true. We now know because of the work of many individuals that prostate cancer risk actually goes up as our testosterone levels fall as we age. We all have our heroes and some of mine
include Dr. Eugene Shippen, author of “The Testosterone Syndrome”, Dr. Jeffry Life author of “The Life Plan” and “Mastering the Life Plan” and a physician by the name of Abraham Morgentaler, M.D. author of “Testosterone for Life”, who is a urologist in Boston that has spent his entire career researching the potential positive and negative effects of testosterone replacement therapy. He has published many articles related to testosterone replacement therapy and his body of research has found no evidence that men who have high testosterone levels are at risk or greater risk of prostate cancer. Actually, quite the opposite was found to be true, the lower your testosterone levels the greater your risk for prostate cancer as you age.

This brings me to important point. In medicine and in life you must always seek the truth for many an incorrect assumption made by singular study will often dictate care literally for decades until the truth finally comes out. In my mind you must always question “what was” and “what is”. Currently the question that I get asked is; “does testosterone cause heart attacks and strokes?” This question is being asked because of all the media attention and dramatization around a couple of misguided, observational studies which in the opinion of many in the field of andrology see as non-informative. There are hundreds of studies that show the benefits of optimizing low hormones and not just testosterone. Taking a proactive approach to your health care, identifying your biomarkers that are in decline or excess, obtaining the appropriate ancillary testing, and then personalizing your program to meet your needs leads to having more energy, leaner and stronger muscles, a high functioning metabolism, and improved overall health and well-being. Your blood pressure will improve, your cholesterol profile will improve, your body’s ability to metabolize sugar will improve, you will have more energy, you’ll feel stronger, you’ll feel more confident about who you and your sex drive will go through the roof!

There will never be a one-size fit all approach that will work in personalized health care. Achieving the best results in your health care means working in concert with your physician, monitoring your biomarkers, making changes in your lifestyle, nutrition, and exercise habits, optimizing your hormones and supplements and making the commitment to your personal program of superior health and fitness.

To Your Health And Vitality,

Dr. Rob Kominiarek