Low Testosterone in Men – Male Hypogonadism Packet

PCCA Document # 98474

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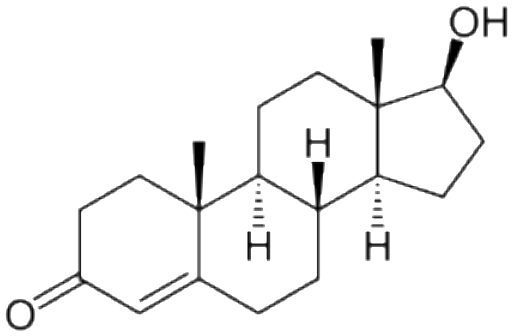

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Male Hypogonadism/Low Testosterone in Men – Patient Screening and Monitoring Guidelines

PCCA Document #97028

Hypogonadism in men is primarily a state involving lower than expected levels of testosterone, and it can occur in men at various stages of life. In many men, it correlates with aging, but low testosterone can also occur in younger men. While there is no officially recognized diagnosis, there are laboratory values and specific symptoms that are clearly identified with low testosterone. Once treatment has begun, patient monitoring is very important, and there are definite markers that should be followed.

SCREENING

There are **two major elements** to consider in determining whether or not a patient should be treated for low testosterone – **laboratory values**, primarily testosterone, and the **presence of symptoms** that may correlate with the laboratory values. Both of these elements are vital in proper patient care.

1. **Key Laboratory Test:**
   Total testosterone, free testosterone, estradiol. LH (Leutenizing Hormone) is very important in determining whether or not patient has primary (hypergonadotrophic) or secondary (hypogonadophic) hypogonadism. Other hormone lab values that can be useful are DHEA, SHBG (sex hormone-binding globulin), DHT (dihydrotestosterone), estrone and prolactin. In addition, PSA, Hemaglobin and Hematocrit should be measured before beginning testosterone therapy. *Due to diurnal variation of testosterone and other hormone production, morning testing is preferred. See Laboratory Value chart below.

Testosterone Serum Levels:

Lab Value	Units	Alt. Units	Comments
Total Testosterone	300-1000 ng/dL	10.4-34.7 nmol/L	Optimal Range: 600-750 ng/dL
Free Testosterone	47-244 pg/mL	190-660 pmol/L	Also expressed as a percent: 1.5-3.2% of total testosterone
Bioavailable Testosterone	130.5-681.7 ng/dL	3-12 nmol/L	Also expressed as 84-402 ng/dL
Note: pg/mL = ng/L	Thus, pg/mL = ng/dL x 10		Example: 47-244 pg/mL = 4.7-24.4 ng/dL

Testosterone and Estrogen Saliva Levels:

Lab Value	Units	Alt. Units	Comments
Free Testosterone	40-200 pg/mL		With topical use, range is likely higher (500-2500 pg/mL)
Estradiol	0.76-2.18 pg/mL	2.8-8.0 pmol/L	Optimal Range: 0.76-1.63 pg/mL, 2.8-6.0 pmol/L

Estradiol (E2) and Estrone Serum Levels:

Lab Value	Units	Alt. Units	Comments
Estradiol	0-50 pg/mL	0-5 ng/dL	Optimal Range: 20-30 pg/mL (2-3 ng/dL)
Estrone	<65 pg/mL		Range: 10-65 pg/mL

Other Important Values:

Lab Value	Units	Alt. Units	Comments
SBHG	13-71 nmol/L	0.5-1.5 mcg/dL	Mean is 0.9 mcg/dL
DHEA	2-9 ng/dL	7-31 nmol/L	Older men are usually deficient.
DHEA(S)	500-2500 mcg/dL	1.3-6.8 µ/mol/L	
DHT	20-50 ng/dL		
Prolactin	7-18 ng/mL		
LH	1.3-13 IU/L		
FSH	0.9-15 IU/L		
Zinc	75-291 mcg/dL		
PSA	<4 ng/mL		
Hct	<52 SI Units		
Progesterone	<1.0 ng/mL	<3.18 nmol/L	

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2. Key patient History and Physical:

A questionnaire such as PCCA document # 94123, Male Screening Form, or the ADAM questionnaire is very helpful in gathering information relative to symptoms of low testosterone. See Symptoms chart below.

3. Key Symptoms:

Decrease in sex drive. Difficulty in establishing or maintaining erections. Decrease in spontaneous early morning erections. Other symptoms include feeling tired more easily, feeling tired more than usual, feeling more irritable and/or depressed than in past. Other symptoms that can be related to low testosterone in men include these: decrease in muscle mass, increase in waist size, loss of muscle strength, loss of height. (Others as listed on screening form.)

Symptoms:

Specific Symptoms	Less Specific Symptoms
Reduced sex drive/spontaneous early morning erections	**Increased fatigue/more tired than usual**
Height loss/Increased joint and/or muscle pains	**Less enjoyment in personal interests/hobbies**
Loss of axillary/pubic hair, reduced need to shave	**Decreased muscle mass/muscle strength**
Small (<5ml) or shrinking testes	Decreased mental sharpness/poor concentration
Difficulty establishing and/or maintain full erections	Changes in usual sleep pattern
Breast discomfort/gynecomastia	Increased body fat/waist size
Hot flushes, sweats	Diminished physical or work performance
	Mild anemia

MONITORING

We will monitor patient both by re-checking laboratory values and assessing patient symptoms.

Relative to testosterone levels, our goal should be to increase testosterone to mid-to-upper levels of the ranges. For most men, there is no increased benefit by raising testosterone above the upper limit. Very importantly, hemoglobin and hematocrit should be monitored; high hematocrit levels, often correlating with high testosterone levels, can pose a patient threat. In some men, an increase in testosterone may raise estradiol to high out-of-range numbers, and it should also be monitored. In addition, PSA should be monitored, as the known presence of prostate cancer is a contraindication to testosterone use, and PSA is one of the markers for prostate cancer. A cautious approach to testing would be to test at one month, three months, six months and one year, in the first year of therapy. Beyond the first year, monitoring levels at six month intervals would be prudent; many patients are managed well after the first year on an annual testing basis.

Physical findings after testosterone therapy has begun may include testicular atrophy, a shrinking of the size of the testes. A decrease in sperm production is also common in testosterone supplementation. Therefore, in men who wish to maintain their fertility and testicular size, options to boost testosterone production (such as HCG and/or clomiphene – information included in PCCA document #94122), rather than supplementation itself, should be considered.

Monitoring:

Monitoring Parameters	Comments
Symptoms, AEs	3 to 6 months after initiation, yearly thereafter, consider formulation-specific AEs.
Testosterone level	3 to 6 months after initiation or dose adjustment, Yearly thereafter. Consider formulation-specific timing.
Bone mineral density	Lumbar spine and/or femoral neck 1 to 2 years after initiation in men with osteoporosis or low trauma fractures.
PSA age >40 years with baseline PSA >0.6	Digital rectal exam prior to initiation PSA 3 to 6 months after initiation. Per prostate cancer screening guidelines thereafter.
Urologic consultation	PSA increase of >1.4 ng/mL in a 12-month period; Increases >0.4ng/mL/year with 6 month level as reference, given >2 years of levels
Hematocrit	3 to 6 months after initiation, Yearly thereafter. Hold therapy if >54% and assess for hypoxia and sleep apnea. Resume therapy if returns to WNL.

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Men's Health Evaluation Form

Today's Date: _____

Name: _____ Birthdate: _____ Age: _____

Address: _____
Street City State Zip

Phone: _____ Email: _____

Height: _____ Weight: _____ Desired Weight: _____

Occupation: _____ Hobbies: _____

How often and how much?

Do you use tobacco/nicotine? ☐ Yes ☐ No _____
Do you use alcohol? ☐ Yes ☐ No _____
Do you use caffeine? ☐ Yes ☐ No _____
Do you exercise? ☐ Yes ☐ No _____
How long have you exercised? (months/years) _____
Type of exercise preferred. _____

If yes, please elaborate (dates/frequency):

Have you ever had a panic attack? ☐ Yes ☐ No _____
Do you have OCD? ☐ Yes ☐ No _____
Any diagnosis of mental illness? ☐ Yes ☐ No _____
Ever had a head injury/concussion? ☐ Yes ☐ No _____

How frequent are your bowel movements? _____

Typical # of hours of sleep per night: _____ Normal bedtime: _____
Uninterrupted? ☐ Yes ☐ No Time and reason for interruption: _____
Do you wake rested or tired (even when getting 7-8 hours of sleep)? _____
Are you or have you ever been a night shift worker? ☐ Yes ☐ No
If yes, please describe when and for how long: _____

My diet is:
_____ Super healthy _____ Mostly healthy _____ Needs work _____ Terrible
What would you like to change about your current dietary choices? _____
_____

Allergies: Please list any allergies and describe the reaction that occurred.
Drugs: _____
Foods: _____
Other: _____

Patient Name: _____

Over-the-Counter Medication History: Please list all non-prescription medications that you are taking. (Include vitamins, herbals and supplements): _____

_____

_____

_____

_____

_____

CBD/THC Use: Please list any products used and frequency:_____

Medical Conditions/Diseases: Please list any conditions/diseases that you have been diagnosed with or suffer from. (Examples include heart disease, high blood pressure, depression, benign prostatic hyperplasia, erectile dysfunction, etc.) _____

_____

_____

Have you ever tested positive for Epstein-Barr virus or Lime Disease? ☐ Yes ☐ No

If yes, please elaborate (dates/current status): _____

When was your last physical exam? _____ When was your last colonoscopy? _____

Any bowel habit changes or blood in stool? _____

Current Prescription Medications:

Medication Name and Strength	Date Started	How Often per Day	Medical Condition Being Treated

Please indicate if you are experiencing the following symptoms:

	Absent	Mild	Moderate	Severe
Weight gain	_____	_____	_____	_____
Dry skin/hair	_____	_____	_____	_____
Hair loss	_____	_____	_____	_____
Anxiety	_____	_____	_____	_____
Depression	_____	_____	_____	_____
Moodiness or irritability	_____	_____	_____	_____
Headaches	_____	_____	_____	_____
Difficulty falling asleep	_____	_____	_____	_____
Difficulty staying asleep	_____	_____	_____	_____
Fatigue	_____	_____	_____	_____

Patient Name: _____

	Absent	Mild	Moderate	Severe
Loss of memory	_____	_____	_____	_____
Foggy thinking	_____	_____	_____	_____
Arthritis	_____	_____	_____	_____
Decreased sex drive	_____	_____	_____	_____
Stress	_____	_____	_____	_____
Sugar cravings	_____	_____	_____	_____
Difficulty losing weight	_____	_____	_____	_____
Decreased height	_____	_____	_____	_____
Difficulty establishing and/or maintaining full erections	_____	_____	_____	_____
Decrease in spontaneous early morning erections	_____	_____	_____	_____
Less enjoyment in personal interests and hobbies	_____	_____	_____	_____
Premature ejaculation	_____	_____	_____	_____
Difficulty reaching orgasm	_____	_____	_____	_____
Difficulty urinating or weak stream	_____	_____	_____	_____
Frequent nighttime urination	_____	_____	_____	_____
Decreased muscle mass	_____	_____	_____	_____
Bone loss	_____	_____	_____	_____
Bone fractures	_____	_____	_____	_____

Other symptoms: _____

I am _____ years old. I feel _____ years old.

What are your goals for taking hormone replacement therapy?

1. _____
2. _____

Doctor who we should contact for this therapy:

Name: _____ Phone: _____

Address: _____

Street City State Zip

*** Please include a copy of all relevant lab work, especially PSA and hormone levels, that you have recently obtained.

Men's Hypogonadism Health Profile/Questionnaire

Points to Consider

1. Decreased sex drive, difficulty establishing and/or maintaining erections and a decrease in spontaneous early morning erections are more diagnostic than others for andropause. However, the patient should receive a complete exam and all symptoms should be considered. These symptoms combined with pertinent lab values will aid diagnosis.

2. A waist circumference ≥ 40 inches increases the risk for men to develop metabolic complications.

3. BMI and waist circumference are very important to the patient's general health. However, new evidence suggests WHR (waist to hip ratio) is more consistently a predictor of metabolic complications.

   General waist to hip ratio guidelines:

Age	Low Risk *	Moderate Risk *	High Risk *	Very High Risk *
20-29	< 0.8	0.8 - 0.9	0.9 - 0.94	> 0.95
30-39	< 0.85	0.85 - 0.9	0.9 - 0.95	> 0.96
40-49	< 0.87	0.87 - 0.93	0.93 - 1.0	> 1.0
50-59	< 0.9	0.9 - 0.95	0.95 - 1.0	> 1.0
60-69	< 0.9	0.9 - 0.97	0.97 - 1.1	> 1.1

* risk of developing metabolic complications

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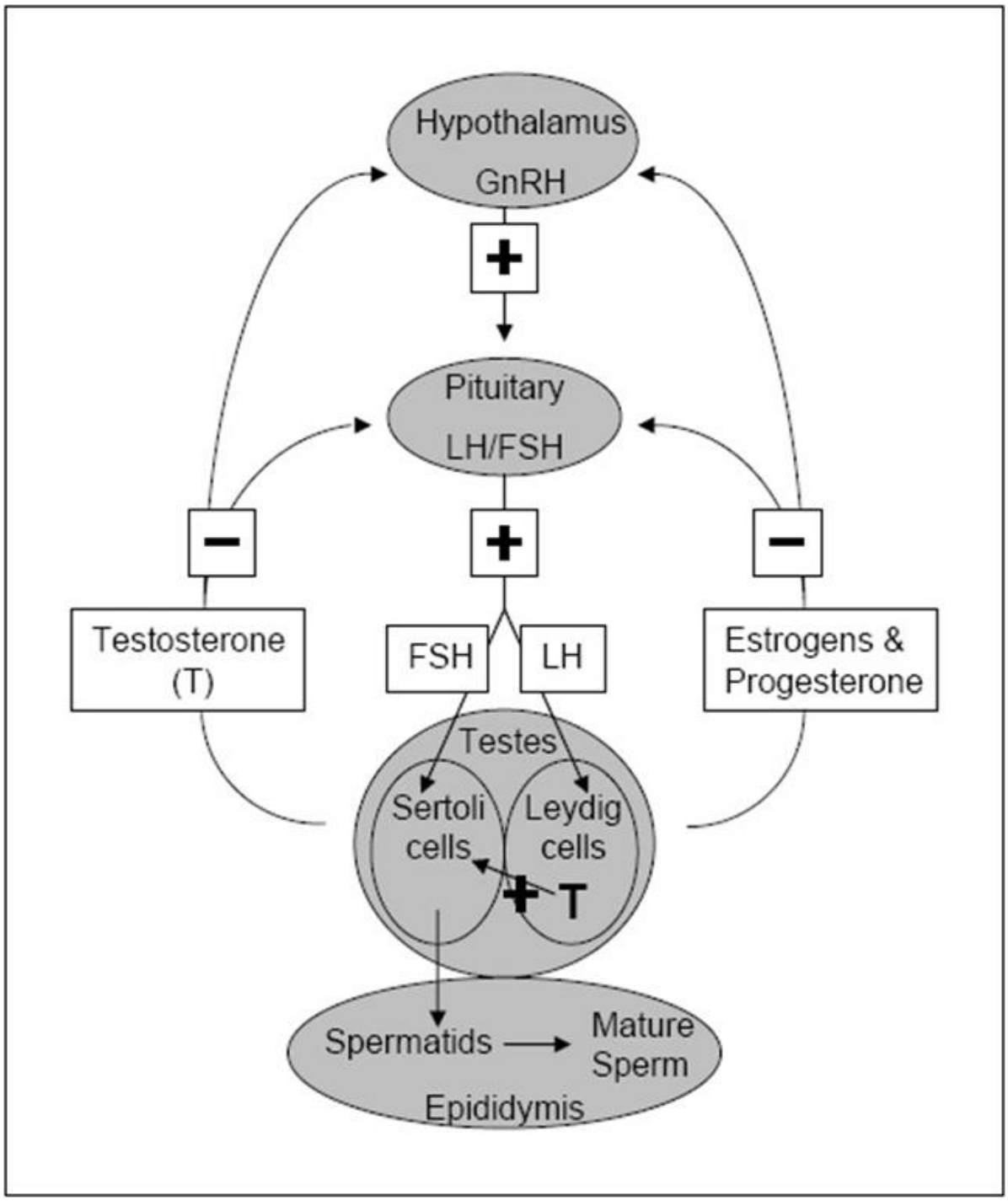
HPA LH/FSH Diagram

PCCA Document #98475



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TREATING MALE HYPOGONADISM:
Options to Boost Low Testosterone in Men

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Hypogonadism in men is primarily a state involving lower than expected levels of testosterone, and traditionally this condition has been treated almost exclusively with testosterone supplementation. However, low testosterone can be fairly complex, involving a myriad of factors including the inability of the testes to produce sufficient testosterone, improper brain signaling, and excess estrogen. (Primarily seen as female hormones, estrogens are also very important in men since declining testosterone can alter the androgen:estrogen relationship. While there is not an established target value for the androgen:estrogen ratio, changes in this relationship can result in complications such as declining prostate health). In some men, clear reasons behind low testosterone can be difficult to determine. The end result, though, can be the same: insufficient testosterone that results in an unhealthy life and is often characterized by symptoms such as loss of libido, erectile dysfunction, depressed mood, and lethargy. After proper diagnosis, including testing for testosterone, estrogen, and luteinizing hormone (LH), properly directed therapy can be dramatically effective in reversing these symptoms and providing a healthier, more robust lifestyle.

In this review, we will consider the following ways to increase and/or maintain testosterone levels within at least the mid-physiologic levels, while also keeping the androgen:estrogen relationship in mind:

1) Lifestyle changes
2) Reduce estrogen levels
3) Increase testicular output of testosterone
4) Testosterone supplementation

1) Lifestyle changes

Lifestyle modifications can boost testosterone production and keep the androgen/estrogen relationship healthy. Sedentary lifestyles, central adiposity, and unhealthy habits such as smoking and excessive alcohol use work against that goal. Whenever and to whatever extent possible, we should recommend an active exercise program that involves both aerobic and weight-resistant activities, along with a healthy eating plan that promotes loss of excess weight and fat. Many men who follow these tenets of healthy eating, appropriate dieting, and adequate exercise will find that their hormone levels correlate positively with their lifestyles. This, by far, is the simplest and soundest basis for hormonal health.

2) Reduce estrogen levels

Adverse effects have been reported with changes in the androgen:estrogen relationship; these changes can occur because of declining testosterone levels and increasing (or even constant) levels of estrogens. As mentioned previously, changes in this relationship are patient-specific and there is not a desired target value. Estradiol has been identified as a primary mediator in the hypothalamus/pituitary axis (HPA, Appendix A) for gonadotropin-releasing hormone (GnRH) and thus luteinizing hormone (LH) and follicle-stimulating hormone (FSH) in men. Thus, it becomes important to monitor estrogen levels (primarily estradiol, but also estrone) so that corrective action can be initiated when estrogen levels are high. Some studies have shown that, instead of actual testosterone supplementation, testosterone levels can be increased by using aromatase inhibitors to decrease the synthesis of estrogen. High estradiol levels, through the negative feedback mechanism, can shut down or slow down GnRH secretion, and thus decrease the levels of LH and FSH. LH is the primary messenger hormone to signal the Leydig cells in the testes to produce more testosterone. Therefore, decreasing the action of estradiol with an aromatase inhibitor increases the production of testosterone. Another reason to be aware of estrogen levels is the role that estrogen plays in the level of Sex Hormone Binding Globulin (SHBG). Estrogen elevation contributes to the elevation of SHBG, a protein that binds testosterone and decreases the level of free testosterone. This free form is the active form of testosterone; therefore, agents that lower estrogen are proposed to increase the amount of active testosterone available.

For many men, the simplest and least invasive steps to reduce estrogen levels are to lose weight, practice good nutrition and engage in regular exercise. Because aromatase, the enzyme system that is responsible for converting testosterone to

estradiol (as well as converting androstenedione to estrone) is more abundant in fatty rather than lean tissue, fat reduction through exercise can improve the relationship of androgen and estrogen levels. A potent aromatase inhibitor that has been studied for use in men with high estrogen levels is anastrozole, available commercially as a 1 mg tablet or as bulk powder. Some pharmacists and physicians have found that it can be very effective in oral doses ranging from 0.25mg three times a week to 0.5mg every other day. It also has been prepared in a sublingual form, with a suggested dose of 0.1mg daily. Another commercially available aromatase inhibitor is letrozole, which is available as a 2.5mg tablet and has been studied with good results in men. Suggested dosing ranges from 2.5mg three times per week to 2.5mg daily. As a means of gauging the effectiveness of these agents, one should obtain baseline levels of estradiol, and then compare them with levels 30 to 60 days after initiation of therapy. (Chrysin, Vitamin C and Zinc have been reported as aromatase inhibitors, but there is little literature supporting these agents.) A very important consideration is that we do not lower estradiol so greatly that we induce hot flashes or contribute to osteoporosis. Another important reason to avoid drastic lowering of estradiol levels is that estradiol may possess libido-enhancing effects in men and these effects may decrease with declining estradiol levels. Some practitioners have suggested the combined use of testosterone with anastrozole, as either a sublingual or parenteral dosage, which may prove to be useful therapy in some patients.

3) Increase testicular output of testosterone

Increasing testicular output of testosterone may be the desired option in the case of secondary hypogonadism, a condition in which the testes may be fully intact but are not receiving proper or sufficient signals to produce testosterone. The signal hormones LH and FSH may be mimicked by Human Chorionic Gonadotropin (hCG); an injection of hCG can often reactivate the testicular secretion of testosterone by binding at LH receptors. Dosage requirements vary from patient to patient, with some responding to injections of 500 units three times weekly and others requiring up to 1500 units three times weekly. For some men this may be a very effective way of restoring testosterone to physiologic levels while not suppressing the male's ability to produce sperm. Testosterone supplementation can decrease sperm production by suppressing FSH thru the negative feedback system. It should be noted that treatment to stimulate testicular output of testosterone would not be useful in a man diagnosed with primary testicular failure, in which the testes are unable to produce testosterone (a condition referred to as primary hypogonadism).

Clomiphene also works to increase testosterone production. It has been known for many years that clomiphene could be used to test the integrity of the HPA, but several papers have been published in recent years that chronicle the use of this agent as a potentially important means of maintaining sufficient testosterone levels on an on-going basis. (Many are familiar with the use of clomiphene in female fertility; it can also be useful in male fertility). At doses ranging from 25mg every other day to as high as 100mg daily, clomiphene acts as a SERM, effectively blocking estradiol from binding to its receptor. With less estrogen binding, GNRH levels increase and lead to increases in LH and FSH secretion. Clomiphene has been compared in at least one head-to-head study with testosterone supplementation and has been shown to be very

effective in both restoring hormone levels and reducing signs and symptoms of hypogonadism. Clomiphene overcomes the previously mentioned problem of decreased sperm production seen with testosterone supplementation. For this reason, clomiphene is one of the best options for men interested in maintaining their fertility. As in the case with anastrozole, the combined use of clomiphene and testosterone seems to have merit; the principle is that the clomiphene would help maintain the level of LH, which usually declines with testosterone therapy. Thus, we have the body making testosterone, and that would combine with the testosterone supplementation. While not yet clinically tested, this combined therapy has generated interest.

4) Testosterone supplementation

Testosterone supplementation: that is the form of treatment most familiar to all. For many men, this will be the treatment of choice – it is easily understood and, when properly administered, can be very effective in boosting testosterone levels. (See discussion on "Male Hypogonadism/Low Testosterone in Men: Patient Screening and Monitoring Guidelines" document)

A. Parenteral Dosing

Giving testosterone by intramuscular injection is probably the most common form of dosing over the past twenty-thirty years, and it seems to work well for many men. However, a serious and confusing drawback is the erratic release of testosterone; there is no way to provide a steady-state release over the 3 to 4 week intervals at which the injections were usually recommended. Many times the physician would measure levels after a three week interval and find them surprisingly low. Not understanding that effective dosing is a matter of finding the proper interval, physicians would increase the dose from, for example 200mg up to 300 or even 400mg. This would not lengthen the duration of action, but would rather sharpen the peaks and valleys associated with testosterone ester injections. The patient would experience supraphysiologic levels in the first week, then have declining levels after that; results of the supraphysiologic levels include increased conversion to estradiol and the previously mentioned polycythemia. Gynecomastia has also been associated with this kind of therapy. It has been proposed multiple times in recent years that a better method of dosing intramuscularly is to give a lower dose at weekly intervals; a suggestion of 75mg to 100mg is quite common. In this way, there is a more continuous release of the hormone without the peaks and valleys of the traditional dosing pattern.

Subcutaneous dosing is being looked at as a potentially more favorably route of dosing, allowing the patient more freedom to dose himself than was possible with the intramuscular injections.

In a pilot study, testosterone enanthate in oil was given by subcutaneous injection on a weekly basis. All of the patients were within the normal range for testosterone following injection. Patients also reported the subcutaneous route was easy to use and well tolerated. In general, subcutaneous injections are preferred over intramuscular injections because they are less painful, more convenient, allow for smoother release of the drug, are patient-controlled, and are associated with better compliance. If testosterone can be incorporated into a pen delivery system, as mentioned in the study on subcutaneous injection of testosterone, patients will benefit even more with the improved convenience.

B. Topical Administration.

At this time, topical administration appears to be the most effective way of dosing testosterone. While creams, solutions, and lotions have been used, over the past dozen years the greatest benefit seems to come from topical gels. We will focus on this type of vehicle as it has more clinical information available compared with other vehicles, and compliance has been shown to be relatively easy to achieve. In most gel formulations, testosterone is completely dissolved; until high concentrations (10% and greater) are used, the gel is easily absorbed and leaves no residue. It has been suggested that gels, unlike creams, do not depot in the skin dermis but rather proceed more directly to blood vessels. From various studies over the past 10-12 years, a topical dosing range when an efficient vehicle is used can be from 40mg -120mg daily. An approximate absorption of 10% of testosterone from gel vehicles has been established, suggesting that an application of 50mg in a topical gel will result in 5mg net absorption. (For comparison with a patch, 50mg of a gel equates to about 5mg from a patch.) Some practitioners prefer a topical solution to a gel, using a propylene glycol/alcohol mixture as the base and a suggested concentration of 6% testosterone. At this time, there is no known benefit to using a smaller volume of a higher concentration, as high concentrations have the downside of leaving a residue. A risk associated with topical dosing is the transfer to a child or female, and every precaution should be taken to mitigate that risk.

C. Sublingual or Buccal Administration

From this type of dosing route, testosterone is best given 3 to 4 times a day to maintain something approaching steady-state release.

While absorption is efficient (higher than topical) and rapid (peak levels can be obtained after approximately 30 minutes), metabolism is also rapid due to the short half-life of testosterone, and levels return to baseline after 4 to 6 hours. Effective sublingual or buccal doses can range from 10mg to 25mg per dose, suggested to be dosed at 6-8 hour intervals. While this is a relatively inexpensive and non-invasive method of dosing, the patient must understand that daily compliance of multiple dosing is necessary to obtain maximum benefit of the hormone. The use of a high dose once daily, for example at 100mg - 200mg, will simply drive the levels very high into the supraphysiologic levels for several hours, making it an unfavorable route of administration. Sublingual dosing may be useful for a male who is already supplementing testosterone but needs an extra testosterone boost to enhance sexual function. Tablet triturates with a polyglycol base are a useful and likely more effective way to dose sublingually or buccally when compared with standard troches, due to the smaller volume and shorter time to full dissolution.

For more discussion on dosage forms for testosterone replacement, see PCCA Document #99637, Atrevis Hydrogel® Dosing Considerations. This document discusses the value of the base used, specifically, Atrevis Hydrogel. Also included are suggestions on how to dose testosterone when changing from one dosage form to another, e.g., from parenteral or buccal to topical.

D. Implantable Pellets

This is a method some physicians prefer, particularly due to the fact it gives them the ability to directly control patient dosing with an in-office surgical procedure. The advantage to the patient is that compliance is not an issue; the patient has the procedure done at a 3 to 5 month interval and does not have to be concerned

with daily or weekly dosing. A disadvantage is that there is no way to adjust the dose during the life of the pellet in the body. For compounding pharmacists, pellets offer the challenge of providing the patient with a product that both releases the hormone consistently and is sterile, requiring compounding procedures that are very unique in methodology.

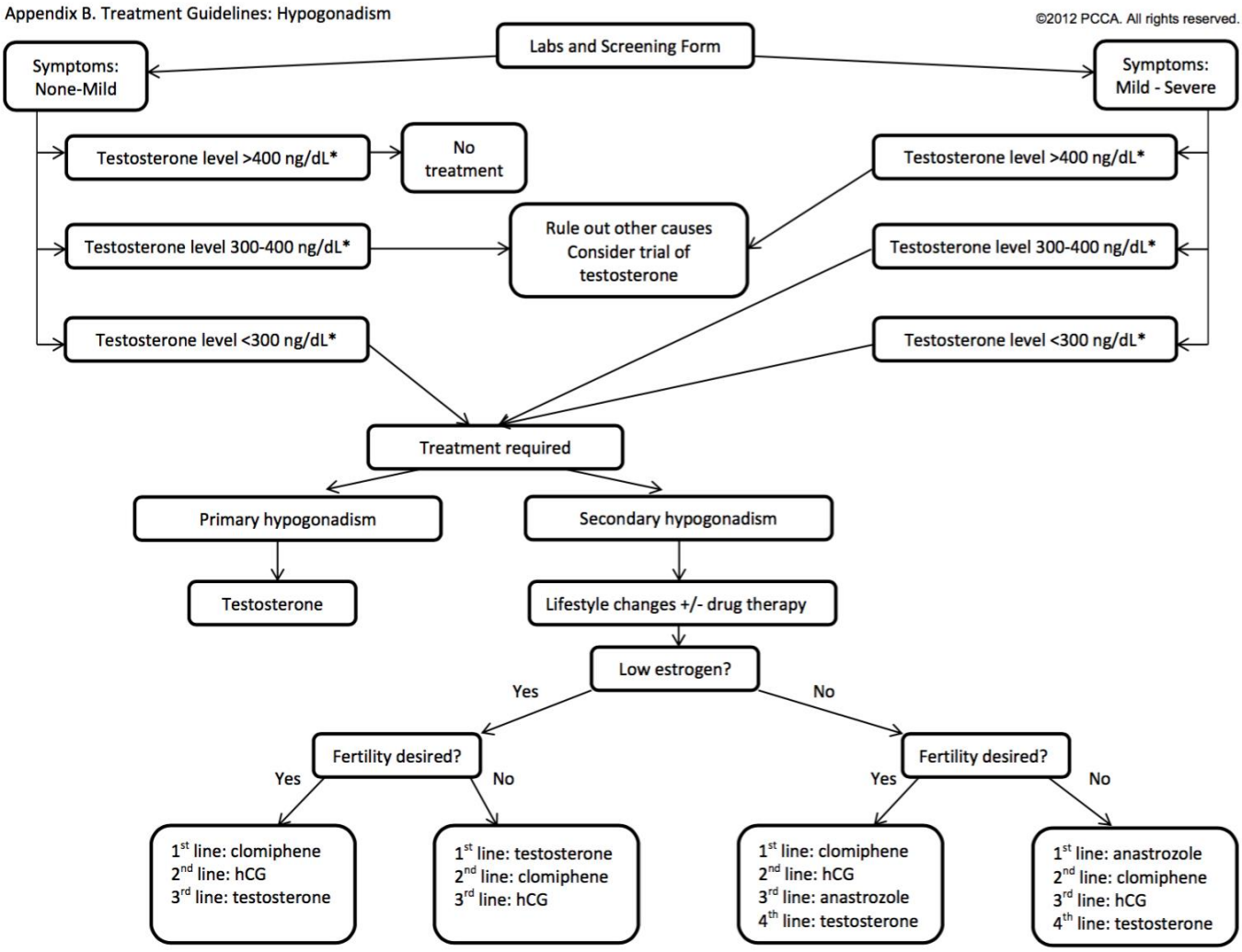
E. Oral Dosing

Oral dosing of testosterone is inefficient unless one is speaking of the long-chain undecanoate ester. This form of testosterone is now available in the U.S. in a commercial product, and is not available as a bulk chemical for compounding. (In many clinical articles, when oral testosterone is discussed, the reference is to hormones that are no longer used in men, such as methyltestosterone, which causes liver toxicities in the doses suggested.)

In summary, male hypogonadism is a common condition widely associated with the aging process. Understanding of this condition is continuing to grow as new information is available. Pharmacists are in a very unique position to work with patients and physicians in achieving better diagnosis and treatment plans for the hundreds of thousands of men in the U.S. who are hypogonadal. Improved management of this condition results in better health for each patient.

Treatment Algorithm

PCCA Document #98476



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Dosing Chart and References

PCCA Document #98477

Appendix C.

Drug	Dosage Form	Dose Range	Notes
Anastrozole	Capsules	0.1 mg daily – 0.5 mg every other day	
	Sublingual	0.1 mg daily	
Letrozole	Tablets	2.5 mg 3x/week – 2.5 mg daily	
hCG	IM injection or SQ injection	500 Units – 1500 Units 3 times per week	
Clomiphene	Tablets or Capsules	25 mg every other day 50 mg daily 50 mg twice daily	
Testosterone	IM injection	75-100 mg weekly	Used to avoid highs and lows associated with every 3 week dosing
	SQ injection	Limited clinical data – Dosing is similar to the IM formulation	Anecdotal evidence shows a benefit
	Topical gel	40-120 mg Initially: 50 mg/mL VersaBase gel OR 5% carbomer alcohol gel Gel should be applied to a 2" by 2" patch of skin once daily (May be divided into 2 daily doses)	~10% absorption For comparison, 50 mg gel = 5 mg patch
	Topical cream	5% in Lipoderm base	Not used frequently
	Sublingual	5-10 mg per dose 3-4 times daily	Level peaks in approximately 30 minutes and returns to normal in 4-6 hours
	Implantable pellets	One dose (multiple pellets) lasts 3-5 months	
	Oral	400-500 mg daily	Inefficient due to extensive first-pass effect

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Clomiphene

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Anastrozole:

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