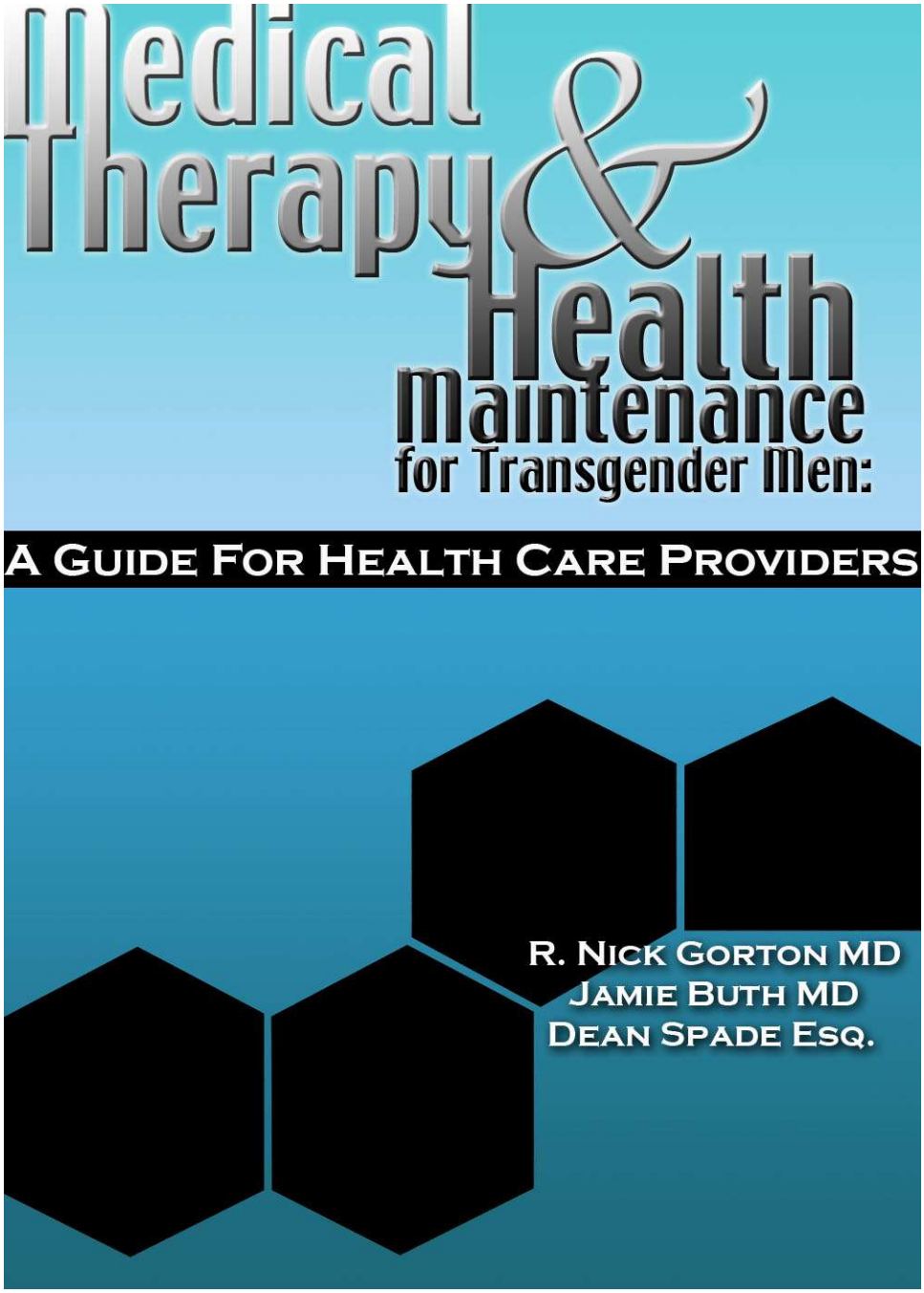
Medical Therapy & Health Maintenance for Transgender Men:
A Guide For Health Care Providers
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Medical Therapy and Health Maintenance for Transgender Men: A Guide For Health Care Providers

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SRLP works to guarantee that all people are free to self-determine their gender identity and expression, regardless of income or race, and without facing harassment, discrimination, or violence. SRLP is a collective organization founded on the understanding that gender self-determination is inextricably intertwined with racial, social and economic justice. Therefore, SRLP seeks to increase the political voice and visibility of low-income people of color who are transgender, intersex, or gender non-conforming. SRLP works to improve access to respectful and affirming social, health, and legal services for our communities.

Lyon-Martin Women's Health Services: www.lyon-martin.org

LMWHS was founded in 1979 in San Francisco and named in recognition of LGBTQ civil rights activists - Phyllis Lyon and Del Martin. The clinic provides high quality individualized care and support services to women and transgender people who lack access to quality care because of their sexual orientation or gender identity, regardless of their ability to pay.

Disclaimer:

Medical science is constantly evolving. New research about treatments, changes in medical standards, and diagnostic testing emerges almost daily. Definitive answers to some questions may not always be known, especially in the treatment of rare conditions such as transsexualism. The authors and publisher of this book have made every effort ensure the information provided within is accurate and up-to-date. However, as medicine is constantly changing and human errors are always possible, the authors and publisher do not warrant the information in this book is complete or accurate. They cannot accept responsibility for errors, incomplete information, or for the clinical results of using this information. Readers of this and every medical text should always confirm information from other sources before using it for patient care. In particular, as none of the medications described in this text are FDA approved for treatment of Gender Identity Disorder, readers are encouraged to consult with other sources including providers experienced in the treatment of transgender patients before using this information. Please consult the package insert for further information about doses, contraindications, and adverse effects before prescribing any medicine.

Contributions, comments, questions, and criticisms for future editions:

Substantive contributions for future editions of this work by the authors are quite welcome. Comments, whether positive or negative, are also welcome. If at all possible we will respond to questions and comments. Please address correspondence by email to: nickgorton@gmail.com. By mail: Nick Gorton; Lyon Martin Women's Health Services; 1748 Market Street, Suite 201; San Francisco, CA, 94102.

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Preface

The provision of care for transgender patients can be extremely rewarding. A knowledgeable provider can guide a transgender patient through a challenging life change and help him emerge whole and healthy in a body finally recognized as his own. Unfortunately, the knowledge necessary to care for transmen before, during, and after transition is rarely taught in medical school or residency. This information is also almost never adequately presented in endocrinology or medicine textbooks.

This book was written to fill that gap. It brings together in a single volume much of what I have found searching within the published medical research literature and in expert opinion. In essence, I wrote the book I would have loved to have, as a physician and a transman, when I began my own transition.

I hope that it will be painfully outdated within months of release by the publication of new research that begins to answer the questions I have presented in this text. However, I also hope that it will serve as a good foothold for anyone wishing to learn about the medical treatment of transgender men - whether transman, provider, or perhaps even both.

If you're reading this and you *are* both, email me. We should talk. nickgorton@gmail.com

This book while it places treatments in context, does not intend to provide definitive guidance on who should be treated. While diagnosis and readiness for treatment are briefly discussed, this book assumes a provider is already considering hormonal therapy for a patient. There are numerous opinions and sources of information on evaluating patients with regards to suitability for hormonal therapy. The interested reader is advised to begin her search with the Harry Benjamin International Gender Dysphoria Association (www.hbigda.org) as well as the *Diagnostic and Statistical Manual of Mental Disorders* (DSM) and *Treatments of Psychiatric Disorders,* both published by the American Psychiatric Association.

Nick Gorton

Chapter 1 – Brief Endocrinology and Metabolism Review

Before discussing treatment of transmen, a *brief and simplified* review of endocrinology and the metabolism of androgens will be helpful.

Steroid Hormone

Steroid hormones are derived from cholesterol. They include ***sex steroids*** (estrogen, progesterone, testosterone,) ***glucocorticoids*** (cortisol, prednisone, hydrocortisone,) and ***mineralocorticoids*** (aldosterone.)

Androgens

The classic definition of androgen is simply a substance that stimulates the growth of the male reproductive tract. In general however, the term androgen is used to refer to sex steroids whether synthetic or naturally occurring that exert their effects primarily at the androgen receptor.

Androgens have two primary effects: ***anabolic and androgenic***. Androgenic effects produce the typical male sexual characteristics. Anabolic effects primarily result in stimulation of muscle and bone growth as well as metabolic changes. While testosterone exerts both effects, certain synthetic androgens have differing relative anabolic and androgenic effects.

The majority of androgen in blood is bound to protein, chiefly Sex Hormone Binding Globulin (SHBG) with the remainder bound primarily to albumin. Only 1-2% is unbound, 'free' androgen. Androgen bound to SHBG is neither bioavailable to exert androgenic and anabolic effects nor vulnerable to metabolism.[1] In individuals with high levels of SHBG such as cisgender (non-transgender) women, the free androgen level is lower, but hormones have a longer half life.[2] Conversely in an individual with lower levels of SHBG more free androgen is bioavailable however, metabolism and destruction occur more rapidly. Normally, women have about twice the circulating levels of SHBG that men do.

SHBG is increased by: estrogen (especially oral estrogens) and thyroid hormone. SHBG is decreased by: obesity, testosterone, high levels of growth hormone, high levels of insulin, and high levels of glucocorticoids.[3] Additionally the binding of testosterone to SHBG varies between individuals. So two patients with similar SHBG and total serum androgen levels might have very different relative androgen effects at the tissue level.[4]

Testosterone Metabolism

Cyt-P-450

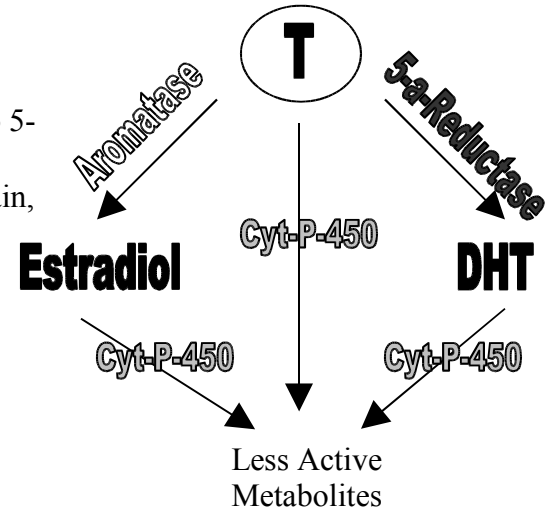
Ubiquitous hepatic oxidase.

5-a-Reductase

- Enzyme that converts testosterone (T) to 5-α-dihydrotestosterone (DHT.) Mainly found in androgen responsive tissue (brain, pituitary, skin, bone, liver.)
- Type 1 – sebaceous glands and liver.
- Type 2 – genitourinary tract, liver, facial/scalp skin, and prostate.

Aromatase

Enzyme that metabolizes 'aromatizeable' androgens to estrogens. (Testosterone is aromatizeable, while DHT is not.) Occurs mainly in adipose tissue and brain.



After testosterone is metabolized in the liver, 90% is excreted in the urine.[5]

DHT is 5-10 times more potent than testosterone. In women, DHT is more highly protein bound, with only 0.5% existing as free DHT. Testosterone is more bioavailable however, with approximately 1.4% unbound.[6]

The varied actions of androgens in different tissues are not the result of distinct androgen receptors but because of *different levels of activity of Aromatase and 5-α-Reductase* and therefore different relative levels of testosterone, DHT, and estrogens.[7]

Both androgens and estrogens are required (in differing amounts) in *both* males and females for optimal health.

Physiologically active testosterone is sometimes roughly estimated by the free androgen index (FAI). FAI is the ratio of total testosterone to SHBG. FAI = 100 x Total Testosterone(nmol/L) / SHBG(nmol/L). However, while used clinically by many practitioners, the utility and accuracy of the FAI in women is still debated.[8] Additionally, in transgender men the FAI may not be as accurate or have values comparable to cisgender men. Moreover, the FAI even if accurately measured may not correlate well with end-organ effects due to the local steroid hormone metabolism that occurs in many tissues as well as the variable binding of testosterone to SHBG.[9,10]

Normal FAI values are age and gender specific:
Male:

- 20-29 years: 30-128
- 30-39 years: 24-122
- 40-49 years: 14-126
- Older than 49 years: 18-82

Females aged 20-49 years: 0.4-8.4. Females older than 49 years: 0.4-6.6

The Illinois State Academy of Science provides an online database of normal hormone levels in humans available at http://www.il-st-acad-sci.org/data2.html.

Chapter 2 - Hormonal Therapy

Readiness for Hormonal Therapy

> "If it looks like a duck, and quacks like a duck, we have at least to consider the possibility that we have a small aquatic bird of the family anatidae on our hands."
> - Douglas Adams in *Dirk Gently's Holistic Detective Agency*

The goal of this chapter is not to provide definitive guidance for providers regarding whether patients are appropriate candidates for hormonal therapy and how to determine when they are ready to begin treatment. The Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) published by the APA describes the diagnostic criteria for Gender Identity Disorder (GID.) The HBIGDA Standards of Care provide the most widely accepted, if not evidence based, guidelines for the provision of therapy for transgender people. However, neither of these documents provides all of the information needed by the physician providing care to an individual patient. Moreover, rigid reliance on these documents is no guarantee of high quality care and they may sometimes inappropriately prevent access of patients to beneficial treatments. It should always be remembered that the goal of medicine is to *heal* and provide our patients with the highest quality and greatest quantity of life possible. So the HBIGDA-SOC and the DSM should be seen as documents that provide useful guidance to clinicians wishing to provide care for *individual* patients.

The current HBIGDA-SOC state that in almost all circumstances, transgender patients must have completed either a three month 'Real Life Experience' (RLE) or a period of psychotherapy (generally of at least three months) before hormones are provided. During the RLE (formerly called the real life test), patients live full time in their new gender identity. However, fulfilling these requirements may not be possible or safe for all transgender people. For patients who must pay for their own care, the cost of three months or more of psychotherapy may be prohibitive. In addition, for many transgender people, a meaningful RLE experience before treatment may not be possible given the limitations of their bodies. This RLE may place some patients at *significant* risk of violence and even death if they are discovered to be transgender. It may in fact, represent a violation of the medical ethics principle of non-malfeasance to require some patients to fulfill a three month RLE as a condition of receiving hormonal therapy. Moreover, while the requirement of a three month RLE or therapy is widely accepted and held as a minimum standard of care, there has never been any medical evidence to support this practice. In fact, the only research available suggests that there may be no differential benefit or reduction in risk of regrets in patents who undergo a RLE versus those who do not.[1]

Therefor, readers of the HBIGDA-SOC should bear in mind that the requirements and readiness criteria do not represent evidence-based guidelines, but rather accepted professional consensus. While careful evaluation of patients is warranted, if adherence to guidelines either places patients in additional danger of violence or prevents their access

to treatment altogether because of financial barriers, the guidelines lose their value. The ultimate goal of improving patient health and welfare is paramount and decisions on who should be treated should bear this in mind.

Overall, testosterone therapy is far more successful at producing desired secondary sex characteristics in transmen than hormonal manipulations are in transwomen. This is due to the fact that in general, the biological plan for the human body is 'Eve' and adding testosterone, whether endogenous or exogenous, will produce significant reversible and irreversible changes to a person's body. With regards to secondary sexual characteristics, going from Eve to Adam is relatively easy, but as transwomen are painfully aware, once you arrive at Adam, going back is difficult if not impossible. So while testosterone is effective and very helpful for transmen, it also represents a more significant commitment to permanent assumption of the male gender role than does estrogen in transwomen. Fortunately, many people with only mild gender dysphoria, who might have regrets if treated, select themselves out and never present requesting hormonal therapy. The additional effect of careful evaluation of candidates readiness makes real regrets in treated transgender patients a true rarity.[2,3,4]

Many transgender men seeking medical therapy will have recently been evaluated and approved for treatment by a mental health professional. However, in some circumstances this will not be the case. While two decades ago, provision of therapy to such patients would not have realistically been considered by primary care physicians, this is not always the case today. In some circumstances patients may not actually require mental health evaluation other than by their primary care provider. Moreover, as some providers who advocate the harm reduction model are aware, often the provision of hormones represents the least harmful and potentially most helpful way to address patients' concerns.

The goal of any evaluation for a patient requesting therapy is to determine whether the patient is transgender and whether he is psychologically appropriate and ready for therapy and its consequences. Moreover, screening for coexisting mental health issues is also appropriate in this population as these may effect and be effected by the physical and psychological effects of hormonal treatment. In some instances, to definitively determine the answers to these questions, a mental health professional should be involved. However, in others when a primary care provider, familiar with diagnosis and treatment of transgender men, is presented with a readily apparent diagnosis in an otherwise very emotionally stable and appropriate patient, further evaluation may not be necessary.

It is important to remember when considering waiving additional evaluation by a mental health professional that there is a long and unpleasant history of distrust and antagonism between the medical community and transgender patients. This is largely due to the historical abuse of power and failure to respect transpatients' autonomy by the medical community. For example, in the past the decidedly homophobic medical and psychiatric community denied sexual reassignment treatment to homosexual transmen (those with a male affectional preference.) In this homophobic paradigm, sexual reassignment was

erroneously seen as a 'cure' for certain 'homosexuals' (i.e. heterosexual transpeople.) Faced with this kind of judgmental rejection, it is not surprising that many homosexual transgender men resorted to fabrication and deception in order to bypass the medical gatekeepers that hindered their access to treatment that was for some, the only perceived alternative to suicide. As a result, it remains the (unfortunately in some cases still accurate) perception by some in the transgender community that if they stray from presenting the 'typical transgender historical narrative' that they will be denied care.

Fortunately, this adversarial and unhealthy situation is gradually changing. One of the authors of this text observed a recent discussion in a group for transgender men about this topic. One member suggested to a relatively new member of the group that it might be necessary that he deceive his psychologist and present the typical transgender narrative in order to approved for hormones and surgery. The reaction of the other members of the group was impressive both in its intensity and its consistency. The new member of the group was advised to be truthful, and if his provider was transphobic, intolerant of non-traditional transmen, or unnecessarily rigid in his interpretation of the HBIGDA SOC, the solution was to find a new therapist rather than lie to his current provider.

The transgender community now knows that there are understanding providers in the medical and mental health fields. The perception is that these providers are highly desirable *precisely because* transgender people can safely be honest with these therapists and receive not just the coveted 'letter' to get hormones, but to actually establish a positive therapeutic environment. It is now up to the medical and mental health fields to similarly seize on this opportunity to heal the rifts between providers and transgender patients that were formed by the previously rigid, homophobic, transphobic, and adversarial attitudes and policies of the medical community.

However, while it is ludicrous and unproductive to assume that every history presented by a transgender patient was regurgitated from the 'acceptable trans-narrative' familiar to every transgender person with access to the internet, this problem can also not be ignored. In order to both assure that an individual transgender patient feels he can be honest about his history as well as work toward eliminating the belief in the trans community that such deception may be necessary, *complete honesty and transparency* from the provider is crucial.

A provider considering primary evaluation for hormones must indicate to her patient that he will not be judged based on his sexual orientation, degree to which he has participated in a checklist of specific sex-stereotypical activities, desire for retaining his reproductive capacity, or his decision whether to pursue certain types of surgeries or treatments. The true goal of such evaluation should be shared with the patient: to ensure that whatever therapy is provided will leave him happier, healthier, and a more whole person.

Patients should be evaluated with respect to the duration and constancy of their gender identity, overall mental health, readiness for therapy, presence of other coexisting mental health problems, and understanding of treatments, as well as their risks and limitations.

We would certainly not advise evaluation by a novice primary care provider for a nineteen year old patient with coexisting untreated significant mental health problems, an unstable home life, and whose decision to transition was made in the past month. However, an experienced provider presented with an otherwise stable and mature patient who has a durable male gender identity could likely make the determination with confidence that such a patient is an appropriate candidate for hormonal therapy.

Perhaps most telling however, is the experience of the authors of this text with this more progressive harm reduction model of treatment. Willingness to provide hormonal therapy based on assessment of individual patients needs, history, and situation with an overriding goal of *achieving the best possible outcome for patients* rather than rigidly adhering to arbitrary rules has been successful. Not only does it demonstrate to *all* patients that their provider's primary concern is their health and well being, but it helps those patients who may *genuinely need* further evaluation and treatment to understand that a mental health referral is not simply to ensure the patient fulfill the requirements of the HBIGDA Standards of Care. Moreover, if transmen see their providers as partners rather than adversaries or gatekeepers, it allows for a more productive, satisfying, and honestly *healing* relationship for patients and providers.

In summary, like any other problem that a primary care provider addresses, some patients require further testing and perhaps consultation with a specialist to determine an accurate diagnosis. However, like the quote at the beginning of this section suggests: if it looks like a duck, walks like a duck, and quacks like a duck, an astute clinician does not always need a tail feather biopsy to rule out goose.

Androgen Therapy – Contraindications

Various authors and clinicians report contraindications for androgen therapy.[5,6,7,8,9,10,11] Below is an *inclusive* summary of those recommendations although no single author lists all of these as contraindications:

Absolute Medical Contraindication in Transgender Men

- Pregnancy or breast feeding.
- Active <u>*known androgen sensitive*</u> breast cancer (evidence suggests in general, androgens may be protective with regards to the stimulating effect of estrogens on breast tissue and may have apoptotic and antiproliferative effects on many but not all breast cancer cell lines.)[12]
- Uncontrolled coronary artery disease.
- Active endometrial cancer.

Relative Medical Contraindications

- Androgen sensitive epilepsy.
- Migraines.
- Severe obstructive sleep apnea.

- Polycythemia (may be due to prior non-medically supervised androgen use.)
- Heart failure, renal failure, or severe hypertension due to the salt retaining effects of testosterone.
- Active substance abuse (Some consider this an absolute contraindication.[13])
- Tobacco abuse.
- Significant hepatic disease.
- Severe acne.
- Controlled coronary artery disease or significant family history of CAD.
- Hyperlipidemia.
- Personal or significant family history of breast cancer (especially if known androgen sensitive.)
- History of uterine cancer.
- Bleeding disorders (for injected testosterone only.)
- History of DVT.
- Significant history of violent behavior.

Androgen Therapy Overview

The half-life of testosterone in blood is approximately 70 minutes, so it is necessary to deliver a continuous supply of the hormone for masculinization. In general parenteral formulations have more consistent pharmacokinetics in a broad range of patients and are able to deliver higher serum levels of androgens.[14] Parenteral forms may be preferable for patients in the early stages of transition who may require greater serum levels than those who are undergoing maintenance therapy. However the most commonly used and least expensive parenteral formulations, testosterone esters, are not ideal and may cause difficulties due to high peak and low trough serum levels of testosterone. Dosage must be individualized and may be lower in post-oophorectomy patients.

The ideal testosterone formulation for transmen would approximate normal male physiologic production of testosterone (4-9mg/day), provide reasonably consistent levels of serum androgens, possess an excellent safety profile, be inexpensive and readily available, and be convenient to use and user friendly. Unfortunately, no currently available testosterone formulation perfectly meets all these criteria. Decisions regarding the best method for testosterone therapy should be individualized with regard to patient preference, likelihood of compliance, cost, and safety.

Testosterone formulations in the US are DEA controlled (schedule 3) primarily due to the risk of diversion and abuse by athletes. All formulations are pregnancy category X.

Prices are estimated based on retail pharmaceutical sales. Some compounding pharmacists are able to make testosterone (including depot, transdermal, and pellet formulations) for a substantially lower cost. The International Academy of Compounding Pharmacists (IACP) (http://www.iacprx.org/index.html) has a referral service for providers or patients searching for local compounding pharmacists.

Types of Therapy

Injected

"Depot" drug formulations are created by mixing a substance with a medicine that slows its release and prolongs the action of the drug. The two commonly used injected testosterone esters in the US are testosterone cypionate (Depo-Testosterone®) and testosterone enanthate (Delatestryl®) which are almost interchangeable therapeutically. Enanthate is purported to be slightly better with respect to even testosterone release, but this is probably more of a concern for body-builders who abuse the drugs at higher doses (250-1000 mg/week) than the replacement doses used by transgender men (50-150mg/week.) The two formulations are mixed with different oils, so some patients may tolerate one formulation better than the other. Enanthate costs more than cypionate and is more typically the one prescribed for hypogonadal males in the US. Cypionate is more popular in the US than elsewhere (especially amongst bodybuilders) and costs approximately $100-125 for a 10 cc (2000mg) vial. Depending on dosing a vial may last from 3-10 months making cypionate the least expensive option overall. Because of its relatively low cost, cypionate is often preferred by transsexual men who must frequently pay out of pocket for care. Other parenteral formulations exist but are more difficult to obtain in the US. For example, Sustanon® is a formulation that mixes shorter and longer acting testosterone which gives more even levels of testosterone release with injections required only every third week. A newly marketed formulation of injected testosterone, Nebido® (testosterone undecanoate in oil) provides significantly improved testosterone delivery with far less variation outside the eugonadal range and with injections required only four times yearly.[15] However, each quarterly dose requires injection of 4ml which may require multiple simultaneous injections. In addition, Nebido® is significantly more expensive and currently unavailable in the US.

With cypionate and enanthate, peak serum levels are achieved within 2 to 5 days after injection, and return to baseline after 10-14 days.[16] The adverse effects of injected testosterone are often associated with high peak levels in the first few days after an injection. Moreover, with injected testosterone esters given every two to three weeks, serum levels of testosterone may be outside of the eugonadal range between 45-55% of the time. These significant changes in serum levels can result in unpleasant fluctuations in mood, energy, and sexual function.[17] Some adverse effects may be ameliorated by using a shorter dosing interval (weekly or every ten days instead of twice monthly.)[18] 100 mg weekly gives much lower peak and higher trough levels of testosterone than does 200 mg every two weeks, while still maintaining the same total dose of androgen. This benefit must be weighed by the patient and provider against the risks and inconvenience of doubling the number of injections.

Injected testosterone is started at a range of doses (25 – 125 mg/week depending on the patient and clinician) and titrated upwards based on clinical effects and trough levels.[19,20] If lower doses are used initially, titration should probably be considered more frequently. After several cycles, trough level around the mid-normal eugonadal range for men of 500

ng/dl is sought. (Normal range for a biological male is 290 to 900 ng/dl.) However, clinical effects *not* specific lab values are the target of therapy. If a transgender man achieves cessation of menses and satisfactory masculinization at relatively low serum levels, titration upwards to reach 500 ng/dl or higher is unwarranted.

With any self-administered parenteral therapy, proper technique is essential. It is imperative for the provider to either teach this skill herself, or arrange for patient instruction to avoid preventable complications such as infection, nerve injury, pain, and inadvertent intravenous injection. The dorsogluteal, ventrogluteal, or anterolateral thigh are the preferred locations as each readily accommodates 1-4ml injections. Patients should be taught either the z-track or air bubble method to decrease seepage. There is some evidence that the air bubble method may be superior.[21] In addition, if patients are self injecting, the air bubble method may be easier to perform. Several excellent websites exist with instructional information for transmen about self-injection. However, this should be supplemental to instruction and preferably initially direct observation to ensure patients are using proper technique. (http://www.forge-forward.org/handouts/injection.pdf) Providers should also assess how patients are disposing of biohazardous sharps. Local and state laws governing sharps disposal vary. If in doubt, the local public works or sanitation departments can provide guidance. Some hospitals and pharmacies have sharps return programs. In addition, there are commercial companies who provide relatively inexpensive sharps mail-back services where patients purchase a sharps container and mail it back when full.

Transdermal

Both testosterone patches and gel are available. Both approximate normal physiological levels of testosterone better than the higher peaks and troughs associated with injection of testosterone esters. Both can cause local skin irritation, however the effect is much more pronounced with patches (about 2/3 of patients) due to substances that increase transdermal absorption, than with gel (about 1/20.)[22] Both also have a risk of inadvertent exposure to others who come in contact with the patient's skin. This is probably most important for patients whose intimate partners are pregnant or considering pregnancy or those who are parents of young children as both of these groups are more vulnerable to the masculinizing effects of androgens. Case reports of significant virilization of young children after exposure to topical androgen preparations (both prescription and 'supplement' products) used by their caregivers demonstrates the very real risk for interpersonal transfer.[23] Additionally, an unpublished study cited in the product literature by the makers of AndroGel® (Unimed Pharmaceuticals) reported that the female partners of males using 10mg/day of AndroGel had serum testosterone levels greater than twice baseline after fifteen minutes daily of vigorous skin to skin contact 2-12 hours after application of AndroGel® by their partners. This transfer was completely eliminated by covering the application area with a tee-shirt.[24]

Delivered doses of both patches and gel are generally in the range of 5-10 mg/day. Unfortunately, in some patients inadequate absorption through the skin occurs.[25] This may

make transdermal testosterone less effective, especially during the first few years of cross-gender hormonal therapy. However, these preparations may be useful during maintenance treatment after adequate masculinization has already occurred or in post oophorectomy patients who often require less overall androgen.[26,27]

Testosterone gel is absorbed quickly when it is applied and produces a temporary drug depot in the skin which diffuses into the circulation, peaking at 4 hours and decreasing slowly over the rest of the day. A steady state is reached within days.[28] Cost is about $160-210/month in the US. Typical dose is 2.5-10g of 1% gel applied daily but must be individualized for each patient.[29] Each gram of the 1% gel contains 10mg of testosterone, of which only 9-14% is absorbed.[30] So if 5 g of gel is applied daily, 9-14% of the 50mg (4.5-7mg) should be systemically available. Genitals should be avoided when applying testosterone gel because a greater proportion of testosterone applied to genital skin is converted to DHT. Applying the gel over a larger surface area may produce a small to moderate increase in total absorption and mean serum androgen levels when compared to application over a smaller surface area.[31]

Because of the risk of interpersonal transfer, consistent hand washing after use and avoidance of skin to skin contact with vulnerable persons after application should be emphasized to patients. If inadvertent exposure happens, the manufacturer of AndroGel® recommends washing the area immediately with soap and water. Testosterone gel should only be applied to clean intact skin. Showering or swimming should be avoided for at least one hour but ideally six hours after application to prevent adverse effects on absorption. In addition, skin to which testosterone gel has been applied should not be covered with clothing until complete drying has occurred.[32]

Two commercial formulations are available in the US AndroGel® and Testim®. A single small study reported somewhat increased serum levels and bioavailability of testosterone with Testim® when compared to AndroGel®.[33] However the clinical significance of this is unknown, and both formulations are used successfully.

Patches (2.5 and 5mg size) slowly diffuse testosterone through skin and are replaced daily. Cost is about $120-200/month in the US. Dosages range from 2.5-7.5mg daily.[34] Because of skin irritation, rotation of sites is probably more important with patches than with gel. Irritation is more severe when patches are applied over bony prominences or areas that are exposed to prolonged pressure.[35] A small open label study demonstrated that skin irritation can be alleviated by applying a tiny amount of 0.1% triamcinolone cream onto the site prior to application.[36] Caution must be taken by patients that their intimate partners (especially female bed partners and young children) not be inadvertently exposed to displaced patches. After removal of the occlusive patches, residual testosterone may remain on the skin temporarily and transfer may occur with skin to skin contact.

Subcutaneous Implants

Testosterone pellets were one of the first effective forms of testosterone replacement in men in the 1930s. Multiple pellets are inserted under the skin with a trocar every three to six months. This must be done in a physicians office, but is a relatively minor procedure done under local anesthetic. The only brand name pellet available in the US is Testopel® (75mg) which cost $15-20 each. The trocar kit sold by the manufacturer (Bartor) costs approximately $150. Other pellet formulations are available in the US through some compounding pharmacies and pellets as large as 200 mg are often used. Absorption approaches zero-order kinetics regardless of pellet size. Three 200mg pellets are therapeutically equivalent to six 100mg pellets.[37] Three to six 200mg pellets (600-1200mg) should provide physiologic testosterone levels for approximately four to six months, with each 100mg of pellet inserted delivering approximately 0.65mg of testosterone daily.[38] Total cost to patients may be greater than injected testosterone when the cost of the physician visit, supplies, and procedure are included but may be less than or comparable with transdermal. The primary advantages of pellets are that they give a much more constant blood level of testosterone than injections yet require attention at most four times yearly. Each insertion is associated with a transient peak of testosterone lasting 1-2 days. However this does not exceed the peak associated with each injection of bimonthly testosterone esters.[39] Pain or local irritation can occur and occasionally the pellets can extravasate.[40] This procedure is performed by some gynecologists (the pellets are inserted in the same manner as estradiol pellets.) Providers unfamiliar with the procedure may wish to refer patients to a gynecologist who is familiar with it. In addition to periodic pellet insertion, transgender men may benefit from an established relationship with a gynecologist sensitive to their medical needs who may help improve compliance with gynecologic screening. The major disadvantage of testosterone pellets is that if need arises for urgent cessation of testosterone, reversal is difficult and requires an invasive procedure.

Oral

Oral testosterone is rapidly absorbed and shunted to the liver via the portal circulation. This testosterone is rapidly degraded by the liver and results in a minimal amount of androgen reaching the systemic circulation. In addition these high levels reaching the liver also increase the likelihood of some of the potential adverse effects of testosterone including lower SHBG levels, hepatotoxicity, and lower HDL levels. Esterification of testosterone or addition of fatty acids decreases the hepatic first pass metabolism, so oral formulations are generally modified in this manner.[41] Moreover if taken with fatty acids, first pass metabolism is decreased which results in increased serum levels.

The 17-alkyl androgens (danazol, fluoxymesterone, oxandrolone) are inherently hepatotoxic and should be avoided.[42] The safest of the oral formulations is Andriol® (testosterone undecanoate.) This drug avoids significant first pass metabolism and much of the hepatotoxicity of oral testosterone by preferentially being absorbed through the lymphatics due to the addition of a long aliphatic chain.[43] Unfortunately, testosterone undecanoate is not currently available in the US, but is licensed in Canada and Europe.

For this reason, oral testosterone is infrequently used in the United States. Serum levels of testosterone are ten times higher when testosterone undecanoate is taken with fatty food when compared to the fasting state.[44] Therefor patients should be instructed to take the drug with food (preferably with some fat) to achieve best possible effects. Non-compliance with this instruction may be the cause of sub-therapeutic testosterone levels and inadequate masculinization.

Oral testosterone provides less fluctuation in serum levels than injected, however the first pass effect of the liver may result in testosterone levels too low to provide satisfactory masculinization and suppress menses.[45] In addition to lower testosterone blood levels, relatively *higher* DHT levels are often found with testosterone undecanoate.[46] Typical dose for testosterone undecanoate is 160-240 mg daily divided bid-qid. Cost is higher than injected, GI upset may occur, and compliance may be an issue due to necessity of multiple daily doses.[47]

Sublingual/Buccal

In 2003 the FDA approved a buccal form of testosterone (Striant®.) Sublingual testosterone can also be made by some compounding pharmacies. Price for Striant® is slightly higher than transdermal testosterone ($180-210/month.) Absorption of sublingual or buccal testosterone through the oral mucosa avoids the first pass hepatic metabolism of oral testosterone as the venous drainage of the oral mucosa is directly into the superior vena cava. Striant® lozenges can cause gum irritation, taste changes, or headache. However the majority of side effects diminish after two weeks. The lozenge is 'mucoadhesive' and will soften but not dissolve completely. It must be removed from the mucosa when the next lozenge is applied. Levels of testosterone peak within hours and remain in the eugonadal range achieving a steady state within 24 hours with consistent twice daily dosing.[48] Serum testosterone levels are reported above the lower limit of normal for males approximately 80-100% of the time with Striant®.[49,50,51] Total testosterone delivered is comparable with or greater than transdermal testosterone.[52,53] However dosage titration is not possible with Striant® (available in a single 30 mg dose) for transmen who may require more or less testosterone. Difference in efficacy and tolerability in transgender males is unknown, and studies in cisgender (non-transgender) males may not be generalizable.

Approximate Cost Comparison

This is based largely on non-compounded prices quoted in late 2004 by several US retail and internet pharmacy chains. Compounded formulations may well be substantially less. The cost for Testopel® is based on the manufacturers information and does not include physician procedure fees.[54]

Formulation	***Dose***	***Approximate Monthly Cost (USD)***
Androgel®	5mg/day	160-210
Androderm®	5mg/day	120-200

Formulation	*Dose*	*Approximate Monthly Cost (USD)*
Testopel®	5 pellets plus trocar kit q3months	80-90
Injected Enanthate	100mg/wk	35-50
Injected Cypionate	100mg/wk	25-35
Testim®	5mg/day	160-210

Non-Testosterone Hormonal Therapy

Depo-Provera®

Generally after the first cycle, menses are greatly reduced or eliminated. This may be useful for transgender men prior to initiation of testosterone therapy to reduce or eliminate vaginal bleeding which may be a source of distress for some transmen. Depo-Provera® is relatively inexpensive, readily available, and also prevents unintended pregnancy in sexually active bisexual and homosexual transmen. In November 2004 however, the FDA issued a black box warning for Depo-Provera which states that prolonged use can result in decreased bone density. The FDA warning states that a woman should use Depo-Provera® long term (greater than 2 years) only if no other birth control methods are adequate. Physicians and patients must weigh the risks and benefits of this treatment, however short term use may be reasonable as a temporizing measure until full hormonal transition is begun.

Andro 'Pro-hormones'

These drugs are available in the US without a prescription as 'dietary supplements.' Androstenedione, 4-androstenediol, 5-androstenediol, 19-androstenediol, and 19-norandrostenediol are purported by their advocates to increase serum testosterone, increase muscle mass, decrease fat, elevate mood, and increase sexual performance (i.e. many of the effects transgender men seek with androgen therapy.) Unfortunately, there is no robust evidence that the pro-hormones do any of these things in cisgender men.[55,56] However, ***there is evidence*** that ingestion of these substances can cause elevated estrogen levels and decreases in HDL cholesterol.[57] In women, oral androstenedione does cause increases in serum androgens, however, increases in SHBG and estrone are also demonstrated.[58,59,60] Additionally, in women with polycystic ovarian syndrome (PCOS,) the oral administration of the supplement dehydroepiandrostenedione (DHEA) results in increased DHT due to increased peripheral 5-α-Reductase activity when compared to normal women.[61] Transmen have an increased prevalence of PCOS, and patients with this disease may possibly increase their DHT levels with use of DHEA. However, in general, DHEA acts as a pro-hormone for metabolites with predominantly *estrogenic* effects.[62] Therefor the effects that DHEA will produce in any particular transgender man are unpredictable.

In women, DHEA has been shown to result in improvements in libido and sexual function, mood and well being.[63] The effect of DHEA on CAD risks are inconsistent and point to no definite conclusions.[64] However, regardless of purported efficacy, the safety of all of these dietary supplements in long term treatment has not been determined, *especially* in the unique population of transgender men. Moreover, as with all dietary supplements in the United States, there is little or no government regulatory oversight with regards to safety and actual content of dietary supplements. Supplements may not contain the substances listed on the label, may contain different amounts of the substances than listed, and may even contain other substances not listed. A study of the content of several DHEA dietary supplement products showed a wide variation in drug levels. Products ranged from no measurable DHEA to 149% the package's stated content.[65]

One useful reference that may be presented to transmen who consider taking dietary supplement pro-hormones is a 2004 Consumer Reports® article on dietary supplements. Androstenedione was specifically cited as one of the "twelve supplements you should avoid."[66] While the medical literature can sometimes seem daunting, unfamiliar, and contradictory, Consumer Reports® is a respected and familiar publication that many patients trust.

In summary, providers should be aware of the use and availability of these 'dietary supplements' and counsel patients about the risks of taking these unregulated drugs. Often, transmen use these as an alternative to testosterone out of desperation because they are unable to access medically supervised cross-gender hormonal therapy. Provision of appropriate and medically monitored therapy may decrease patients use of these alternatives which are of questionable safety and efficacy.

GnRH Agonists

It is increasingly recognized that gender identity disorder is not only a disorder of adults. While GID in children often does not result in transgender identity in adulthood, transgender adolescents generally have a stable gender identity that will persist as it does in transgender adults. Therefor, while somatic therapy could not be recommended in children, adolescents are increasingly presenting with requests for treatment. Moreover, early treatment has notable advantages with regards to final outcome. While treatment in adults in many ways seeks to undo the pubertal changes previously experienced by patients, treatment in adolescence could theoretically prevent some of these changes. In addition the desperation, suffering, and intense feelings of isolation experienced by transgender youth going through a puberty alien to their gender identity might be partially ameliorated. However, cross-gender hormonal therapy will produce irreversible changes in adolescents before they are able to make informed decisions and fully consent to treatment. Therefor therapy to delay puberty may aid in treatment of transgender youth to delay this decision to a later time.

In both sexes, the hypothalamus releases GnRH (Gonadotropin Releasing Hormone) to stimulate the pituitary to produce LH (luteinizing hormone) and FSH (follicle stimulating hormone,) which in turn signal the gonads to produce sex steroids. In transgender adolescents of either sex, GnRH agonists may be considered to delay puberty which will make subsequent therapy in adulthood more effective.[67,68] GnRH agonists initially over-stimulate the pituitary then rapidly desensitize it to the effects of GnRH. Over a period of weeks, gonadal steroid production is greatly reduced. The most significant problems with this therapy are the *very* high cost, the medical and psychological risks associated with a developmental delay in children who would otherwise be pubertal, and a risk of local reactions to injected forms (occasionally severe.) An additional benefit for transgender boys treated for years with GnRH agonists may be the potential for a modest (about 1cm/year of treatment) increase in final adult height.[69] However, in studies of children treated with GnRH agonists to induce growth, a delay in puberty may be associated with impaired bone development which may predispose to later osteoporosis.[70,71]

Depo-Lupron®, the most frequently used GnRH agonist in the US has been found effective in 95% of children with central precocious puberty (pathologically early pubertal maturation in children due to increases in LH and FSH released by the pituitary) who were given 11.25 mg depot preparation every 3 months.[72] The lowest price found in a recent web search for Depo-Lupron® at this dose was $870. (www.e-DrugsCanada.com) Using this price, the cost for treating a pubertal transgender child from age fourteen to eighteen would be approximately $14,000. However, some physicians are beginning to advocate treatment of very select adolescents with cross gender hormonal therapy at an earlier age.[73,74] Unfortunately, little has been published to date regarding this treatment. This early cross gender hormonal therapy would, in the case of transgender adolescents, be significantly less expensive than GnRH agonists. In addition, it would allow transgender adolescents to experience a more normal puberty appropriate to their gender identity.

HBIGDA is currently evaluating the provision of care to adolescents and it is expected that version seven of the SOC will provide more guidance for the treatment of transgender youth.

Other Uses For Androgen Therapy

- At low doses, testosterone is increasingly used to improve sexual function, muscle and bone mass, and energy levels in post-menopausal women. This is especially the case in those who may have a relative deficiency of androgens such as after bilateral oophorectomy or adrenal failure.[75,76]
- AIDS wasting in men and women (for the anabolic rather than androgenic effect.)
- Hypogonadal men – whether from disease or age related changes.[77]
    - In healthy men there is a normal age related decline in testosterone levels.
    - This decline is generally gradual rather than the abrupt decline in hormonal activity found in menopausal women.

- This decline is not as universal or profound as menopause, with many elderly men having normal testosterone levels.
- Only some older men who have low testosterone levels will have clinical symptoms of testosterone deficiency.

Chapter 3 - Risks of Non-Provision of Hormonal Therapy to Transgender Patients

Transsexual patients who present for treatment are almost universally highly motivated and often anxious to pursue medical and surgical sexual reassignment. By the time a transgender man seeks medical care to pursue hormonal therapy, he has often acquired a great deal of information from reliable as well as possibly more dubious sources. Often he has seen a psychotherapist who may or may not have diagnosed him with Gender Identity Disorder (GID) and referred him for therapy. Occasionally he may have already begun non-medically supervised hormonal therapy with its increased risks.

The provider approached for hormonal therapy therefor must have a frank and open discussion with her patient with regards to his knowledge, expectations, and previous use of androgens. It is critical to discuss this with a non-judgmental attitude as patients may be less than forthright if they feel their access to hormones may be jeopardized by full disclosure.

In some cases providers may feel a patient is unready for social, medical, or psychological reasons to undertake hormonal therapy. If this is the case, it is *critical* to discuss this honestly with patients and to fully disclose provider concerns. It is also imperative to indicate the steps that the provider and patient may take to rectify the provider's concerns to meet the patient's ultimate goal of satisfactory and safe sexual reassignment.

Providers must however, consider not only the adverse effects of providing hormones but the adverse consequences of *denying access* to medically supervised hormonal therapy.

Patients unable to access medically supervised therapy may use 'dietary supplements,' buy hormones on the street, and may share prescriptions for hormones as well as needles for injection. The risks of blood borne infections can be substantial in some transgender populations.[1] If illicit use is known, providers may counsel against such use. However, even if the provider does not wish to prescribe hormones, provision of clean needles to patients is one harm-reduction option available. This will help assure the patient both that he may feel safe disclosing his practices and that his provider's primary desire is to protect his health. Moreover, patient honesty regarding non-prescribed hormonal use may allow providers to more appropriately provide medical screening which will be described later. As is the case with patients who are non-compliant with other recommended health behaviors (smoking cessation, safe sex practices, diet, etc.) care and monitoring should still be provided to minimize the adverse consequences of *actual* patient choices and behaviors. Just as a patient with diabetes mellitus would not be denied appropriate prevention, screening, and treatment despite non-adherence to an ADA diet, patients who choose to use non-prescribed hormones should be monitored and treated appropriately based on the hormonal therapy they *are actually using*.

Moreover, in addition to the purely medical risks of unsupervised hormonal therapy, non-treatment of transgender patients can result in significantly worse psychological outcomes. Suicide rates are significantly lower in treated transgender patients than in non-treated. Untreated transsexual patients have suicide rates as high as 20% while treated transmen have suicide rates of less than 1%.[2,3] Interestingly, while in the general population, cisgender females attempt suicide more than twice as frequently as cisgender males, studies of transsexual patients show a higher number of suicide attempts in transgender females rather than transmen.[4] It appears that in this psychological variable, transsexual women more closely resemble cisgender women and transsexual men more closely resemble cisgender men.

Transgender patients, by virtue of their gender identity are also at significant risk for harassment and hate-related violence.[5] Unlike many transgender women, some transmen report a decrease in such dangers of interpersonal harassment and violence when they transition as the effects of testosterone make them more readily able to 'pass' in society.

Another concern sometimes expressed by providers as a reason for hesitating to provide hormonal therapy is the possibility that patients will be unhappy with the results of sexual reassignment and will regret having undertaken such treatment. This is especially a fear in transmen due to the efficacy of testosterone in producing dramatic and sometimes irreversible male secondary sexual characteristics. However in actual practice, the vast majority of patients are satisfied with therapy and true regrets are quite rare.[6,7,8]

In summary, providers should realize that while there may be some risks for patients who undertake hormonal reassignment, there are *probably far greater* risks associated with non-provision of such care. While the dictum *primum non nocere* is important, it is crucial to consider the entire quote from Hippocrates' *Epidemics*: “As to diseases, make a habit of two things - ***to help***, or at least do no harm.” Inaction due to an unrealistic fear of *possible* adverse events may actually harm the patient more than the proposed treatment itself.

Therefor the personal feelings of reticence individual providers may have toward prescribing cross gender hormonal therapy as 'altering' a normal healthy body should be examined. For a transman, a female body is *neither normal nor healthy* and failure to address this may have disastrous consequences for the patient. No provider would hesitate to offer a largely safe and effective treatment that *decreases the relative risk of a life threatening outcome by 2000%!* Yet providers do hesitate to offer androgen therapy to transsexual male patients despite a decrease in sucidality from approximately 20% to less than 1%. (Absolute risk reduction ~ 20%, relative risk reduction ~ 2000%.)

Simply because a disease or patients with that disease challenge societies norms or may engender personal discomfort in us, this does not relieve us of our responsibility as health care providers: to provide our patients with the care that offers them the best quality and quantity of life possible. Indeed, it is these situations precisely that allow us to perform the service for which most providers initially entered medicine: healing.

Chapter 4 - Informed Consent

Testosterone therapy causes permanent physical changes as well as a risk of possible adverse effects. As such, informed consent is imperative. With hormonal therapy for sexual reassignment, the physician's task may be complicated by the pre-existing knowledge that many transgender patients bring with them. This knowledge can be both a benefit and a detriment to ensuring that patients make a truly informed decision. Many patients have read extensively about hormonal therapy and may already have a significant understanding of testosterone use (occasionally surpassing their provider's!) However, their sources of information may not have been entirely accurate or may have downplayed the possible adverse effects while suggesting unrealistic expectations for outcomes.

In addition, some patients who believe they are well informed may perceive a discussion of risks, benefits, and alternatives as unnecessary, intrusive, and occasionally even offensive. However, while this may complicate the provider's task, it does not obviate the need for such a discussion. Moreover, while some patients might be less than appreciative of provider education, many transmen report that they would prefer more knowledgeable providers who can inform them of the risks, benefits, and alternatives of testosterone therapy.

The following is an example of an informed consent form that might be utilized to start this discussion with patients. Additional examples of informed consent information for transgender patients has been previously published.[1]

Patient Informed Consent Information

Testosterone treatment will cause some permanent and many reversible changes in your body. Some of these changes you may want (like facial hair and a deeper voice) but some you may not (like baldness.) Before you start taking testosterone, it is important that you have a good understanding of these effects as well as the risks involved in taking testosterone. If while reading this form you have any questions, make sure you discuss them with your health care provider so you have a realistic expectation of what ***will*** happen and what ***may*** happen.

It is also important that you understand that testosterone is not the only way that all FTM transgender patients choose to be treated. Just as chromosomes and genitals do not define your gender identity, neither does which hormones are in your body or what surgeries you choose to have. So it is important that you decide what goals you would like to achieve in your treatment and discuss these with your health care provider. Deciding not to take testosterone, to delay taking testosterone, or to take a lower dose than others does not make you 'less trans.' Gender identity can only be determined by you based on how *you feel inside*, not the choices you make about your medical care.

Permanent Changes

These will <u>not go away</u> if you stop taking testosterone
Will Happen:

- Increased facial and body hair. Not just on your face, chest and stomach. You may also get hairs on your back, buttocks, and even in your ears.
- Deepened voice.
- Clitoromegaly (enlargement of the clitoris to an average of 4-5 cm after 1-3 years).

May Happen:

- If you have not finished puberty, you might have a growth spurt and closure of growth plates.
- Male pattern baldness (may be partially treatable with certain medicines.)
- Changes in your ovaries that may make it difficult or impossible for you to produce eggs or get pregnant even if you stop taking testosterone.
- Possible but uncertain increases in risks of ovarian or uterine cancer.
- Changes in your uterus (like fibroids) or ovaries (like cysts) that may make hysterectomy (removal of uterus) and oophorectomy (removal of ovaries) more difficult if you eventually choose to have these surgeries.
- Rarely, benign or malignant liver tumors or other liver disease (mostly with transmen who take testosterone pills by mouth.)
- Possible but uncertain increase risk of developing osteoporosis (thinning and weakening of bones) that may become worse after oophorectomy or if you stop taking testosterone.

Reversible Changes

These occur with testosterone treatment but generally will go away if you stop taking testosterone

- Increased libido (sex drive) and changes in sexual behavior.
- Increased muscle mass (especially upper body strength.)
- Redistribution of fat to a more typical male pattern (to the stomach instead of the hips and thighs.)
- Interference with other medications that you may take.
- Increased sweat and changes in body odor.
- Increased appetite, weight gain, and fluid retention.
- Prominence of veins and coarser skin.
- Acne of the face, back, and chest, especially in the first few years of treatment (which if severe, may cause ***permanent*** scarring.)
- Emotional changes (both good and bad.)
- Worsening of blood cholesterol levels which might increase your risks of heart attacks and strokes.
- Increase in red blood cell count (which rarely, if severe and untreated can make you more likely to have strokes, heart attacks, or blood clots.)
- Stopping menstruation (periods.) This may take several months or may be immediate.

- Vaginal dryness and itching that may even occasionally cause pain with vaginal penetration.
- Worsening of or increased chance of getting certain diseases. If you think you have or are developing these diseases, it is important to tell your doctor. They can be treated and having them doesn't necessarily mean you have to stop taking testosterone.
    - Type 2 diabetes
    - Liver disease
    - High blood pressure
    - High cholesterol
    - Heart disease
    - Migraine headaches
    - Sleep apnea
    - Epilepsy (seizures)

Consent

I have read and understand the above risks and benefits of testosterone therapy. I have had a chance to discuss this with my health care provider, _____ and to ask and have answered any questions I might have.

I understand that there are very few total number of transgender patients who have been treated with testosterone and that because of this, the long term effects are not well-studied or fully understood. There may be important risks or benefits that are not listed above that medical science does not yet know.

I identify as having a male/masculine gender identity and therefor wish to be treated with testosterone.

I understand that testosterone treatment may make it necessary that I have more health care screening tests than other female-bodied people my age.

I understand that taking testosterone does not make me immune to, and in fact may possibly increase my risk to develop certain gynecological problems including cancer. I understand that even if I have a hysterectomy (removal of the uterus) and oophorectomy (removal of the ovaries) I must still continue yearly gynecological exams and screenings (either with my provider or another provider of gynecological care who is aware of my transgender status.)

I have discussed with my provider options for retaining my fertility. I understand that being transgender does not necessarily preclude future reproduction and/or parenting. However I understand that pursuing hormonal therapy may make it more difficult or even impossible for me to have a genetic offspring in the future. I have discussed my desires

and choices with my provider and feel comfortable that I have made an informed decision about my future reproductive options.

I understand that fertility (ability to become pregnant) will not immediately cease when I start testosterone. I understand that it is imperative that if I have vaginal sex with men, I must use a barrier method until my periods stop for at least two months. I understand this is because testosterone can cause major birth defects if I become pregnant while taking it.

I understand that testosterone is a DEA controlled substance (like narcotic pain medicines and some sedatives) and that it is illegal to share these medicines to other people. I also understand that sharing needles with anyone can place me at risk for blood borne diseases like HIV/AIDS and hepatitis.

I understand that an open and honest relationship with my health care provider is essential to keeping me healthy and safe. I agree that I will share with my provider any physical problems or side effects that I may develop especially if I think they are caused by testosterone. I understand and expect that I will never be penalized for my honesty about my body.

Signed _____

Printed Name _____

Date _____

Witness _____

Printed Name _____

Date _____

Chapter 5 – Surgical Summary

It is not the goal of this text to provide detailed information about the surgical procedures that transgender men may choose. However, the following brief description of some of the more common procedures will provide a background from which providers may seek further information.

It should be remembered that not all transgender men may be candidates for, may choose to have, or may be able to afford any or all of these procedures. What medical and surgical therapy a transgender patient has or will undertake should neither cast doubt on the veracity of his diagnosis nor suggest that he is not 'yet' a male. A transgender man who is unable to afford a desired mastectomy is no 'less trans' or 'less male' by virtue of his socioeconomic status than is a diabetic 'less diabetic' because he cannot afford medications. Moreover, as with any diagnosis, a patient who chooses not to have surgical intervention because for him the risks outweigh the benefits should not generally have his diagnosis subjected to further scrutiny. Just as with any other medical condition, patient autonomy and right to make a truly informed decision is paramount.

Of all surgical procedures, the most common is some form of chest reconstruction to provide transgender men with a more normal appearing male chest. Many transmen also choose to have some form of gynecological surgery to remove female reproductive organs. Only a minority due to personal preference, medical constraints, or financial difficulty are able to have some form of true genital reconstruction.

Chest Reconstruction Procedures

Mastectomy, Bilateral Periareolar

This procedure involves the removal or reduction of the breasts by making a small incision around the nipple and removing most of the tissue and fat from under the skin. This results in a chest shape that appears more masculine but does not completely approximate the male chest in that nipple size and position may be more female in appearance. This is often not feasible for transmen with breasts larger than A or B cup or breasts that are significantly ptotic, and in general the larger and more ptotic the breast, the worse the outcome. Subsequent procedures to alter the location and contour of the nipple may be needed.

Mastectomy, Bilateral Complete with Nipple and Areola Reconstruction

This procedure involves removal of the breasts by making incisions below the breasts, performing a complete mastectomy, resizing the nipple/areola complex (NAC) and grafting it into a more typical male position. Compared with periareolar mastectomy, there are larger scars, more damage to sensation of the chest (and permanent loss of sexual sensation in the nipples,) and more danger of losing the grafted nipple permanently due to subsequent necrosis and sloughing. The result, while less aesthetically pleasing

because of scars more closely resembles a true male chest in contour, nipple size and location. This procedure may be done on transmen with even quite large and ptotic breasts and may afford them the best aesthetic result overall.

Mastectomy, Bilateral Complete with Nipple Pedicle

This procedure is similar to the bilateral complete mastectomy with NAC reconstruction however, instead of removal of the NAC, it is left in place via a stalk of tissue, and is threaded through the chest at a more normal position. This is a more complex technique and may not give as ideal cosmetic results as reconstruction of the NAC, but it may allow for preservation of sexual sensation to the nipples.

Mastectomy, Scar Revision

While the scars created by a patient's first surgery may be large because of the necessity of other components of the procedure, these scars may be electively revised later when healing is complete from the first surgery (generally after at least six months to a year.) While the goal is creating scars that are cosmetically less apparent, complete removal of scars is never possible.

Genital Reconstruction and Related Procedures

Metoidioplasty

This procedure involves the creation of a very small penis (neo-phallus) by extending and repositioning the clitoris that has been enlarged by testosterone therapy. The skin and tissue around the clitoris is modified so that the clitoris can extend from the pubic region and appear as a small penis. Liposuction in the pubic area may help create a more male appearance by making the neo-phallus appear more pronounced. Some surgeons also augment the size of the neo-phallus by bulking it up with other tissue. The resulting penis is however, significantly smaller than the smallest adult male penises and its use in penetrative sexual intercourse is severely limited. However it is felt by many patients that with this procedure, the greatest amount of sexual function and pleasure is preserved for the transman. Additionally, unlike a phalloplasty, the resultant penis is generally able to gain erections naturally.

As with any genital surgery however, the risk to sexual function is significant and this or any genital surgery may rarely result in complete or near complete genital sexual dysfunction. Additionally, this surgery cannot be performed until the individual has been on hormonal therapy for two or more years and the clitoris has enlarged sufficiently to produce the largest possible penis for the patient. Of genital reconstructions, this is probably the most common and the least expensive for transmen who undertake genital surgery.

Metoidioplasty With Urethroplasty

This procedure is a metoidioplasty as above with the additional of an extension of the urethra through the neo-phallus which is generally created from harvested vaginal mucosal tissue. This procedure is performed so that patients may gain the additional frequently desired functionality of urinating through the neo-phallus while standing. Risks include fistula formation, incontinence, and recurrent urinary tract infections with resulting risk of damage to the entire urinary tract.

Abdominoplasty

An abdominoplasty (tummy tuck) may also be desired either prior to or concurrently with a metoidioplasty in order to make the neo-phallus appear larger by decreasing the visual effect of the protruding abdomen.

Free Flap Forearm Phalloplasty

This procedure involves construction of a neo-phallus from non-genital tissue of the forearm and attaching it in the appropriate position to approximate a male penis. The neo-phallus is generally formed from tissue taken from the inner forearm skin (on the patient's nondominant side) as well as vaginal tissue to form the neo-urethra. The forearm tissue including nerves and vasculature are grafted after the neo-phallus is formed into a tube around a catheter. The neo-urethra is attached to the native urethra and allows for urination while standing. The nerves of the clitoris are sometimes attached to the grafted cutaneous nerves and hopefully will grow into the neo-phallus after surgery allowing for some retention of sexual arousal and gratification. Some surgeons, however, leave the clitoris intact beneath the neo-phallus or within the constructed neo-scrotum so that it can be stimulated independently of the neo-phallus. Advantages include a larger neo-phallus that may more closely resemble the normal male penis. However phalloplasty often requires multiple surgeries and up to a year of recovery. Moreover, the significant scarring and risk to function of the forearm and hand (as well as the risks of any genital surgery for sexual dysfunction and urinary complications) make the procedure unacceptable for many transgender men. Lastly, in general, phalloplasty is significantly more expensive than metoidioplasty so it may not be an option for many transmen even if it is the procedure they may prefer.

Abdominal Pedicle Flap Phalloplasty

This procedure is similar to the forearm flap technique except that the donor site is tissue on the abdomen or waist. The tissue is rolled into a tube and, over a period of up to two months, is progressively shaped and separated from all of its original blood supply except for the small pedicle that attaches it to the lower abdominal wall. Later, when the phallus has developed a reliable blood supply, it is further detached to hang in the groin area and subsequently shaped to look more like a typical male penis. Complications are similar to those with forearm flap phalloplasty, but sensation is often considered to be inferior. The main advantage is trading a more readily apparent forearm scar for a less visible scar on the abdominal wall. Again multiple procedures are required and recovery can be

prolonged. This is probably the least common of the currently used genital reconstructions for transsexual males in the United States.

Penile Erectile Prosthesis Implantation

Often techniques like those used in impotent cisgender men, can be performed after completion and full healing from phalloplasty to achieve erectile function in the neo-phallus. While these techniques do not reproduce erections in genetic men or improve sexual sensation, they do allow for penetrative intercourse. Complications can include component failure, device erosion or migration, sizing problems, and auto-inflation. Infection occurs in approximately 2-3% of primary implant surgeries and may require removal of the prosthesis and result in significant scarring of the neo-phallus.

Scrotoplasty With Insertion of Testicular Expanders

This procedure produces a male appearing scrotum from skin and soft tissue of the labia. Subsequent insertion of testicular expanders that can be enlarged slowly over months increases the size of the neo-scrotum until it can accommodate typical male size scrotal implants. This is an additional procedure to either phalloplasty or metoidioplasty but frequently is performed with them in transgender males who pursue genital reconstruction.

Colpectomy (Vaginectomy)

This procedure removes the vagina to approximate a more male appearing perineum. The principal risks of this procedure are significant blood loss, damage to the bladder, and damage to the rectum even in the hands of an experienced gynecologist. Blood loss requiring transfusion is not infrequent and carries all of the intendant risks. Additionally, the blood loss itself may pose a more serious surgical risk to people with other medical problems, making this a less frequently performed procedure. When undertaken, it is sometimes performed in conjunction with scrotoplasty.

Colpoplasty (Vaginoplasty)

This is a newer procedure to reconstruct the perineum that involves closure of the perineal opening of the vagina while opening the cervical end of the vaginal vault into the abdominal cavity. This results in an 'inversion' of the vagina and has less operative risk than full vaginectomy. This is a more recently developed technique and may come to replace colpectomy as the procedure of choice for transsexual men who require reconstruction of the perineum. However, unlike a colpectomy, residual vaginal epithelium exists- now as part of the abdominal cavity. This should not result in any increase in malignant transformation, however it would prevent easy surveillance for vaginal cancer by pelvic exam and PAP smear. Moreover, unlike cervical cancer, vaginal cancer is more multifactorial in etiology. Known risk factors include HPV infection, history of cervical neoplasia, immunosuppression, radiation and chemotherapy, infection with herpes simplex virus or *Trichomonas vaginalis,* and tobacco abuse. However, some women with vaginal cancer have no known risk factors, so there is no female-bodied person (transman or cisgender woman) who can be thought to have zero risk.[1] Moreover,

while fortunately primary vaginal cancer is much more rare than cervical cancer with an incidence of 0.1-0.2 per 100,000 women[2], this is likely in part due to detection while at the stage of VAIN (VAginal Intraepithelial Neoplasia) from surveillance PAP smears. A colpoplasty that leaves residual vaginal tissue that is not available for surveillance would almost certainly increase the risk of *progression of* vaginal carcinoma if it developed in a transman.

Colpocleisis

A third alternative to perineal reconstruction is colpocleisis. In this procedure, the mucosa of the vagina is ablated and the muscular walls of the vagina are fused together. This procedure is generally performed in older women who are no longer sexually active as a treatment for severe vaginal vault or uterine prolapse. Even in the frail elderly patients in whom this procedure is generally performed, there is a low complication rate. The advantage to this procedure is that it has much less risk of damage to pelvic organs or of blood loss significant enough to warrant transfusion as in colpectomy. In addition, little or no vaginal mucosa unaccessible for monitoring remains as it does with colpoplasty.

Other Transgender Related Surgical Procedures

Hysterectomy with Bilateral Salpingo-Oophorectomy

This is essentially the same procedure performed in cisgender women which involves removal of the uterus, both ovaries, and both fallopian tubes. While not required for most transgender men to have a functional external male presentation and male hormonal milieu, some transmen find that this surgery is 'emotionally necessary' (they feel uncomfortable as males who have female internal genitalia.) In addition, removal of these organs decreases (but does not eliminate) the risk for subsequent gynecological tumors. Since transgender males historically have had difficulty securing adequate and sensitive gynecological preventative care, removal of these organs may be the only way that the risk of advanced ovarian, uterine, or cervical cancer is acceptably decreased. Risks include incontinence, injury to bladder or bowel, formation of abdominal adhesions (and the subsequent risks of chronic pain and bowel obstruction that come with any abdominal surgery.) Additionally, with oophorectomy any chance of further reproduction (even with assisted reproductive technology) is completely eliminated unless ovarian tissue banking or embryo banking is used.

Notably, if patients plan further eventual genital reconstruction, it would be advisable to consult with their planned genital surgeon first, as hysterectomy technique may effect future surgical outcome. Consultation in advance with the gynecologist performing the hysterectomy may improve subsequent reconstruction outcome.

Liposuction to Reduce Fat in Hips, Thighs, Buttocks

While testosterone therapy alters body fat composition and fat location, with some transmen, this process is not adequate to produce a sufficiently male body contour.

Liposuction can be done to improve body contour but this procedure is more often than not, unnecessary.

Chapter 6 - Health Maintenance for Transgender Men

The following is a theoretical ***ideal*** health monitoring schedule for transmen *in addition to* other age-appropriate health maintenance.[1,2,3,4,5,6] It represents the *sum* of all recommendations from a number of different sources. No single author has included all of these and it should *not* be assumed that these are all a requirement for provision of quality, safe cross gender hormonal therapy. It is presented to help providers consider the spectrum of monitoring possibilities when deciding which regimen she will ultimately select for her patients. At the end of this chapter, the authors' own preference for clinical monitoring will be presented as an example of what we choose to undertake in actual clinical practice.

In general, it is probably safest to assume that patients should be screened according to whichever sex has the greater risk for the disease being considered. For example, with osteoporosis transgender men should be assumed to have the risk of a woman, for cardiovascular disease that of a man.

The monitoring suggested for transgender men on testosterone therapy is often more extensive than that suggested for cisgender males receiving the same medications in the same doses.[7,8,9,10,11,12] This is likely is due to two motivations on the part of providers. First, the evidence for the safety and efficacy of testosterone therapy in transgender men is minuscule when compared to studies of testosterone replacement in cisgender males. This is due to both the fact that transmen are a much smaller target population as well as the fact that studies of transgender patients may be inadequately supported or funded.[13] While evidence of safety for testosterone replacement in cisgender males is reassuring, there is a real possibility that these results may not be completely generalizable to the transgender male population. The second motivation for providers to perform more intensive monitoring is that testosterone is considered largely a 'foreign' hormone for female-bodied patients. Providers are aware that men have shorter life expectancy and are at greater risk of developing certain health problems. The most obvious systemic difference between men and women is the difference in sex steroids, so it seems logical to attribute the increase risk in cisgender males to the ongoing effect of sex steroids. Therefor providers may see testosterone therapy for female-bodied patients as an *inherent* risk that may jeopardize the principle of *primum non nocere*. Naturally a provider, when using a therapy she perceives as inherently risky or potentially harmful, will tend to advocate more intensive monitoring to detect any adverse effects that may be caused by the therapy. (If a provider cannot 'do no harm' she would at least like to detect any harm as early as possible!) However, the increase risk in cisgender men may be a correlation rather than a causation, and studies have actually demonstrated *decreased* cardiovascular risk in cisgender males with testosterone levels at the higher end of the normal range.[14] So the *post hoc ergo propter hoc* assumption may be invalid in this case.

Unfortunately, a simple definitive answer to these questions is not known. However these uncertainties are presented here so that providers will understand that these suggested

screening schedules are often a cautious 'best guess' of professionals in the field rather than truly evidence-based screening recommendations.

There are however, some recommendations that are reasonably consistent between both the literature regarding transmen as well as cisgender men. They represent the *minimum monitoring* that has been advocated for *any* population treated with testosterone (in addition to other appropriate health maintenance screening based on individual risk factors.) These include: follow-up assessment every 3-6 months during the first year or two and yearly or biannually thereafter, assessment of symptomatic response to therapy at each visit, monitoring clinically for signs and symptoms of diseases that may be unmasked or made worse by testosterone therapy (like obstructive sleep apnea,) as well as possible interval monitoring of hematocrit (especially in older patients.)[15,16,17,18,19,20] If the list presented below is the sum (maximum) of all recommendations, these are the consistent recommendations included by almost all sources, that is the bare minimum.

Lastly, providers should remember that the bulk of recommendations for health maintenance and screening are *irrespective of the sex of the patient* and are based on guidelines that are appropriate to both men and women whether or not they are transgender.

Costs

It is important for providers to be aware that their patients frequently pay for part or all of their transgender related care out of pocket either because they lack insurance or their insurance plan refuses to pay for transgender related care. Providers should be sensitive to this when deciding what tests patients should undergo. Moreover providers may be called upon to advocate for patients with regard to insurance reimbursement if patients request this. While some insurance providers may reject out of hand payment for a PAP smear for a patient who is listed as male on his insurance policy, a letter from the patient's provider explaining the circumstances may help. Some patients, however, prefer this information withheld from their insurance providers because of sometimes realistic fears that they will lose some or all of their coverage. So individual patients should be consulted regarding preference. Patients are justifiably cautious about such revelations because transmen have historically experienced significant discrimination from health insurance providers when transgender status was disclosed. While many insurance companies deny payment for 'transgender related care,' some have in the past taken this to mean *any* care for a transgender patient. For example, transgender people have been denied care for bronchitis, shoulder bursitis, and extremity lacerations simply because these illnesses occurred *in a transgender patient*.[21]

Fortunately, this medical-insurance based discrimination toward transgender patients is gradually being successfully challenged. Several countries now include transgender related care within national health insurance plans. Medi-Cal (the California Medicaid program) now pays for transgender related care and Medicaid exclusions in other states are being challenged currently.[22,23] In addition, recently a large US insurance provider

(Aetna) concluded that the scientific evidence supported the medical necessity and safety of transgender related care and has changed their corporate policy of excluding transgender related care from all insurance policies.[24] Kaiser has also amended their policy and pays for some transgender related treatments.

However, most transgender patients in the US still pay out of pocket for some or all of their medical costs. Therefor it is important that providers balance appropriate screening with reasonable expenditures for their patients. Patient autonomy, safety, confidentiality, and the adverse consequences of non-treatment or non-medically supervised treatment must be carefully weighed when making these choices. Decisions are not easy and should always be individualized.

Before Initiation of Testosterone Therapy

- Complete History - including social, occupational/educational, sexual, family, and gender history. Emphasis should be placed on the potential effects of testosterone therapy on each of these areas. Includes assessment of prior hormone use (especially non-medically supervised treatment.) If patients have not yet had complete psychological evaluation, particular attention should be paid to psychological history as dual diagnosis is not uncommon in this population. The emotional and mental toll of longstanding gender non-conformity in a society that infrequently condones such behaviors can cause or exacerbate many other psychological illnesses. Family history should include: familial gynecologic and breast cancer syndromes and premature atherosclerotic disease as well as its risk factors such as hypertension, hypercholesterolemia, and diabetes. Use of tobacco, alcohol, and other drugs of abuse should be documented and appropriate counseling provided.
- Complete Physical - Physical exam must be approached with patience and sensitivity as patients may be uncomfortable revealing or even acknowledging some gendered aspects of their body. Exam should include palpation of the liver, clinical breast exam, pelvic exam (if not recently performed by another provider,) and assessment for pre-existing masculinization. Notably if a clinical chaperon is used for gynecologic or breast exam, when possible the patient should be consulted as to his preference for gender of chaperon. The assumption that transmen would prefer a female chaperon for gynecologic exam is sometimes wrong. Particular attention should be paid to diagnosis of polycystic ovarian syndrome (PCOS), as this disorder is much more prevalent in transgender men. Pre-existing masculinization may be due to PCOS, prior use – possibly unsupervised – of androgens, or rarely an undiagnosed intersex condition such as non-classical congenital adrenal hypertrophy. The prior use of androgens should be approached non-judgmentally as it is more likely to do with delay, desperation, and a lack of reliable providers than a preference for the patient to take hormones unsupervised.
- Informed Consent.
- Weight and Blood Pressure.

- Fasting Lipid Profile if indicated.
- Fasting Glucose or Hgb A1C.
- If sexually active with men, pregnancy test (if positive, testosterone therapy is ***absolutely contraindicated*** until the pregnancy is completed or terminated.)
- +/- Kidney Function (with or without urinalysis.)
- +/- Liver Function Panel (or ALT.)
- +/- Hormonal or Genetic Studies – possibly including estradiol, testosterone, prolactin, cosyntropin stimulation test, and LH (if indicated by history and physical.)
- +/- PAP and STD Screening (if not recently performed and/or if indicated by history and physical.)
- Mammography for pre-mastectomy patients if indicated according to general guidelines for females.
- Sleep study to assess for sleep apnea if this diagnosis is suggested by history and physical.

3-4 Months Follow Up After Initiating Testosterone Therapy

- Directed History and Physical again including social, occupational/educational, sexual, and gender history. Emphasis on the positive and negative effects that have occurred in these areas and any anticipated future problems. Gynecologic history should assess effects on menstruation. Assess for signs/symptoms of adverse effects of testosterone: fluid overload, sleep apnea, hyperglycemia, etc. Particular attention should be paid to the integument exam as acne is one of the most common adverse consequences of testosterone therapy.
- Weight and Blood Pressure.
- CBC or Hemoglobin/Hematocrit (to rule out polycythemia.)
- Fasting Lipid Profile.
- Trough Testosterone Level.
- Liver Function Panel (or ALT.)
- Fasting Glucose or Hgb A1C.
- Consider testosterone dose titration.

Every 6-12 Months

- Directed History and Physical which should include yearly pelvic exam if not performed by another provider. Breast/chest exam should also be included.
- Weight and Blood Pressure.
- PAP (if not otherwise eligible for less frequent screenings.)
- If pre-mastectomy, mammography based on standard guidelines for females.
- Once on appropriate stable dose for 6 or more months, if masculinization is inadequately progressing - LH level. (*It is not necessary to test* if adequate masculinization occurs *or* if LH is found to be adequately suppressed on a stable regimen.)

- Hemoglobin/Hematocrit.
- Liver Function Panel (or ALT.)
- +/-Trough Testosterone.
- +/- Lipid Panel (depending on age, risk factors, and previous results.)
- +/- Glucose or Hgb A1C (depending on age, risk factors, and previous results.)
- Consider dose titration as needed.

Endometrial Ultrasound

Every 2 years prior to hysterectomy or if any bleeding occurs after cessation of menses. (Endometrial biopsy is also indicated if performed to evaluate bleeding after cessation of menses.)

Bone Density

DEXA (Dual Energy X-ray Absorptiometry) scan within two years after oophorectomy and if indicated by prior results or by assessing risk factors every 1-3 years thereafter.

Hepatic Ultrasound

Every 3-5 years[25] to assess for hepatic tumors. This is probably only important for patients taking oral testosterone and is probably not necessary in patients on parenteral, transdermal, or buccal/sublingual testosterone.

Authors' Recommendations

While the above enumeration of possible monitoring and testing options was intended to encompass every possible suggestion made in the literature, it is not a standard recommendation for actual patient monitoring in clinical practice. Even in medical fields where there is a large body of clinical evidence there are often significant disagreements about optimal monitoring between clinicians and between professional organizations. Therefor, the above *inclusive* list was presented so that providers have an idea of the debate surrounding monitoring of patients.

This book is however, designed as a practical guide for clinicians seeking to treat transmen. Therefor we present the following summary of health screening that the authors use in clinical practice. We believe this is a reasonable screening guideline in our population of transgender men who often pay out of pocket for most trans related care. Of course it must be recognized that this is intended to guide monitoring for the average transgender patient. Transmen with other significant medical problems or risk factors may require more intensive monitoring.

Initial visit: Generally a clinical evaluation only - complete history and physical. Labs only if indicated based on history and physical (including assessment of pregnancy risk.) Gynecologic referral if no evaluation in the past year. Mental health referral if indicated.

Start on dose of 100-150 mg every two weeks. It should be noted that the reason we do not screen for lipids and fasting glucose at the initial visit is that documentation of the development of hyperlipidemia or glucose intolerance after instituting testosterone therapy may be used by insurers as a reason to deny payment for treatment of those illnesses as 'transgender related.' We only perform lab evaluation of patients who present a clinical reason for such testing.

1-2 months: Telephone or if necessary, in person follow-up. If no significant adverse effects, consider increasing dose to 150-200 mg every two weeks. If significant side effects occur consider *increasing frequency and lowering dose while maintaining same total administered amount of testosterone*. We suggest 50-75 mg per week instead of 100-150 mg every two weeks and plan to reevaluate the patient after 4 weeks on his new dose.

2-3 months: Clinical reevaluation – directed history and physical. ALT, fasting glucose, lipid profile, CBC. Consider titrating dose (generally with an ultimate goal of 100mg per week in most transmen.)

3 months after stable and effective dose achieved (generally 5-6 months after initiating therapy): Clinical reevaluation – directed history and physical. Trough testosterone level, sometimes LH level, ALT, fasting glucose, CBC, and if indicated by other risk factors – serum lipids.

Yearly thereafter: Clinical reevaluation – screening history and physical with special attention to systems affected by testosterone. ALT, fasting glucose, CBC, if indicated by other risk factors – serum lipids.

Yearly thereafter: Gynecologic evaluation or referral.

Chapter 7 - Testosterone Effects

Cardiovascular

Testosterone is often presumed to produce adverse cardiovascular effects because people with higher endogenous testosterone levels (men) have a higher risk of early cardiovascular disease than people with lower endogenous levels of testosterone (women.) However, whether this is causative or merely a correlation is the important question when considering the risks and benefits of testosterone therapy (for both transgender men as well as cisgender men with hypogonadism.) It may be that other biological sexual dimorphisms or differences in environment and behaviors account for the increases in morbidity and mortality in cisgender men. Indeed, in the few small studies in the literature of castrated males (mostly institutionalized males and Castrati – singers castrated before puberty) there was no significant decrease in cardiovascular disease mortality when compared to non-castrate males.[1]

In biological men, testosterone levels that are *either significantly above or below normal* are associated with increased cardiovascular risk.[2,3] A single retrospective study in the medical literature of 293 transmen treated with testosterone (range of 2 months to 41 years) by the Amsterdam Gender Dysphoria Clinic from 1975 to 1994 showed no increase in cardiovascular mortality or morbidity when compared with the general female Dutch population.[4] *However the absence of evidence is not evidence of absence*. A small to moderate detrimental or even advantageous effect is quite possible, though a very large effect is unlikely.

In cisgender men, androgen therapy (especially with oral testosterone or with supraphysiologic doses) *can* adversely affect the blood lipid profile by causing decreases in HDL, increases in LDL, and increases in triglycerides and homocysteine levels. However, these effects are less significantly and consistently found with normal replacement doses of testosterone and with non-oral formulations. Studies have even shown decreases in LDL or total cholesterol with non-oral testosterone therapy.[5]

The definitive answer is unknown however. In transgender men, testosterone may cause negative changes in lipid profile which is a known risk factor for cardiovascular disease. Androgen therapy also, while tending to decrease overall body fat, redistributes fat toward the typical male pattern of abdominal obesity[6], which is associated with worse cardiovascular risk than fat carried on the buttocks and hips. Cross gender hormonal therapy is also associated with an increase in visceral fat mass in transmen[7] which is a known risk factor for CAD. In addition, androgen therapy can cause weight gain and decreased insulin sensitivity (worsening any predisposition to develop Type II diabetes.)[8] Androgen administration in transgender men has also been associated with an increase in plasma homocysteine, which is a known independent risk factor for CAD.[9] Endothelin levels have also been shown to increase in transgender men on androgen therapy.[10] Endothelin is a potent proinflammatory vasoconstrictor that is associated with increased risk of CAD and pulmonary arterial hypertension. Serum adiponectin levels also decline

with testosterone use.[11] Adiponectin is a hormone secreted by fat cells that regulates glucose and lipid metabolism and exerts an anti-inflammatory effect on vascular endothelium. Higher levels are associated with a decreased risk of coronary artery disease. A small study demonstrated that vascular reactivity assessed by peripheral vascular response to a vasodilator measured by ultrasonography is impaired in transmen after androgen treatment.[12]

Moreover, supra-physiological levels of androgens (generally due to steroid abuse in athletes) may be associated with *significantly* increased risks of cerebrovascular accidents and heart attacks even in young otherwise healthy patients.[13,14,15,16] Unfortunately the only published literature about supraphysiologic androgen levels and vascular accidents in otherwise healthy adults are case reports. As the denominator consisting of all individuals who abuse anabolic steroids is unknown, a meaningful determination of true incidence and relative risk is not possible. However, the more than a dozen published cases of vascular catastrophes in otherwise *exceptionally* healthy young athletes abusing androgens suggests a link may exist. So it is critical to emphasize to patients that with regard to androgen therapy, *more is **not** better and may be significantly more risky!*

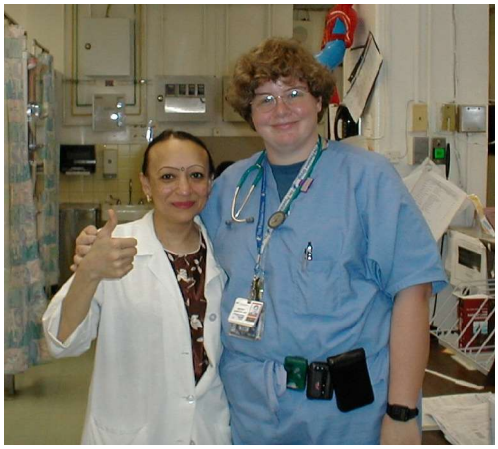
Androgens are not necessarily entirely detrimental though. Acutely testosterone causes dilation of the coronary arteries,[17,18] and in men with testosterone levels *within the normal physiological range*, higher levels may actually be associated with a slight *decrease* in cardiovascular disease.[19] In a recent review, of thirty nine papers in the medical literature studying the association between testosterone levels and CAD in men, none found a positive association, 23 showed no association, and 16 showed an association between lower serum testosterone levels and higher rates of CAD.[20] In older hypogonadal men, testosterone replacement (at doses comparable to doses prescribed to transgender men) demonstrated no evidence of increase in risk for cardiovascular disease.[21] Moreover, the decrease in HDL cholesterol seen with testosterone therapy may not reflect an actual increase in atherogenesis. It may be that this reflects an accelerated reverse cholesterol transport producing a net anti-atherogenic effect.[22]

One interesting hypothesis but unstudied however is that if present, any increases in CAD risk in transmen may not be due entirely to androgen administration, but in fact may be due to pre-existing increased risk conferred by the very mechanism that may result in or be associated with transgenderism. It has been suggested that FTM gender identity disorder is due to prenatal androgen influences that imprint the brain causing a male differentiation of the CNS.[23] It has also been suggested that prenatal androgen imprinting causes other sexual dimorphisms that predispose to increased CAD.[24] In addition, transgender men have a much higher incidence of Polycystic Ovarian Syndrome and the resultant pre-existing androgenization.[25,26] PCOS in turn has a much higher incidence of hypertension, glucose intolerance, and dyslipidemia.[27] The very mechanisms that may promote development of a male gender identity in transmen may be the actual cause of any increase in CAD incidence.

For health maintenance and screening it is probably safest to be conservative and assume that transgender males cardiovascular risk is greater than that of a biological woman of similar age and health status but probably no worse than that of a male of similar age and health status. Because of this possible additional risk with androgen therapy, improving modifiable cardiovascular risk factors becomes more important. The most important modifiable risk factor for many transmen is **tobacco abuse**. However, smoking cessation should not be presented as an absolute requirement for hormonal therapy as this not only disregards patient autonomy but will increase the likelihood that patients will feel the need to conceal information from providers. As with any other patient, persistent education, encouragement, and assistance are the best path to the ultimate goal of improving health behaviors.

Other modifiable risk factors that should also be discussed with patients include: diet, exercise, and control of hypertension, hypercholesterolemia, and diabetes. Discovery of hypertension, hypercholesterolemia, or diabetes should be treated as with other patients, and should not reflexively require cessation or even a significant decrease in testosterone dose. A physician treating a middle-aged cisgender male who develops diabetes would not consider testosterone deprivation to treat her patient's illness, nor should this necessarily be the case with a middle aged transman.

Providers may have an additional advantage however when counseling transgender men on healthy lifestyle behaviors when compared to other patients. With relief of lifelong dysphoria, transmen may have a newly kindled desire to improve diet and exercise. Once the patient's body image becomes one that is more comfortable, he may find himself more motivated to improve that body image. One of the authors of this text had a substantial and sustained weight loss of approximately 40 kg after finally being treated for lifelong gender dysphoria.



Pre-transition 5'10" ~ 125kg

Post-transition ~ 85kg

Integument

Hair

The androgenic effect on hair follicles of the face and scalp is mainly due to the more potent androgen, DHT. However, testosterone alone is sufficient to stimulate male pattern growth of axillary and pubic hair.[28] Testosterone is irreversibly converted (within hair follicles) by Type II-5-α-Reductase to DHT. With androgen therapy in transmen as with cisgender men, genetics primarily determines how much hair will develop (and where) as well as whether androgenic alopecia (male pattern baldness, MPB) will develop. Thinning of scalp hair is related to duration of testosterone therapy and is present in approximately fifty percent of transmen after thirteen years on hormonal therapy.[29]

Propecia® (finasteride) is a Type-II 5-α-Reductase inhibitor that works by blocking the conversion of testosterone to DHT. Type-II 5-α-Reductase is present in facial and scalp hair follicles as well as prostate tissue. Because of the distribution of Type-II 5-α-Reductase finasteride's primary therapeutic use is for prostatic hypertrophy and MPB. In facial hair follicles, DHT increases hair growth while in the scalp DHT decreases hair growth in susceptible individuals. Males with congenital deficiency of Type-II 5-α-Reductase have little or no beard growth and do not develop MPB. Inhibiting the enzyme in transmen would therefor be expected to both decrease hair loss in the scalp *and* slow or stop facial hair growth (although growth that has occurred should not regress.) It is important to discuss this effect with patients as they may begin to develop MPB prior to achieving the quantity of facial hair they desire. If further beard growth is desired, treatment of MPB might be delayed, although this risks suboptimal results with finasteride. Alternatively, topical minoxidil might be used while awaiting sufficient beard growth.

Gynecomastia occurs in patients taking finasteride, however it was observed in less than 2% of patients taking 5mg daily (the dose for prostatic hypertrophy) for four years. Similarly, at the 5 mg dose reductions in libido were found in 6-7%, however this tended to resolve over time in the majority of patients.[30] In addition to local tissue effects, finasteride also decreases serum DHT levels by as much as 65%.[31]

Finasteride is sold as 5mg tablets as Proscar® for prostatic hypertrophy. As of late 2004, it is approximately $2.40/pill in the US (or $0.60/day if quartered to take approximately 1.25 mg daily.) As Propecia® it is $1.60/1 mg tablet ($1.60/day to take 1mg daily.) Providers should be aware of and discuss the cost difference with patients when prescribing this medication. Patients should be warned however, Proscar® tablets are not scored and are somewhat challenging to equally divide.

Finasteride is not approved for use in women, has not been studied with respect to long term safety, and is teratogenic in pregnancy. However it has been studied and used off label to treat hirsutism in women.[32]

Rogaine® (Minoxidil – available without prescription) is sold as 2% and 5% solutions. The 5% solution is not recommended for use by women because it may cause the adverse effect of unwanted facial hair growth in a small minority of patients. However this hair is finer and may not resemble normal male facial hair, so it may not be advantageous to transmen desiring a beard. Minoxidil may cause skin irritation and itching. 1 cc is applied twice daily to the scalp (predominantly in the areas where hair loss is greatest.) It may take several months to show effects and may cause a slight paradoxical worsening of hair loss initially (which does eventually recover.) Minoxidil does not work by the same mechanism as finasteride, so it should not have adverse effects on beard growth.

With both minoxidil or finasteride the beneficial effect will be lost within months upon ceasing use of the drug. With both, best results occur when they are started *before* significant hair loss has occurred.

In addition to using finasteride as a treatment for male pattern baldness, it may also be useful in some transmen with very hirsute male relatives who are concerned about too brisk facial hair growth with testosterone therapy. Every transman does not necessarily desire to have heavy facial hair (just as not every adolescent boy who develops it is happy with it.) A desire to avoid facial hirsuteness or MPB is not, however an indication that a transman is not 'really transsexual,' but rather that like all people, he has preferences and desires for his own ideal body image.

With testosterone therapy new hair growth will gradually occur on the face and torso, but hair number and thickness will also increase on the arms, legs, and genital area. Facial hair growth should follow the typical pubertal pattern of development. One interesting finding about hair growth comes from research on women given physiological (low dose) androgen replacement. In women receiving low-dose androgens who developed hirsutism, almost all had *decreased levels of SHBG* (and thus increased free testosterone levels.)[33] This might suggest that transgender men who are not experiencing adequate hair growth (as expected when compared with their male relatives) in the face of adequate serum levels of testosterone might have decreased bioavailable testosterone due to higher levels of SHBG. This would be reflected by a lower FAI. However this has not been directly studied.

Transgender men not infrequently report dissatisfaction with facial hair growth when starting testosterone. It is important to counsel them that beard growth normally occurs very gradually. From the onset of adolescence to the to the time when a young man can produce a full adult beard may be as long as 8-10 years. After two years on testosterone it is not unusual for transmen to have facial hair reminiscent of what one would find on a fifteen or sixteen year old boy. In addition, due to genetic factors, some men will never grow a dense beard.

One helpful suggestion to transgender men in the early phases of therapy or even those not yet on testosterone therapy is to actually strive to maintain a 'close shave.' The soft

downy 'peach fuzz' type hair that is present before testosterone is not cosmetically unapparent, but rather suggests that the wearer is either a prepubescent boy or a female. A sparse growth of facial hair similarly suggests that the individual is an early pubescent male. This may contribute to the often unpleasant experience that many transmen report of being perceived as much younger than their actual age. One of the authors was in medical practice during his transition and found that simply shaving again halfway through a twelve hour clinical shift significantly lessened the number of inquiries: 'Are you *old enough* to be a doctor?'

Skin

Increased activity of oil and sweat glands stimulated by testosterone will result in increased sebum production. Some transgender men also report a change in body odor – less sweet and musky, more metallic and acrid. This may not be viewed by all patients as an adverse effect. If severe odor is a problem, washing with an antibacterial soap like Hibiclens® (chlorhexidine) in the axillae may help by decreasing skin carriage of odor causing bacteria. After 1-2 weeks of daily cleansing, a noticeable decrease in odor should occur. If ineffective, topical antibiotics like clindamycin or erythromycin may also be of help.

Most transgender men will develop at least some physiologic acne on the face and frequently back. More severe clinical acne will develop in a smaller minority.[34] Acne is generally worse the first few years of testosterone therapy (mimicking a second puberty) and can be treated with standard acne therapy. Initial treatment is with increased cleansing (at least twice daily) with an anti-acne or oil reducing scrub like Cetaphil®. If this does not improve acne, more aggressive therapy as would be offered to any patient, including systemic antibiotics, is warranted *before* permanent scaring occurs.[35] Some physicians who treat transgender men see severe clinical acne as a contraindication to increasing testosterone dose. However, this should only be a consideration after other medical treatments for acne have been exhausted and changing the route and/or frequency of testosterone administration is unsuccessful.[36] One of the authors of this text's clinical acne was rapidly reduced to mild physiologic acne by changing from 200mg of testosterone cypionate every two weeks to 100mg weekly.

Fortunately, acne in adult transgender men should be less severe than in adolescents because they do not have other physiologic inducers of acne such as the elevated growth hormone levels found during puberty.[37]

Wound Healing

There is some evidence that testosterone exerts a negative effect on wound healing.[38,39] However, just as anti-androgen therapy or estrogen supplementation is not recommended for cisgender males undergoing surgery, testosterone therapy need not necessarily be suspended for SRS. Moreover the effect of cross gender hormone therapy may actually be overall a positive one in transmen facing surgery. Testosterone is anti-thrombotic and may decrease risks of other serious post-surgical complications like deep venous

thrombosis which have been shown to be increased in transwomen on hormonal therapy.[40]

Gynecological Effects

Menses

Menses cease due to anovulation caused by the suppression of the hypothalamic-pituitary axis by testosterone.[41] Menses may cease after the first testosterone injection, however many patients may have one or more periods before complete amenorrhea occurs. All patients should be amenorrheic within five months of treatment.[42] If bleeding continues past five months with otherwise adequate testosterone dose, gynecologic and possibly endocrine evaluation may need to be undertaken. Typically it requires 200mg of parenteral testosterone esters every two weeks to stop menses. However, patients may require from 100-400mg every two weeks to achieve amenorrhea.[43] If doubt exists whether continued bleeding is due to insufficient testosterone dose versus pathological bleeding, testosterone levels, endometrial biopsy, and LH levels may clarify the cause. Although LH levels are quite variable throughout the day, very low levels generally indicate that testosterone dose is adequate to fully suppress the pituitary-gonadal axis and suggest that bleeding is not due to inadequate testosterone. However, failure of complete suppression of LH, when occurring in transgender men on typical doses of testosterone who are experiencing adequate masculinizing effects and have complete suppression of menses does not indicate a need for an increase in dose. Occasionally, especially in patients with lower serum testosterone levels, the addition of a progestin such as medroxyprogesterone acetate 5 to 10 mg may be required to induce complete cessation of menses.[44,45]

Gonadal Hormone Production

In non-oophorectomized transmen, testosterone may not completely suppress estradiol, LH, and FSH levels even with adequate dosing to induce satisfactory masculinization and cessation of menses.[46] Moreover, the suppression of gonadal steroidogenesis is neither the goal nor actually necessary for successful masculinization. In addition, higher estrogen levels may be beneficial. They are protective against acne by decreasing sebum production[47] and may be more protective than testosterone alone against osteoporosis. Clinical evaluation is more important than laboratory values and treatment must be individualized.[48] As was stated above, while complete suppression of LH indicates adequate dosing of testosterone, failure to completely suppress LH *does not necessarily indicate inadequate dose*. The goal of treatment is satisfactory masculinization and suppression of menses, so clinical evaluation is paramount.

One additionally useful application of a completely suppressed LH in the authors' clinical practice is patient reassurance. Transgender men may be impatient for the salutatory effects of hormonal therapy and may erroneously believe that 'more is better' or will cause a more rapid response. If a patient has a completely suppressed LH level, they can be reassured that their testosterone levels are adequately filling tissue receptors to the

greatest extent that can be reasonably expected. Further increases in dose and serum levels are unlikely to increase desired clinical effects but may come at the cost of far greater side effects. This reassurance may decrease the likelihood that patients will choose to surreptitiously increase their doses without provider knowledge or approval. However, LH levels may be expensive, especially if patients must pay out of pocket for treatment and they are less frequently used in transmen than transwomen.[49]

Clitoral Development

Clitoromegaly occurs, and frequently reaches its apex within 1-3 years of therapy. Sizes generally range from 3-7 cm with 4-5 cm being about average.[50] In a minority this may be sufficient to engage in penetrative intercourse with a partner.[51] This is genetically influenced, but some physicians advocate topical clitoral testosterone cream as an adjunct to growth before metaidioplasty (surgical reconstruction of the hypertrophied clitoris to more closely resemble in structure, location, and function a penis.)[52] There is no definitive evidence for this practice, but anecdotally it seems to be effective for some patients. However, this testosterone is absorbed and should be calculated into a patient's total regimen. In addition, a greater proportion of testosterone absorbed through genital skin will be converted to DHT than if applied elsewhere. This may produce stronger masculinization as well as an increase in adverse effects. Patients should be counseled that higher parenteral dosages of testosterone have not been shown to significantly increase clitoral size in individual patients when compared to more normal dosing.[53] Like other effects of androgens, time and genetics seem to be the primary determinants.

Increased clitoral sensitivity and responsiveness to stimulation is expected and may predate any noticeable clitoromegaly. Occasionally transgender men, especially in the initial phases of testosterone therapy, have reported clitoral discomfort. This may be due to increased sensitivity from hormonal effects alone or may represent abrasion or minor trauma from the increased sexual activity that may result from androgen therapy which is discussed further below.

Ovarian Effects

After long-term androgen therapy, ovaries may develop PCOS (Polycystic Ovarian Syndrome) morphology.[54,55] Untreated PCOS is associated with an increased risk of endometrial cancer, an uncertain increase in risk of breast cancer, and a possible increase in the risk of ovarian cancer, as well as decreased fertility.[56,57] In both PCOS and transgender men treated with testosterone there is a significant up-regulation of androgen receptors in the ovaries.[58] In addition to any effects of exogenous testosterone, a significant proportion of transgender men may have hirsutism and menstrual irregularities prior to initiation of testosterone therapy and as many as half of these men may have pre-existing PCOS.[59,60] This contrasts with an incidence of approximately 6% in the general adult female population.[61] However, interestingly, self-identified lesbians also have higher rates of PCOS that are intermediate between heterosexual women and pre-treatment transgender men.[62]

It is unknown whether the risk of ovarian cancer is increased, decreased, or unchanged in transgender men compared to the general female population. Unfortunately it will probably never be known since ovarian cancer is a relatively rare disease with an overall lifetime risk in women of only 1/70, with a median age of onset of 60 years.[63] Because ovarian cancer is uncommon, the overall population of transgender men is very small as well as currently relatively young, and even within the transmale population many patients are at decreased risk due to prior oophorectomy, it would be virtually impossible to do the appropriate epidemiological study to definitively answer that question. However, ovarian cancer has been reported in transgender men (Robert Eads as well as two other transmen reported in the medical literature.)[64] Particularly worrisome about these cases is that in *all three*, the malignancy occurred in younger transmen. Eads was 52 years old at his death, and both cases in the literature were reported in transmen under age 50. Moreover in both cases described in the literature, a family history of ovarian cancer was not present. Because of this uncertain but possibly increased risk, *it has been recommended by some physicians that transgender men have a hysterectomy and oophorectomy within 2-5 years of starting androgen therapy.*[65,66] In addition, this may also be advisable because some transmen find it difficult or may be reluctant to access appropriate and consistent gynecological care.

Another advantage of oophorectomy is that testosterone dose can then frequently be decreased, often by as much as 50%.[67] Caution should be taken when decreasing dose however, because if lowered too much it may precipitate vasomotor symptoms.[68] However, in oophorectomized transmen, vasomotor symptoms may develop even without changes in testosterone dose. This is likely due to the abrupt decrease in circulating estrogens. Altering route, dose, or intervals of androgen treatment may relieve these symptoms. It is generally not necessary to add-back estrogen after oophorectomy because like cisgender men, transgender men should produce some estrogen by aromatizing testosterone.

If prophylactic oophorectomy is undertaken, it is important to remember that, especially in transgender men who are at increased risk for ovarian cancer (such as those with BRCA mutations, hereditary site specific ovarian cancer, and Lynch Syndrome II) removal of the ovaries alone does not *completely eliminate* risk. In cisgender women with high risk for ovarian cancer, removal of the fallopian tubes and even total hysterectomy is often recommended in addition to oophorectomy as the risk of cancer of the fallopian tube and the uterine stump of the fallopian tube is also increased. In those transmen with congenital predisposition to ovarian cancer, this may be used as a justification to encourage insurers to cover the costs of surgery.

Transmen, like all female-bodied people should be screened regarding both maternal *and paternal* family history of malignancies that may indicate familial cancer syndromes. BRCA1 and BRCA2 mutations are suggested by an increased prevalence of malignancies (especially at a young age or when two primary cancers develop in a single individual) of the breast -especially in males, ovaries, and pancreas. BRCA mutations are also more prevalent in certain ethnic groups such as Ashkenazi Jews. Lynch Syndrome II is

suggested by an increased prevalence of non-polyposis colon cancer (especially right sided) as well as increases in endometrial, ovarian, and other genitourinary malignancies.[69]

Endometrial Effects

Some of the uncertainty of the relative risk for ovarian cancer holds true for endometrial malignancy in transgender men. Endometrial cancer is known to have a three times greater risk in patients with PCOS.[70,71] Androgen receptors have been detected in endometrial carcinomas.[72] Moreover, high serum androgen levels are associated with an increased risk of endometrial hyperplasia and cancer. However, this increase may not be directly due to androgen effects and might be due to associated elevated estrogen levels.[73] A high prevalence of endometrial hyperplasia has been noted in a small study of transgender men undergoing hysterectomy.[74]

In particular, it is important to remember to educate patients who retain their uterus that frequently the first sign of endometrial cancer is bleeding in post-menopausal women. Transmen with ***any bleeding*** after the cessation of menses with adequate uninterrupted androgen therapy ***must*** have an endometrial biopsy (and generally an ultrasound) done to rule-out endometrial cancer. *Like post-menopausal women, any bleeding in transmen on continuous testosterone therapy who have previously ceased menstruation should be considered* ***cancerous until proved otherwise****.* While malignancy is not the only cause of such bleeding, it *must* be ruled-out.

Some sources recommend endometrial ultrasounds every two years until hysterectomy is performed.[75] Testosterone typically causes atrophy of the endometrium. However, endometrial hyperplasia has been reported in some patients.[76] Any transgender man with endometrium that is not thinned on ultrasound after several months or more of adequate dose testosterone therapy should have an endometrial biopsy to evaluate for endometrial dysplasia and may require progesterone to cause sloughing of the endometrium. Vaginal bleeding from progesterone may be unpleasant for a transman, but the consequences and risk of endometrial cancer should be emphasized to the patient. Timing of such progesterone induced bleeding can however be discussed with the patient so that it can be planned for a time when it is least disruptive for him.

Uterine Effects

With the cessation of menses, some transmen who previously suffered dysmenorrhea may experience a relief of symptoms as menstruation eventually ceases. In addition, there is evidence that prostaglandin metabolism may be enhanced in hormonally treated transmen. The principle prostaglandin metabolizing enzyme found in myometrium, 5-hydroxyprostaglandin dehydrogenase (PGDH,) is significantly up-regulated by testosterone administration in transgender men.[77]

Cervical Screening

It goes without saying that any patient with a uterus/cervix should ideally have yearly pelvic exams with Pap smears. The only exceptions to this is in patients over thirty with either three consecutive normal Pap smears or negative Pap and HPV-DNA testing as indicated by the 2003 ACOG guidelines.[78] A few transgender men have never had penetrative vaginal sex, and may therefor be at decreased risk of cervical cancer due to minimal if any exposure of the cervical epithelium to human papilloma virus. In this population it may also be reasonable to perform pap smears only every 3 years.[79] However, even if a Pap smear is not required, ACOG still recommends yearly pelvic exams for any adult female-bodied person. This need for screening should be emphasized to transmen who have historically been reticent to seek out appropriate gynecologic care. However, rigid adherence to guidelines in the face of patients who suffer significant physical or emotional discomfort with exams may have the reverse of the desired effect. It should be remembered that the goal is to preserve patient health and well-being. A pap smear and pelvic exam done regularly every 2-3 years is far superior to no preventative examinations at all.

Providers unable to provide gynecologic well-checks should assist patients by referring to sensitive providers in the their area. These referrals should be discussed in advance with the gynecologic provider to ensure that she and her staff are comfortable providing care for transgender men and will be sensitive to their individual needs.

Vaginal Effects

Especially after oophorectomy, transgender men may experience vaginal atrophy and dryness, which may result in dyspareunia for those patients who desire to have penetrative receptive vaginal intercourse. This can sometimes be alleviated as it is in post-menopausal women with topical vaginal estrogen. Also like in post-menopausal women, this estrogen is absorbed systemically. However, depending on the formulation and dosage, this amount is far less than with oral estrogens prescribed for post-menopausal HRT (which is lower still than the levels normally found in reproductive age women.)[80] Especially in transmen who have already achieved satisfactory hormonal transition this is unlikely to represent a significant problem, but it does carry with it the risks and benefits of *any* estrogen therapy.

Breast Effects

Some transgender men report a decrease in breast size with androgen therapy. However, no histological changes were found when this was studied and likely it is due to loss of fat in the breasts.[81]

Although there may be no ultrastructural alterations in breast tissue, there is evidence for biochemical changes after long term androgen therapy. The female breast is second only to the prostate in tissue concentration of prostate specific antigen.[82] (Originally named prostate 'specific' because older, less sensitive assays only detected PSA in the prostate which has orders of magnitude higher concentrations than other tissues.) PSA levels

increase up to twenty fold after prolonged androgen therapy in transmen but fall by about half after mastectomy, hysterectomy, and oophorectomy. Breast tissue is likely the source of elevated levels of PSA in hormonally treated transgender men when compared to cisgender women. It has been suggested that the residual breast tissue (including the nipple) is the source for this persistently elevated PSA in post-surgical transmen.[83] Moreover, in women with breast cancer, some studies point to elevated tissue PSA as a positive prognostic indicator, although this remains controversial.[84] However it should be noted that even though serum levels in hormonally treated transmen are significantly increased compared with baseline levels, PSA levels in transmen remain significantly lower than those in cisgender men. PSA screening levels in cisgender men are reported in *nano*grams/mL, while the elevated levels found in transmen are in the range of 35-45 *pico*grams/mL.[85]

Breast cancer risk is likely significantly lower in the transgender male population simply because many transmen have bilateral mastectomies which decreases (but does not eliminate) the amount of breast tissue in which malignancy can potentially develop. Moreover, the effect of testosterone may be protective in contrast to the stimulating effect of estrogen and progesterone on breast tissue. Testosterone may also have apoptotic and antiproliferative effects on many but not all breast cancer cell lines.[86] Additionally, in women with PCOS (who have higher circulating androgen levels,) the incidence of breast cancer is no greater (and may be lower) than the general female population.[87] One retrospective observational study of testosterone in postmenopausal women suggested that testosterone supplementation may be protective against breast cancer even when co-administered with estrogen/progestin.[88] However, no mastectomy can completely remove all breast tissue and patients must understand that their risk of breast cancer, while much lower, is not zero. It should be emphasized to patients that any suspicious lumps must be evaluated by a health care professional. In addition, a portion of administered testosterone will be aromatized to estrogen. This estrogen may have stimulatory effects on breast cancer cells. So this is yet another point that may be presented to patients as a reason not to take higher than appropriate doses testosterone, as excess testosterone may also lead to higher amounts of circulating estrogens.

Transmen who do not choose to have mastectomies should have breast self exams, clinical breast exams, and screening mammography according to appropriate age and family history based guidelines for cisgender women. As with gynecologic screenings it is a general dictum that screening *should continue* ***until the patient no longer has the screened organ.***

Sexual Function

Natural testosterone levels peak in women just before ovulation which may account for the mid-cycle increase in libido many women experience. Studies of women with high normal testosterone levels across the menstrual cycle have shown more sexual gratification and less depression than women with low normal levels of testosterone.[89] Moreover, numerous studies over the past five decades of low dose androgen

supplementation in women (especially oophorectomized women) report improvements in sexual desire and gratification.[90]

Almost all transgender men report a *significantly* increased libido with testosterone therapy. This is often one of the first noticeable changes and is, in many ways, comparable to the increased sexual drives experienced in pubertal males. However, while these significantly elevated libidos are almost expected in teenage boys, they may be unexpected and even unwelcome in educated, mature, adult males. Some of the distress that such elevated sex drives may cause patients can be alleviated by reassurance that this is a normal response. Some transmen report that this effect decreases somewhat after several years of therapy – much like the changes seen with completion of normal puberty in cisgender males.

Patients sometimes also report feeling changed as a sexual being and sexual relations may become more intense and frequent. Patients have occasionally even reported and expansion of their sexual attractions. It is not rare for patients with exclusive sexual attraction to one sex to report an unexpected additional new attraction to the other sex.[91] Some female partners of heterosexual transmen may become anxious or distressed if they are unprepared for the significant increase in their partner's libido. Office counseling including anticipatory guidance may be helpful for *both* patients *and* their partners.

Urinary Tract Effects

In addition to the gynecologic effects of testosterone, urologic effects may be seen. The muscles of the lower urinary tract, especially the levator ani and urethral sphincter contain large numbers of androgen receptors and are sensitive to this hormone. Women with stress incontinence have lower levels of urinary androgens than matched controls without incontinence, and treatment with androgens has been suggested as a therapeutic option for these women.[92] Urodynamic studies have shown that higher androgen levels are related to larger residual bladder volume and this suggests androgens may be involved in increasing bladder relaxation.[93]

Fortunately the most worrisome genitourinary risk from testosterone therapy is not relevant to transgender men. The greatest concern for most men is the possible stimulation of prostatic malignancy. Transgender men need not be concerned about this, so it is possible that testosterone therapy in transgender men actually carries less of an overall risk than similar replacement therapy in hypogonadal men.

One case report in the literature describes a patient accidentally taking double the prescribed dose of testosterone who developed persistent dysuria and hematuria.[94] On evaluation he was found to have hypertrophy of the periurethral glands which appeared to be the source of his symptoms. Biopsy specimen of the glands showed a remarkable similarity to prostatic tissue, and stained heavily for prostate specific antigen. This supports the long-standing hypothesis that the female periurethral glands are homologous

to the prostate. This suggests also that this is an androgen responsive tissue that may be positively or adversely effected by androgens.

Reproduction

As the age at which transgender people begin therapy decreases, retention of reproductive potential becomes more important. However, preservation of reproductive capacity for transmen may be more challenging than for transgender women for whom sperm banking is readily available and relatively inexpensive. Future reproductive capability and plans should be discussed with all transgender patients before the initiation of medical but especially surgical therapy. Particular attention should be paid to younger and nulliparous transmen. Some transgender patients (and their physicians) have historically felt that sterility is the 'price to pay' for transition. However, it is important for providers to inform patients that transsexualism is not mutually exclusive with retaining reproductive potential.[95] Moreover, provider sensitivity to reproductive issues in transpatients has historically been at best neglectful, at worst antagonistic.[96] Unfortunately, in the experience of one of the authors, when questioned about preservation of reproductive potential, many transmen report little or no discussion by their providers and a few are even surprised to learn that preservation of reproductive potential is possible.

To complicate matters, some jurisdictions unfortunately require surgical sterilization to alter identity documents (especially birth certificates.) This legal practice, while obviously detrimental to patients, must be understood as a possible motivation for some transgender men to seek hysterectomy and oophorectomy. Due to this practice, it is appropriate for providers to both press for change in these governmental policies as well as serve as individual patient advocates in efforts to change identity documents while (if desired) preserving reproductive capacity.[97]

If a transgender man has not undergone oophorectomy, he *may* regain fertility on cessation of testosterone. If a patient has not had a hysterectomy, pregnancy may be possible and transmen have successfully given birth to children after hormonal transition was started. However, with the ovarian changes produced by long-term androgen therapy it may require months of cessation of testosterone and possibly assistive reproductive technology to regain fertility and if desired, become pregnant. For transgender men desiring pregnancy, testosterone *must* be withheld prior to and for the duration of pregnancy. With patients desiring pregnancy, particular sensitivity in obstetrical care should be taken and the patient's primary providers should educate other providers and staff with regard to the pregnant transman's unique needs. Labor and delivery nurses used to referring to intrapartum and postpartum patients as 'Mommy' should be sensitive to the fact that the transgender patient may consider himself 'Daddy.'

If a transgender man is planning on having a hysterectomy/oophorectomy, future reproduction may still be preserved, and should be discussed with patients at length before irreversible sterilization is undertaken. Options for preserving fertility include:[98]

- Oocyte banking – hormonal stimulation to induce hyper-ovulation with transvaginal oocyte harvest for freezing. With current technology, there is very poor survival of banked oocytes, and this method is not recommended outside of research protocols.[99]
- Embryo banking – oocyte harvest as above with immediate fertilization and banking of the embryo. Best survival of all techniques, but the sperm donor (whether known or anonymous) must be chosen before oophorectomy.
- Ovarian tissue banking – probably the most flexible option for many transmen especially those unsure of future reproductive desires, but still experimental and performed in only certain centers. Ovarian tissue is cryopreserved after oophorectomy. Even after long term androgen therapy,ovaries usually retain usable follicles. Eventual use of frozen ovarian tissue will likely require replantation into the transgender man for stimulation and harvest, but may eventually be possible in a lab as techniques for tissue culture improve. This technique has been successfully used to preserve fertility in cisgender women undergoing therapy for cancer.[100] Moreover in a proof of concept trial, after cryopreservation of ovarian tissue from a transman who had been on testosterone for a year, secondary and pre-antral follicles were induced after thawing, transplantation, and FSH stimulation in SCID mice.[101]

Voice

Voice changes are frequently one of the most desired effects sought by transgender men. For some patients a feminine range voice may often be *the* major impediment to assuming full male gender role. Fortunately decreases in vocal pitch are also one of the more rapid and reliable effects of androgen administration, with noticeable changes generally present by 6-8 weeks.[102]

Patients should be warned however that like pubertal males, their voice will often experience cracking and squeaking as it deepens to its final male pitch. This may present unexpected and embarrassing difficulties for transmen, both personally and professionally. Occasional transmen may, like adolescent males, experience transient throat pain or vocal weakness during transition. Additionally, professional or amateur singers and speakers should be warned that frequently voice changes occur that may be significantly detrimental to vocal performance. These changes are both unpredictable and irreversible. Like transwomen, those patients with significant speaking or singing concerns may be helped by speech therapy as well as singing or vocal coaching.

Musculoskeletal

Bone is not static. It is constantly being reabsorbed and generated. Osteoporosis results when bone formation occurs at a rate less than bone reabsorption. Androgens and estrogens exert significant influences on bone mineral density (BMD) in both sexes. In adolescent and premenopausal women, higher androgen levels are associated with higher

BMD.[103,104] Women with complete or near complete androgen insensitivity syndrome have lower bone mass than either male or female patients even when compliance with estrogen replacement is adequate.[105] Moreover lower SHBG levels (indicating greater bioavailable testosterone) is associated with a higher BMD in premenopausal women. Similarly in males, higher BMD is associated with higher serum estrogen levels.[106] Additionally, males deprived of estrogen exhibit greater biochemical evidence of bone loss than when testosterone deficiency is induced.[107] So while naturally occurring in different relative proportions, estrogens *and* androgens are necessary in both males and females for optimal bone health.

Specific Sex Steroid Hormone Effects on Bone

Estrogen is the predominant sex hormone that slows bone loss (even in men.) Both estrogen and testosterone stimulate bone formation (especially at puberty in the case of testosterone.) In one study, testosterone caused an increase in cortical bone thickness in transgender men, however this does not necessarily translate to greater mechanical stability.[108] This is consistent with evidence that testosterone stimulates while estrogens depress periosteal bone formation.[109] A second more recent study in transmen demonstrated that after two years on hormone therapy that was sufficient to elevate testosterone levels to upper normal male ranges and suppress estradiol levels to near menopausal ranges, a clinically and statistically significant increase in BMD was found.[110]

However, specific effects of androgens and estrogens on bone have been difficult to study. Much of the significant salutatory effect that testosterone was originally assumed to have on bone in studies of androgen replacement in hypogonadal men has been demonstrated to be largely due to aromatization to estrogens.[111] While androgens certainly exert important effects on bone metabolism, the magnitude is less than that of estrogens. In transmen therefor, the salutatory effects of testosterone on bone should be considered to be due to both the androgen effect as well as estrogenic effects from both the aromatization of testosterone as well as residual ovarian production.

Hormone Effects after Oophorectomy

In menopausal women (which may more closely represent the situation in oophorectomized transmen with corresponding extremely low serum estrogen levels) the association between androgen levels and BMD is less definite. Some studies of post-menopausal women show a protective effect of higher androgen levels, while others show no effect. This lack of protection from osteoporosis may be due however, to lower levels of estrogen rather than differing levels of testosterone. In osteoporotic women treated with hormonal therapy, *combined* estrogen and androgen therapy has been shown to be more effective than estrogen therapy alone.[112] In cisgender women, androgens may therefor be protective *in the presence of sufficient estrogen*, but may be insufficient alone. However, this comparison may not be completely direct as there is some evidence that transgender men, even prior to hormonal therapy, tend toward a more typical male body shape which may represent pre-existing differences in hormonal milieu.[113]

The idea that testosterone is protective in the presence of sufficient estrogens is supported however, by a study of post-oophorectomy transmen which demonstrated that testosterone alone was insufficient to completely retard bone loss. In this study researchers demonstrated that elevated LH levels correlated to lower BMD. This suggests that LH might be a useful indicator of adequacy of hormonal replacement in transmen who are post-oophorectomy, with elevated LH indicating increased risk of osteoporosis.[114]

Taken together current research suggests that pre-oophorectomy *in an environment of higher estrogen levels*, testosterone may have protective effects. These effects may be decreased after sterilization when estrogen levels may drop precipitously.

Estrogen Supplementation

Transgender men who have been oophorectomized ***must*** continue some hormonal therapy to avoid premature osteoporosis. Estrogen supplementation should theoretically not be necessary in normal transmen for prevention of osteoporosis because some of the administered testosterone will be aromatized into estrogen sufficient to maintain bone (as it is in cisgender men.)[115] However if accelerated bone loss is detected in post-oophorectomy transmen, low dose estrogen may be one possible means to slow such loss. However, just as in cisgender women, estrogen therapy carries risks which must be considered when choosing therapy. As in post-menopausal women, if the only indication for estrogen supplementation is bone loss, other treatments such as bisphosphonates may have a superior risk-benefit profile. If estrogen replacement is prescribed, transdermal therapy is preferred because oral estrogens cause a significant elevation in SHBG and therefor lower free androgen levels.[116,117] Daily calcium supplementation is probably a good idea for most transmen as it is for most cisgender women, but it is even more important after oophorectomy. Vitamin D supplementation may also be beneficial for many transmen.

Monitoring

Some physicians advocate a DEXA scan at the time of oophorectomy and periodically thereafter to diagnose osteoporosis in the pre-symptomatic stage when it is more easily treated.[118] Providers should be sensitive to cost however as many transmen pay out of pocket for transgender related care. (In 2005, cost for DEXA in the US ranged $150-400 depending on the center.)

Muscle Effects

In addition to the relationship between decline in BMD and likelihood of some of the adverse outcomes from osteoporosis (fractures from falls in the elderly,) there may be an additional effect due to loss of muscle mass following menopause. Elderly patients with lower muscle strength may be more prone to falls. Additionally, the load muscle exerts on bone has a significant (if not greater) effect on BMD than does gravitational loading.[119] So the increased muscle mass gained with testosterone therapy in transgender men may itself be protective. Therefor resistance training should be encouraged in transmen

because it may have significant protective effects against loss of BMD in addition to both the overall health benefits and the gender confirming effect of producing a more masculine body habitus.

Hematologic

Erythrocyte Effects

Polycythemia in transmen is generally from marrow overproduction stimulated by high serum testosterone levels. Testosterone increases renal erythropoietin production, which in turn induces increased marrow production of red blood cells. This stimulatory effect on erythropoietin induced RBC production is the reason that testosterone was used prior to the advent of epoetin alfa (and sometimes even today) to treat anemia from bone marrow failure.[120]

A transgender man's hematocrit should only be judged high when compared to normal values for *men*. While levels vary with altitude, normal male hematocrit is generally 40.7 - 50.3% (Female normal levels are 36.1 - 44.3%.) However, not all transmen will achieve normal male range hematocrit, so evaluation of anemia should only be triggered by either a hematocrit lower than normal for women or a significant decline in the patient's previous stable level.

Polycythemia is a greater concern for older transmen as the tendency to become polycythemic worsens with age. Moreover, the adverse consequences of polycythemia are more worrisome in the elderly. Higher blood viscosity produced by polycythemia is more likely to cause unfavorable outcomes in patients with preexisting vascular disease found more often in older populations. Severe polycythemia predisposes to both venous and arterial thrombosis. Low does aspirin therapy may decrease the risk.[121]

Polycythemia is more frequently found in patients receiving parenteral testosterone (predominantly injected esters but to a lesser extent with pellets.) It is likely related high peak testosterone levels (especially in the few days after intramuscular injection) as opposed to the more consistent but lower levels produced by oral, buccal, or transdermal.[122,123,124] This complication may be alleviated either by changing patients to an alternative non-parenteral testosterone formulation or by decreasing both the dose and interval of injected testosterone. Decreasing dose and increasing the frequency will lower the peak testosterone levels without decreasing the total testosterone administered. For example, a patient receiving 200mg of testosterone cypionate every two weeks might be changed to 100mg weekly. With more frequent administration of lower doses, peaks and troughs will vary less from normal levels but the AUC should be roughly equivalent. However, if dosage adjustments are not possible or effective, traditional therapy for polycythemia via scheduled phlebotomy may be helpful.

While hematocrit increases, no statistically significant difference in plasma iron, total iron binding capacity, and serum ferritin were detected in transmen before and after androgen therapy.[125]

Leukocyte Effects

In addition to the stimulatory effect on RBCs, testosterone also increases granulopoiesis. In a study of transmen treated with testosterone, there were statistically significant increases in granulocyte count as well as lactoferrin (a transferrin like protein released by neutrophils.)[126] Though, while statistically significant, this amounted to a difference that would be clinically insignificant in healthy transmen. However, while small increases in leukocyte counts may be clinically insignificant, there is evidence that cellular level alterations in leukocyte androgen receptors (AR) and hence cell function occur which may be clinically significant. It is theorized that some of the sex related alteration in risk for inflammatory disorders (including atherosclerotic cardiovascular disease) may be due to alteration in leukocyte function. In an elegant study of the effects of endogenous and exogenous androgens on leukocyte function comparing transmen, hypogonadal males, engrafted genetically female leukocytes in male bone marrow transplant recipients, and normal males, a markedly different effect of exogenous versus endogenous androgens on AR expression in leukocytes of *both* men and women was demonstrated. That is, both male and female leukocytes have higher leukocyte AR expression with endogenous androgens, but both have a down-regulation of AR with exogenous testosterone (whether in hypogonadal cisgender males or transgender males.)[127]

Thrombocyte Effects

Androgen receptor transcripts are also present in platelets. In an ex vivo study of human megakaryocytes, androgen receptors mRNA was upregulated by low testosterone concentrations, but were suppressed by higher concentrations of testosterone.[128]

Coagulation System Effects

Testosterone increases the anticoagulant effects of warfarin. It suppresses clotting factors II, V, VII, and X.[129] Patients who require concomitant anticoagulation may need lower doses of warfarin. Additionally, with warfarin therapy, intramuscular injections should be avoided.

Neurological/Psychiatric

Obstructive Sleep Apnea

OSA may be worsened or unmasked by androgen therapy.[130,131] Risk is greater in patients who are obese, smoke, or have chronic obstructive pulmonary disease. In addition, OSA is more common in Polycystic Ovarian Syndrome patients.[132] So transmen with pre-existing androgenization and PCOS may be at higher baseline risk. Untreated OSA may have significant negative effects on the heart, blood pressure, and mood, as well as possibly unmasking or worsening headache and seizure disorders.

Patients should be informed of the symptoms of OSA: noisy sleeping (snoring,) excessive daytime sleepiness, morning headache, personality changes, and problems with judgment, memory, and attention. These symptoms should be elicited on follow-up evaluation, especially in transmen with predisposing medical conditions or illnesses that could potentially be exacerbated by untreated OSA.

Patients with OSA may develop a reactive erythrocytosis which can be mistaken for polycythemia from testosterone. Any patient with abnormally elevated hematocrit should be screened for possible sleep apnea.[133] Sleep studies are indicated if OSA is suspected as a complication of androgen therapy. While cessation, reduction, or alteration in dose, route, and frequency of androgen therapy may be effective, other modalities to treat OSA are also effective and may allow continued and appropriate hormonal therapy.

Epilepsy

Some seizure disorders are sex-steroid-dependent. These may be improved, worsened, or (*very* rarely) unmasked with androgen therapy. The effect of testosterone on any given epilepsy patient is not readily predicted.[134] Overall, the effect of androgens and progesterones is *anti*-epileptogenic, while estrogens are epileptogenic.[135,136] Moreover there is a positive correlation between estrogen:progesterone ratio and seizure frequency. In women with catamenial epilepsy there is evidence of a relative progesterone deficiency in the luteal phase of the menstrual cycle.[137] However indirect effects of sex steroids on the hepatic metabolism may also be responsible, as lower antiepileptic drug levels are found around the time of menses in women with catamenial seizures.[138]

Sleep deprivation also worsens many seizure disorders, so concurrent OSA unmasked or exacerbated by androgen therapy may also be responsible for worsening seizure control.

Headaches

Known androgen sensitive migraines are a relative contraindication for testosterone therapy.[139] However like epilepsy, the effect that androgens will have on any given patient with a headache syndrome is unpredictable. A small case control study showed a non-significant trend toward lower levels of testosterone in post menopausal women with migraines compared with those without.[140] In addition, two limited open label studies of testosterone in the 1950s suggested that testosterone may actually prevent migraine.[141] As migraines are often associated with changes in hormone levels around menses and as a putative causal relation between estrogens and migraines is accepted, this would suggest that some transmen with migraines might actually have an improvement of their symptoms on testosterone. However as described earlier in this text, it should be remembered that testosterone therapy sufficient to suppress menses and masculinize patients may not fully suppress ovarian steroidogenesis. So the effect of continued estrogen and progesterone production by the ovaries as well as the estrogen:progesterone ratio may have unpredictable effects on any individual patient's migraine syndromes. Even more so than the case of epilepsy, the role of androgens in headache syndromes is not well elucidated and research is sparse.

Peripheral Nervous System Effects

In addition to the effects on the central nervous system, there is evidence that sex steroids exert effects on the peripheral nervous system.[142] Generalized paresthesias are reported as adverse reactions from testosterone.[143,144] Anecdotally transmen have reported this as a side-effect after institution of hormonal therapy.[145] In addition to generalized symptoms, injected testosterone has been reported as a cause of an isolated peripheral neuropathy after intramuscular injection.[146] This may have been due to either direct neurotoxic effects of the drug or pressure on the nerve following intramuscular injection. For patients who self-inject, the importance of good technique in appropriate and safe areas must be stressed to avoid such adverse effects.

Mood and Psychiatric Issues

Historically, transgender people have been perceived to have higher rates of other mental illness than non-transgender people. This may have been at least partially due to the trauma of experiencing discrimination and abuse by living in a society that is often unaccepting of gender non-conforming behavior. However, more recent studies suggest that this may not be entirely true, or may be true to a much lesser extent than it was previously thought.[147,148] This may be due to increasing societal acceptance of transgender people in recent years resulting in decreased development of co-morbid psychiatric disease as a result of discrimination and transphobia.

Some transgender men report mood swings, increased anger, and increased aggressiveness after starting androgen therapy (similar to the effects reported with body builders who abuse androgens.) Androgen administration in transmen has been associated with a reported increase in aggression proneness.[149] However it has also been associated with an overall decrease in affective intensity (both for positive and negative emotions.)[150]

Increases in anger or aggression that may occur should be less severe however than the 'roid rage experienced by athletes engaged in illicit use because with transgender men the more significantly supraphysiologic levels associated with abuse are generally not present. Moreover, in a research study in which biological men were given supraphysiologic doses of 600mg per week, more than four fifths experienced no or minimal psychiatric symptoms.[151] So while providers should be aware of the possibility of adverse psychological reactions, the actual risk for clinically significant effects is likely small. Additionally in a larger study, during and after reassignment, transmen showed more contentment, greater extroversion, and less somatization than pretreatment.[152]

Many transgender men actually report *improved* mood, decreased emotional lability, and a *lessening* of anger and aggression. Likely this is not entirely a physiologic effect but also due to the alleviation of psychological distress from long-standing gender dysphoria. Overall this is best reflected by the decrease in depression and suicidality found in treated transgender patients than in non-treated patients.[153] While testosterone may have some risk of adverse psychological consequences, overall, treatment of transgender patients results in improved psychological health.

Providers should be alert for the infrequent complication of significant affective and/or psychotic symptoms that are rarely possible with androgen therapy.[154]

In the authors' experience the partners and emotional intimates of transgender patients can often provide useful information about mood changes and adjustment to gender role. Patients should be encouraged to feel comfortable bringing their partners or close intimates with them to appointments. When adverse mood changes occur these can often be managed by in office counseling and reassurance. If more significant difficulties arise, appropriate referral to a mental health professional should be made.

Alterations in mood are also sometimes reported by some transmen using injected testosterone during the few days before their next injection or the first few days after an injection. This may be the result of subtherapeutic or supraphysiologic testosterone levels respectively. Changing dosing, interval, and/or route may be effective in alleviating many of these symptoms.[155]

Cognitive Effects

Interestingly when studying the effects of testosterone on cognitive function, researchers found a significantly improved spatial ability in transmen that, after prolonged androgen therapy approximates cisgender male scores. A possible decrease in verbal fluency has been reported but not replicated.[156,157,158] A study comparing transgender men with cisgender women (as opposed to comparing transmen pre and post androgen therapy) revealed lower verbal memory performance (typical of cisgender males) in transmen than in cisgender women. However the authors of the study suggested this was possibly due to prenatal brain organization alterations which may reflect the biological etiology of transsexualism rather than any effect of testosterone.[159]

Gastrointestinal

Hepatic

There is a theoretical risk of developing liver injury or malignancy with all testosterone formulations, but this is minimal with all forms except oral or unless very high doses are administered. Typically, yearly (or even more frequent) monitoring of LFTs is recommended for transmen. However, a recent literature review in the New England Journal of Medicine suggests that unless oral forms are used or supraphysiologic doses are administered, periodic monitoring of LFTs is unnecessary in hypogonadal males on long term testosterone replacement.[160] Unfortunately, this has not been studied adequately in transgender men, so this conclusion may not be generalizable to this population. If an initial LFT profile is normal and a transgender patient has no other risks for hepatotoxicity, it is probably reasonable to limit further monitoring to periodic ALT only.

If elevations of transaminases are discovered, it may be prudent to temporarily discontinue testosterone therapy while this is further evaluated – *especially* in patients taking oral testosterone. However, in patients taking normal doses of non-oral testosterone, LFT abnormalities (especially when large) should only be attributed to testosterone when other causes of liver pathology have been excluded. If testosterone is determined to be the cause of mild hepatotoxicity, permanent cessation of androgen therapy is not necessarily indicated. Cautiously reintroducing testosterone at a lower dose and with different frequency and/or route of administration may provide a safer means of hormonal reassignment.[161]

In addition health care providers who treat transgender patients should remember that some members of this population may be at increased risk of acquiring blood borne pathogens. Therefor viral hepatitis should be considered as a cause when evaluating elevated transaminases.[162] Because of this increased risk, patients who have not been previously vaccinated should be offered hepatitis immunization.

Metabolic

Weight

Testosterone generally increases appetite and body weight. Appetite increases may be due in part to a decrease in serum leptin levels that occur in transgender men treated with androgens.[163] While testosterone tends to decrease the total body fat mass[164], in an individual patient the form that any weight gain will take depends on diet, exercise, and genetic factors. Because of testosterone's anabolic effects, gain of lean muscle mass will be easier than it was previously for transgender men. Moderate amounts of exercise will produce larger gains in muscle mass and may ameliorate some of the adverse metabolic consequences of testosterone.

Anecdotally some transgender men report an increased energy level, decreased need for sleep, and increased alertness after starting testosterone therapy.

Insulin Resistance

Elevated levels of *either* androgens or estrogens are associated with decreased insulin sensitivity in women. The elevations of sex steroids found during puberty, during pregnancy, and even during the luteal phase of women's menstrual cycles are all associated with a reduced glucose tolerance.[165] Additionally, in *both* male and female transgender patients, a decreased insulin sensitivity has been demonstrated after cross-gender hormonal therapy was administered for four months.[166] A study of non-transgender women given exogenous testosterone also demonstrated the development of insulin resistance even in the short term.[167]

In biological men, *abnormally high* ***or*** *low* levels of testosterone are both associated with insulin resistance. So mid-normal levels of testosterone are the target for androgen therapy in any patient. However treatment of non-insulin dependent diabetes mellitus (NIDDM) that appears before or after androgen therapy need not necessitate cessation or even a significant decrease in dosage of androgen therapy. (Providers would not consider androgen deprivation as a reasonable treatment for cisgender men.)

Treatment of Impaired Glucose Tolerance and Diabetes

While therapeutic trials specific to transgender men who develop insulin resistance have not been published, the experience with PCOS patients may be applicable both because PCOS and androgen treated transmen share common physiological features and because a large proportion of transmen may have pre-existing PCOS. Among women with PCOS, 40% have impaired glucose tolerance and 10% have frank NIDDM by the fourth decade.[168] Metformin is the agent most widely used and studied to treat insulin resistance and NIDDM in PCOS patients, and may be a good initial choice for transmen with impaired glucose tolerance. However the salutatory effects that metformin has on other pathogenic changes in PCOS may not occur (or be desired) in transgender men. Metformin is associated with a decrease in serum androgens and an increase in SHBG in PCOS patients as well as clinical improvements in acne, menstrual irregularities, and infertility.[169] However, in transmen exogenous androgens would not decrease with metformin so changes in ovarian morphology and acne would likely remain unchanged.

Although studied less extensively in PCOS patients, the thiazolidinediones have been shown to improve metabolic abnormalities and hyperandrogenemia.[170] However, these drugs are significantly more expensive, have a shorter history of use in clinical practice, and at least one member of this drug family (troglitazone) has been withdrawn from the market due to hepatotoxicity.

Uncertainties

Testosterone may not have an entirely deleterious effect on glucose tolerance however. In contrast to cisgender women, the relationship between sex-hormone levels and insulin

sensitivity is less clear in men. Lower testosterone and higher SHBG levels have been associated with *impaired* glucose tolerance in men.[171] However this effect may not be an independent association with androgen levels, as increased adiposity itself is associated with lower testosterone levels and higher SHBG levels in men.[172]

Moreover, it should be emphasized, especially to patients with pre-existing overweight or obesity that any deleterious effect that testosterone may have on metabolic profile would likely be overshadowed by improvements through diet and exercise. With NIDDM, PCOS, and obesity, weight control through exercise and diet remain a cornerstone of therapy.

Thyroid Effects

Testosterone may decrease levels of thyroxine-binding globulin (TBG), resulting in decreases in total T4 levels and increases in T3 and T4 resin uptake. However despite these alterations in lab values, changes in free thyroid hormone levels and clinical thyroid dysfunction do not occur.[173]

Athletic Performance

Elite athletes must be advised that testosterone therapy will very likely result in disqualification for competition (at least within the female category.) Androgens will usually disqualify participants even if they have a physician's prescription for these medications. Recently though some transgender athletes have been successful in their attempt to compete in their post-transition gender. However, transgender men, if allowed to compete in male sports may not remain as competitive. Androgen administration certainly increases muscle mass – especially with resistance training. It also raises hemoglobin levels which improves athletic performance. However, when hormonally treated transgender patients were compared at one year, the mean muscle mass of the FTM group remained lower than that of the MTF group though the gap had narrowed considerably.[174] Moreover, unless treated before the end of puberty and closure of the physes, transgender men remain shorter and have a lower bone mass than cisgender men which is often a competitive disadvantage.

Drug Interactions

Testosterone (like all sex steroids) is metabolized by the Cytochrome P-450 enzyme system in the liver (specifically CYP3A.) There are numerous drugs that increase or decrease the activity of this enzyme. This change in P-450 activity may cause increased or decreased levels of sex steroids as well as other drugs metabolized by this system.

- Cyt P-450 Inducers – May cause decreased levels of testosterone (and other sex steroid) levels: Phenobarbital, Dilantin, Rifampin, and *Alcohol* are examples.
- Cyt P-450 Inhibitors – May cause increased levels of testosterone: Serzone, Prozac, Paxil, Sporanox, Diflucan, and other ‘azole’ antifungals, Tagamet (which can cause gynecomastia in men because of this effect.) Biaxin and other macrolide antibiotics, and protease inhibitors.

The above listed drugs are a ***small*** example of the drugs that cause these effects so as when prescribing any new drug, interactions should always be considered.

Testosterone can also alter the effects of certain drugs:

- Increases the anticoagulant effect of Coumadin.[175]
- Decreases the effectiveness of propranolol.
- Increases the hypoglycemic effect of oral diabetes medicines and can decrease the insulin requirement and predispose to dangerous episodes of hypoglycemia.[176]

Chapter 8 – Emergency Medical Care Issues

Introduction

In our society the emergency department is the one place where we all expect care will be available regardless of time, type of medical condition, or person seeking care. It is seen as a refuge where patients will have some measure of safety and protection. Emergency personnel are expected to be professional, non-discriminatory, and knowledgeable about a variety of medical conditions. Unfortunately, for many transgender patients, a trip to the emergency department is often a source of unusual anxiety. While many transgender people are able to establish ongoing relationships with providers who are both knowledgeable about transgender issues and sensitive to the special needs of their patients, and estimated 30-40% may not have a primary care provider and rely upon emergency departments and urgent care facilities for care.[1] When seeking care at an emergency departments, patients have no guarantee that they will find a provider who is respectful or knowledgeable about transgender issues. Indeed, anecdotal stories related by transgender patients in emergency departments have been anything but reassuring.

Compounding the concern faced by any patient with a rare diseases that the provider they encounter in an emergency department may be unfamiliar with their illness, transgender patients face an even greater worry. While transsexuality has a higher incidence than Wegener's Granulomatosis, SCID, and Ewing Sarcoma, patients with those diseases could reasonably expect a physician has received at least some minimal formal education about their illness and would be able to refresh her memory relatively easily by consulting common medical texts. Even a patient with bubonic plague with a yearly worldwide incidence of about 1:2,000,000 could more readily expect a physician to be able to understand at least some of the etiology, pathophysiology, and treatment of his illness. However, unfortunately few if any medical schools or residency programs offer any formal education in the care of transgender patients.

In addition to any knowledge deficit, transgender patients also justifiably fear they may encounter transphobia from providers and staff in the emergency department. While certainly there are numerous caring and open-minded physicians and nurses in emergency medicine, transgender patients have reported blatant and egregious discrimination while seeking emergency care. So it is not surprising that transgender patients often avoid seeking emergency care out of the real concern that they will experience discrimination, humiliation, and even substandard treatment from providers who are ignorant of or insensitive to transgender issues. Transmen have reported everything from subtle forms of discrimination such as refusal to use proper pronouns and lack of respect from office staff to frankly inappropriate treatment such as outright refusal of care, inappropriate questioning of sexual behavior, performance of genital examinations that were not indicated, questioning why patients had 'mutilated' their bodies, and even public ridicule by inappropriate discussions with other health care providers. Unfortunately, these sorts of experiences are not of only historical interest but are reported by transmen as having occurred within the past several years. So it is no surprise that many transgender

individuals express *significant* anxiety at the prospect of seeking care from any other than trusted providers. This fear and refusal to seek care has resulted in fatalities. For example, in 1989 Jazz musician Billy Tipton died of an untreated ulcer that eventually caused exsanguinating gastrointestinal hemorrhage. After Mr. Tipton's death, it was discovered that he had a female body though he had lived for decades as a man.

Fortunately there are specific actions that providers can take to make emergency care more accessible and less frightening to their transgender patients. In general, prior planning for urgent and emergent medical problems can help transmen stay healthier and safer.

Specific Emergency Problems

Genitourinary

Transgender men who experience gynecologic emergencies may be extremely reticent to seek care in the emergency department. This underscores the need for continued ongoing gynecologic care for every transman. An established relationship with a gynecologist will not only help prevent the need for emergency gynecologic care, but provides patients an established provider with whom they have already developed a comfortable relationship.

Just as some emergency problems can be prevented, there are other common problems for which advance planning can be instituted. Patients with a history of occasional urinary tract infections or yeast vaginitis can be prescribed prn short course antibiotics and antifungals to have at home in case they develop symptomatic infections when their provider is unavailable. This will both prevent delayed treatment as well as perhaps prevent the need for a late night or weekend trip to an emergency department.

In addition, it is even more important for transgender patients that they be aware of the health care facilities with which their primary care provider and/or gynecologist is affiliated. While some emergencies are so acute that the closest available facility must be accessed, in the vast majority of cases patients have a choice of hospitals.

Surgical Complications

Because patients may need to travel in order to receive surgical treatments from experienced transgender surgeons, many patients may not be completely healed by the time they return home. Primary care providers or emergency physicians may therefor be visited by patients with post-operative issues who normally would seek evaluation from their surgeon. As with all post-operative patients, many problems can be adequately treated by primary care providers, if needed in telephone consultation with the patients surgeon. However, problems may occasionally arise that require more urgent surgical expertise. Ideally primary care providers should have in mind one or more local general and gynecologic surgeons who would be open to providing consultation and assistance should the need arise. Discussing this in advance with a colleague may allow both for the

education of that college about transpatients' special needs and help ensure that patients receive competent and respectful care.

Navigating the Emergency Department

Registration and Identity Information

Even the process of registering and providing insurance information in the emergency department can be a daunting task for some transmen. Not infrequently, patients have identity documents and even insurance cards with names and gender markers that are not congruent with their appearance and gender identity. This may prove awkward for patients to explain to triage and registration personnel especially if registration or triage is in a relatively public area. (Fortunately with the advent of the HIPAA law, these privacy issues are becoming less prevalent as hospitals and emergency departments develop increasing sensitivity.) This also underscores the need to address cultural sensitivity and respect issues not just with physicians, PAs, NPs, and nurses, but also with other hospital staff and even emergency medical service personnel.

One helpful technique that may be employed by patients in this situation and others is a 'carry letter.' This is a letter from the patient's primary provider or psychotherapist that identifies the patient as a transman. The letter should be general and identify the patient by both his original name as well as his current correct name and gender. Presenting such a letter from a physician may serve as a buffer for patients that will make mistreatment by hospital staff somewhat less likely. It will also serve to answer questions that the patient may find awkward or unpleasant to answer.

In addition to providing assistance when accessing emergency care, this letter may also be helpful in other situations. For example, a patient who has difficulty assessing sex segregated facilities or who encounters the police may find such a letter useful. Society often places great weight on evaluation and diagnosis by health care providers, and such an 'official' letter on the provider's stationary may, in the eyes of people unfamiliar and perhaps even antagonistic toward transgender issues, grant legitimacy to patients' status.

The following are two examples of such letters.

Letter for patient currently/newly transitioning and/or living full time as male without fully changing all identity documents or insurance:

To whom it concerns:

[Patient's full chosen name] is a patient under my care. Mr [surname] is transgender and is undergoing medical treatment in order to reassign his sex to match his true psychological gender identity, which is male. As part of this process, Mr [surname] is living in an appropriate male gender identity full time.

The process of changing one's sex both medically and legally is complex and sometimes may take up to several years to complete fully. Because of this, Mr [surname] may have identity documents which may not all reflect his true gender identity or name. Mr [surname]'s prior name was [former full name.]

As part of this medical process, Mr [surname] is expected to live full time in his true psychological gender role. This includes using the appropriate male facilities such as restrooms.

Thank you in advance for affording Mr [surname] assistance and understanding as he carries out his medical sex reassignment. Your efforts are integral in the treatment of this complex condition.

If you have any questions regarding Mr [surname,] please feel free to contact me at the number below.

Letter for patient who is well into transition and/or has changed gender marker and name on most or all documents:

To whom it concerns:

[Patient's full chosen name] is a patient under my care. Mr [surname] is transgender and has completed treatment in order to reassign his sex to match his true psychological gender identity, which is male. With the completion of this process, Mr [surname] should be considered male for legal or identification purposes.

If you have any questions about Mr. [surname,] please feel free to contact me at the number below.

Sincerely,

Mary Smith, MD, FACP
Office address and phone.

Patient Advocates

Patients should also be advised that bringing an advocate with them when they visit the emergency department can be very helpful. It is sometimes easier for persons who are not directly affected by discrimination and transphobia to object to inappropriate treatment. In addition, the advocate may not feel disempowered due to illness, injury, or simply being in the patient-role. Ill or injured patients sitting on a gurney wearing only a thin hospital gown may not feel as confident in demanding appropriate and respectful treatment as an accompanying advocate.

Additionally, most people who are transphobic, like those who are racist, sexist, or homophobic, may be less willing to overtly express their discriminatory beliefs if friends or family are present.

Consultation with Emergency Providers

Primary care providers may be called by emergency providers with questions about their transgender patients who do seek care in the emergency department. Just as other providers caring for patients with relatively rare illnesses, availability of providers well versed in transgender care can be an important resource for emergency providers. So availability of primary care providers for consultation is critical.

In addition, if providers are aware in advance that their patients will be seeking care in an emergency department, a short call ahead to emergency providers may help prevent problems before they develop. Interacting with another physician who understands that transsexuality is simply a rare illness that can be successfully treated with appropriate interventions may make providers unfamiliar with transgender medicine more accepting and understanding. Transphobia may often result from lack of knowledge rather than actual intent to harm, and providing anticipatory information may prevent this type of reaction on the part of providers.

Education and Awareness

In addition to provider contact, the ideal prior preparation and education for emergency medical providers, nurses, and other personnel should take place well ahead of any actual need for emergency care. Especially if a provider cares for numerous patients in a community that may be otherwise unfamiliar with transgender issues, provider education may be very helpful. A short discussion at an ED staff meeting may raise awareness that transgender patients live in the community and may present to the emergency department. This information might also be addressed as part of a larger sensitivity or awareness continuing education program for ED staff. Contacting the nurse-educator for the hospital or emergency department may be helpful in determining the best method for this information to be presented.

Ideally this sort of education should provide brief information about transsexuality as a medically treatable diagnosis as well as specific suggestions for how to sensitively and respectfully care for transgender patients. The unfamiliar and unknown seem odd and even sometimes threatening to all of us. Providing even a small amount of familiarity with transgender medicine may therefor significantly impact the way patients are treated in the emergency department.

A valuable resource for these discussions can be transgender patients themselves. Some transpatients may be willing to accompany their provider to an educational session such as this. This valuable resource can help put a human face on the issue and demystify it for providers and staff.

Intervention After Emergency Department Visits

In addition to addressing problems before they occur, patient experiences in emergency departments can serve as events that may help change care in future. If transpatients experience sub-standard, insensitive, or frankly discriminatory care in an emergency department, providers should address this deficiency directly with the department or hospital administration. While patient complaints – especially in municipalities where discrimination based on gender identity is illegal – are taken very seriously by hospitals, *provider* complaints can be even more effective in bringing about positive changes.

Perhaps even more importantly however, letters of compliment for care that is sensitive, respectful, and clinically competent can have an immeasurable effect on future care. While people respond very well to positive reinforcement, unfortunately complaint letters generally outnumber complimentary letters by several fold in any public service field. So a letter of commendation for appropriate and sensitive care in an emergency department may be even more noticeable and may help ensure such treatment becomes the standard in one's community.

Patient Privacy and Disclosure

Because of possible drug interactions as well as other health related problems specific to transgender patients, it should be emphasized to every patient that in general he should inform any provider that treats him that he is on androgen therapy (and any other medication or supplement that he may be taking.) However, patients may not feel comfortable revealing to every provider that he is transgender (especially for non-trans related care.)

If a patient expresses this concern, it may be helpful for him to inform other providers he is on testosterone for primary hypogonadism. While not entirely truthful, this will at least allow the patient to inform other providers that he receives testosterone therapy. Transmen have also successfully stated that they had surgery for gynecomastia to explain chest scars. Paradoxically, provider ignorance of transgender issues may actually assist patients in this regard as transsexuality may not even be considered as a possible explanation for surgical scars or medication. One transman reported that he was evaluated for blunt abdominal trauma in an emergency department after a motor vehicle crash. *A digital rectal exam was performed by his physician*, but his transgender status was only discovered when the radiologist subsequently read the CT as incongruent with the reported gender of the patient. Cognitive dissonance can sometimes work to a patient's advantage in these situations. However, the ultimate solution to this problem is to eliminate transphobia and ignorance of transgender health issues from the medical community. The task of provider education to ensure sensitive and quality care for transgender people seems massive. However, it is hoped by the authors that this book will be a small step toward that goal so that transgender patients never again have to face the tragic results of such ignorance.

Chapter 9 – Medical Documentation for Legal Name and Gender Changes

Introduction

The legal status of transgender people is gaining increased attention, and significant changes are being made currently. Over the last decade, numerous jurisdictions, including the states of Minnesota, New Mexico, Illinois, Rhode Island, and California,[1] have added protection against discrimination on the basis of gender identity to their anti-discrimination laws. Additionally, many changes have occurred and are occurring with regard to the rules for changing name and sex designation on various identity documents. Finally, increasing challenges to exclusions of transgender health care from state-supported care (Medicaid programs, health care for foster youth, youth in juvenile justice, and adults in state custody) are being brought, often with success.

In most realms of transgender law, medical evidence is still a central component of making out any legal claim or applying for any adjustment in sex designation. For this reason, a health care provider who is treating transgender patients should be prepared to be asked for letters confirming her patients' gender identity or documenting their treatment protocol for various legal purposes. This section is designed to help in drafting those letters, giving providers an understanding of what information is most helpful to the clerks, administrators, and judges who may be reviewing the medical information from providers with substantially less understanding of the transgender health than providers or their patients have. This section will provide a basic understanding of the most useful medical evidence in the areas of identity documentation and state support of transgender health care, and provide model letters for use in clinical practice.

Name Changes

When applying for a name change in most jurisdictions, a patient should not be required to document his medical status. The general legal approach to name change is that name changes should be permitted by courts unless the petitioner is seeking to change their name to defraud someone (usually creditors). Transgender name change petitioners are not seeking to defraud anyone, just to have a name that better suits their identity. However, some courts have erroneously viewed transgender name change petitioners as fraudulent and required medical evidence from them. Cases in several states have confirmed that this higher evidentiary standard for transgender name changes is not in keeping with the law.[2] However, many judges have not researched the issue and may still ask patients for this information, or a patient or his lawyer may decide to submit an affidavit from a provider with the application for name change just to avoid any delays in case the court is going to request it. Hopefully, as time passes more judges and lawyers will become informed that this evidence is not necessary, and providers will have less of these requests to meet.[3]

For now, however, providers may be asked to write such an affidavit. Ideally, this should be a basic affidavit supporting a patient's application for a name change. Below

is some sample language that may be useful in guiding providers in drafting such a affidavit.

Civil Court of the City of New York
County of New York

In the Matter of the Application of CURRENT LEGAL NAME for Leave to Assume the Name of REAL/PREFERRED NAME	AFFIDAVIT Index No. _____

DOCTOR'S FULL NAME being duly sworn, testifies and deposes that:

- I have been licensed to practice medicine in the State of New York since __(year) __ and have been a board-certified family physician in the State of New York since ____(year)___.
- I began working as a physician at _____(hospital)_____ in ___(year) _____.
- Since ___(date)____, CURRENT LEGAL NAME has been my patient. This patient is popularly known as "REAL NAME" as (s)he feels uncomfortable being known by his legal female name. In his professional and personal life, he has been using consistently and habitually the name REAL NAME.
- It is my medical opinion that REAL NAME is a transsexual. Under my medical supervision, REAL NAME is undergoing hormone therapy for his transsexualism.

- In my professional opinion, REAL NAME's desire to change his name from an identifiably female name to an identifiably male name is completely consistent with his male gender, and I strongly feel that it is in his best interests to allow this change.
- By adopting the male name "REAL NAME" in place of the female name "CURRENT LEGAL NAME," REAL NAME will be able to retain the name he has used consistently and habitually, while eliminating the very significant embarrassment and bias he experiences when forced to disclose his legal name, which currently does not match his gender identity or physical appearance. For these reasons, his name change will not be a fraudulent act, but a true expression of his gender identity.

_____

DOCTOR'S FULL NAME

Sworn to before me this

_____day of _____ 2005

_____

Notary

Identity Documents

Obtaining identity documents that match the new gender identity and name is an essential step in transition for an transgender person. Without basic ID that comports with gender identity, obtaining employment, applying to educational programs, getting

medical care, or even getting a speeding ticket or buying alcohol can become a context for discrimination or even violence. Most people believe that each of us has a specific "legal" gender that the government recognizes, and many transgender people and their providers initially think that there is one simple step to changing that sex designation. However, in reality, each agency that issues identity documents (the Social Security Administration, the Passport agency, Departments of Motor Vehicles, Medicaid programs, public assistance programs, Bureaus of Vital Statistics, Immigration Services, etc.) has their own standard and method for changing sex designation. Worse yet, they are very inconsistently applied (usually depending on what clerk a transgender applicant ends up seeing) and also frequently change.

For this reason, the overall approach that medical providers should use is a generally worded letter. No matter what kind of treatment a patient has undergone, if a provider believe he is at the point in his transition where his well-being or safety would be benefited by having identity documentation that comports with his gender identity, providing a general letter will likely be of most help to him at the various agencies he must visit and contend with.

Why is a generally worded letter so useful? First of all, at most agencies a patient approaches for sex designation change, the front line workers will not know the agency policy for sex designation change, and they are also likely to know very little about transgender health care. In my experience, when clients approach these agencies with letters detailing specific medical protocols, the agency clerks often see this as an indication that they should evaluate the sufficiency of the medical care the applicant has undergone to determine if it is "enough" to merit a change of sex designation.[4] The lack of knowledge that most clerks have about transgender medical care, combined most times with lack of familiarity with their agencies policies regarding these applications (especially as the policies are changing frequently) results in routine denials. In my experience, my clients who have applied for sex designation change with more generally worded letters, especially when seeking a drivers' ID, passport, Social Security, Medicaid, or public assistance sex designation change, have had the greatest success. The focus of the letter should be less upon the details of the medical treatment, and more upon the fact that a provider considers his patient to be the new gender. Sample language is below:

> Dear Sir or Madam:
>
> I am Dr. _____. I am a licensed _____ in [State Name]. [Insert 2-4 sentences about provider qualifications, institutional affiliations, etc.]
>
> Mr. John Doe is a patient in my care. I have been treating him for the past [number of months or years]. In my medical opinion, Mr. Doe is a transsexual man. I have determined that his male gender predominates and have given him appropriate sex reassignment treatment.
>
> As a result, Mr. Doe has now successfully undergone all necessary medical procedures to fully transition from female to male. Mr. Doe should be considered male

for all legal and documentation purposes, including on his passport, driver's license, and social security records. Indicating his gender as male is accurate and will eliminate the considerable confusion and bias Mr. Doe encounters when using identification that does not reflect his current true gender.

Sincerely,

Dr. _____

In some instances, particularly birth certificate sex designation change, such a letter may not be useful, although in any situation starting with such a letter and seeing if the agency making the sex determination asks for further detail is a good approach. This general wording, if read by someone who knows very little about transgender health care, will usually be sufficient, whereas providing details about hormone therapy or other treatment will only open up questions if they've never heard of the treatment and decide to investigate. Providing a general letter, in my experience, is likely to expedite the process because it prevents people without much medical knowledge from getting bogged down in details they are not qualified to assess. Also, because the standards regarding what treatment, specifically, is required are inconsistently applied and change frequently, this general wording will usually avoid confusion.

Other Uses of Medical Evidence in Legal Contexts

Identity documents and name changes are probably the most common areas in which transgender patients will request supportive documentation for legal recognition of their new gender. However, medical evidence has often also been a central issue in many other areas of transgender law. When determining whether a transgender marriage is legitimate for immigration or estate purposes[5], when determining the child custody rights of a transgender parent,[6] when assessing whether discrimination has occurred in a workplace or place of public accommodation,[7] and in many other contexts, courts incorporate medical evidence into their assessment of transgender people's rights. Attorneys frequently use medical experts to help a court understand what transsexuality is, what transgender health care entails, and what mental health effects transgender identity can have on a transgender person's family members. Working with transgender rights attorneys on cases like these, either as a treating physician when an individual provider's patient is involved in a case, or as an expert on transgender health care generally, can be an important way to contribute to improved understanding of transgender people and transgender health care.

These issues are becoming increasingly important as the issue of the legitimacy of transgender health care comes to the fore in many contexts. Private health insurance companies, Medicaid systems, prison systems, juvenile justice systems, and foster care systems are all being pushed by transgender advocates to recognize the legitimacy and medical necessity of transgender health care and to allow for access and insurance

coverage for this care. The push for this reform is happening with varying degrees of success in courts, legislative arenas, and administrative negotiations. Medical professionals who administer transgender health care can be an important part of these processes, dispelling myths that transgender health care is "cosmetic" or "experimental" and supporting updated understandings of this care in insurance companies and government agencies.

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Version 1.2, November 2002

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1 For updated information about the most current anti-discrimination legislative initiatives, go to the Transgender Law and Policy Institute website, www.transgenderlaw.org, or the National Gay and Lesbian Task Force Transgender Civil Rights Project, http://www.thetaskforce.org/ourprojects/tcrp/index.cfm.
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3 The Manhattan Civil Court recently invited one of the authors (DS) to train the Civil Court judges about this and other transgender legal issues, and currently uses *In Re Guido* to train all new judges on the issue of transgender name changes. Hopefully other courts will soon follow suit in working to raise awareness amongst judges about transgender legal matters that come before them and prevent unfair rulings.
4 This is often especially true in the birth certificate context. Birth certificate sex designation change remains one of the most difficult areas for transgender rights. Forty-seven states currently allow transgender people to change sex on a birth certificate, but the majority require evidence of sex reassignment surgery in order to make such a change. What constitutes sex reassignment surgery, especially in the case of FTM's, remains hotly debated, and inconsistently applied. See Ala.Code, § 22-9A-19 (2002) (order of court of competent jurisdiction and surgery required); Ariz.Rev.Stat. § 36-326 (2001) (change may be made based on sworn statement from licensed physician attesting to either surgical operation or chromosomal count, although registrar may require further evidence); Ark.Code Ann. § 20-18-307 (2002) (order of court of competent jurisdiction and surgery required); Cal. Health & Safety Code. § 103425, 103430 (2002 Supp.) (court order and surgery apparently required); Col.Rev.Stat. Ann. § 25-2-115 (2002) (same); D.C. Code Ann. § 7-217 (2002) (same); Ga.Code Ann. § 31-10-23 (2002) (same); Haw.Rev.Stat. § 338-17.7 (2002) (physician affidavit and surgery required; registrar can require additional information); 410 Ill. Comp. Stat. 535/17 (2002) (same); Iowa Code § 144.23

(2002) (physician affidavit and surgery "or other treatment"); La.Rev.Stat. Ann. § 40:62 (2002) (order of court of competent jurisdiction and surgery required); Mass. Ann. Laws ch. 46, § 13 (2002) (same); Mich. Comp. Laws § 333.2831 (2002) (affidavit of physician certifying sex reassignment surgery); Miss.Code Ann. § 41-57- 21 (2001) (registrar may correct certificate that contains incorrect sex on affidavit of two persons having personal knowledge of facts; not clear whether restricted to initial error in certificate or includes gender change); Mo. Rev. Stat § 193.215 (2001) (order of court of competent jurisdiction and surgery required); Neb.Rev.Stat. § 71-604.1 (2002) (affidavit of physician as to sex reassignment surgery and order of court of competent jurisdiction changing name required); N.J. Stat. Ann. 26:8-40.12 (2002) (certificate from physician attesting to surgery and order of court of competent jurisdiction changing name); N.M. Stat. Ann. § 24-14-25 (2002) (same); N.C. Gen.Stat. 130A-118 (2001) (affidavit of physician attesting to sex reassignment surgery); Or.Rev.Stat. § 432.235 (2001) (order of court of competent jurisdiction and surgery required); Utah Code Ann. § 26-2-11 (2002) (order of Utah District Court or court of competent jurisdiction of another State required; no specific requirement of surgery); Va.Code Ann. § 32.1-269 (2002) (order of court of competent jurisdiction indicating sex has been changed by "medical procedure"); Wis. Stat. § 69.15 (2001) (order of court or administrative order) *cited in Matter of Heilig*, 2003 WL 282856 (Md.). See also, Lambda Legal Defense and Education Fund's chart at http://www.lambdalegal.org/cgi-bin/iowa/documents/record?record=1162.

5 See *In re Estate of Gardiner*, 42 P.3d 120 (Kan.2002); *Littleton v. Prange*, 9 S.W.3d 223, 224 (Tex.Ct.App.1999); *M.T. v. J.T.*, 140 N.J.Super. 77, 355 A.2d 204, 205 (N.J.Super.Ct.App.Div.1976); *Anonymous v. Anonymous*, 325 N.Y.S.2d 499 (N.Y. Sup. Ct 1971); *In re Ladrach*, 513 N.E.2d 828 (Ohio App. 1987).

6 See *In re V.H.,* 412 N.W. 2d 389 (Minn. Ct. App. 1987); *In re D.F.D. and D.G.D.,* 261 Mont. 186 (1993);*In re T.J.*, Minn. App. LEXIS 144 (1988); Kantaras v. Kantaras, Florida 2/21/03 see NCLR website for cite (finding a transsexual father to be legally male, his marriage to be valid, and awarding him custody of his children, after a three-week trial with extensive medical evidence); But see *Christian v. Randal*, 516 P.2d 132 132 (Co. Ct. App. 1973).

7 See e.g., *Goins v. West Group*, 635 N.W.2d 717, 87 Fair Empl.Prac.Cas., Minn. (1999); *Oiler v. Winn-Dixie Louisiana,* 2002 WL 31098541 (2002); *Doe v. Bell,* 2003 WL 355603; *Doe ex rel. Doe v. Yunits*, 15 Mass.L.Rptr. 278 (2001).