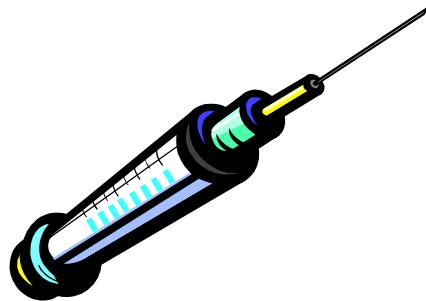


HORMONE THERAPY
IN
TRANSSEXUAL
PATIENTS



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HORMONE THERAPY IN TRANSEXUALS

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GENDER REASSIGNMENT PROCESS

For a person diagnosed as transsexual ('TS') by a properly qualified specialist, a process of *Gender Reassignment* takes place. The steps of the process are:

- **Diagnosis** made by an appropriate specialist.
- **Counselling** and/or **Psychotherapy** as required.
- **Hormones** to change the body shape and characteristics.
- **Electrolysis** to remove facial (and possibly other) hair.
- **Real Life Test**, living in the new gender role.
- **Surgery** to change the genitals. Possibly other surgery too, such as breast augmentation or facial cosmetic surgery.

DESIRED OUTCOMES:

Some common patient desired outcomes include:

1. For MTF

Decreased facial/body hair
Increased breast size/breast growth
Change in body fat distribution to gynoid "pear"
Weight loss/weight gain
Softening of facial skin and other features
Decreased or elimination of erection/ejaculation
Maintain a strong transgender identity
Maintain a strong feminine identity
Change in voice tone or quality
Decreased or reverse male pattern baldness
Vaginoplasty and/or other surgeries
No surgery

2. For FTM

Facial hair with or without body hair
Increased body musculature
Maintain a strong transgender identity
Maintain a strong male identity
Mastectomy
Phalloplasty
No surgery
Masculine body

The process of hormonal reassignment is slow; maximum effects may be achieved after 2-3 years of therapy.

GENERAL INFORMATION ABOUT HORMONE THERAPY

Once the patient has been diagnosed as transsexual, the Consultant Psychiatrist will normally decide to initiate hormone treatment. This involves administering large doses of female sex steroids (oestrogens, usually accompanied with progestogens) to induce the development of female secondary sexual characteristics. In a pre-operative subject this will normally be accompanied by some form of anti-androgen treatment to reduce the effect of the patient's endogenous male sex hormones.

The effects of feminising hormones vary greatly from patient to patient. Younger patients generally obtain better and more rapid feminisation, although genetic factors are also highly significant.

With appropriate dosage, most patients experience noticeable changes within 2--3 months, with irreversible effects after as little as 6 months. Feminisation continues at a decreasing rate for a period of two years or more, often with a 'spurt' of breast growth and other feminisation when the testes are removed by orchidectomy or GRS.

MAIN EFFECTS OF FEMINISING HORMONES

The main effects of feminising hormones are as follows:

- Fertility and 'male' sex drive drop rapidly, this may become permanent after a few months. Erections become infrequent or unobtainable. Patients report increased 'female-type' sex drive. In time the penis and scrotum may atrophy to some extent, requiring the patient to regularly stretch them by hand to maintain adequate donor material for eventual GRS. The testes and prostate also atrophy.
- Breasts develop. Typical final breast size is somewhat smaller than that of close female relatives. The nipples expand and the areolae darken to some extent, but breast development may be unsatisfactory particularly in older patients, in which case implants may be desired. Breast growth can be greatly augmented by use of an appropriate progestogen, causing a more natural breast to form with lactative and ducting tissue as well as the fatty tissue laid down by oestrogen treatment.
- Body and facial fat is redistributed. The face becomes more typically feminine, with fuller cheeks and less angularity. In the longer term, fat tends to migrate away from the waist and be redeposited at the hips and buttocks, giving a more feminine figure.

- Body hair growth often reduces and body hair may lighten in both texture and colour. There is seldom any major effect on facial hair, although if the patient is undergoing electrolysis, hormone treatment does noticeably reduce the strength and amount of regrowth.
- Scalp hair often improves in texture and thickness, and male pattern baldness generally stops progressing. Some patients find that some recently-lost hair will grow back to some extent, but severe hair loss will necessitate hair transplants or a hairpiece or wig. Some studies suggest that topical application of minoxidil (2 % or 5 % solution; the 2 % is available without prescription under the brand name 'Regaine') may reverse hair loss to some extent when it is used alongside hormone therapy. Studies have found it to be of marginal benefit in normal males (due presumably to the continuing effects of dihydrotestosterone) but beneficial in females or androgen-suppressed males. See also Finasteride (Section [9.1.4](#)).
- The skin and hair become less greasy; spots and acne generally improve. Some patients find their skin becomes very dry; many patients will need to change their skin-care regime after starting hormones.
- Metabolic rate decreases; many patients gain weight. Additionally, muscle mass is often lost.
- Many patients report brittle fingernails; some patients have claimed improvement in this case by taking various nutritional supplements.
- Many patients report sensory and emotional changes: heightened senses of touch and smell are common, along with generally feeling more 'emotional'. Mood swings are common for a while following commencement of hormone therapy or any change in the regime.

ADMINISTRATION

Hormones are most commonly administered orally; however, depot injections or skin patches are sometimes used, especially in patients with liver problems, as they avoid the 'first pass' through the liver after absorption in the digestive tract. Typical dosages listed are for oral administration.

There has been debate in recent years over whether to administer a constant dosage of hormones every day, or whether to mimic a natural menstrual cycle by reducing or stopping oestrogen for 7--10 days per 28 and adding or increasing a progestogen during that period. No advantage has been found to the cyclic method; its principal effect seems to be to induce extreme mood swings similar to PMS. There is some evidence that the non-cyclic approach produces slightly more rapid feminisation, and so a non-cyclic regime is widely regarded as preferable today.

HIV DISEASE AND TRANSGENDER PEOPLE

HIV infection is unfortunately prevalent among the transgender population. There is no evidence in the medical literature or in our experience that the natural history of HIV disease differs in transgender people. HIV is not a contraindication or precaution for any of our protocols. While drug-drug interactions may occur, we know of no specific dangerous interactions or likely causes of drug failure. Treatment with hormones is frequently an incentive for patients to address their HIV disease and providers of care for transgender people should enhance their HIV expertise.

CONSENT

The use of medications for gender reassignment is off-label. There are potentially life-threatening complications. The medical provider should obtain a signed consent indicating agreement to and understanding of treatment from the patient.

MTF HORMONAL THERAPY

Male to female hormonal reassignment of gender is based on the ability of medications to effect demasculinization by blocking production and action of Androgens (testosterone) and to effect feminization by responsive but latent tissue.

RISKS AND MONITORING

There are also some risk factors associated with hormone therapy, the most serious of which is a risk of deep-vein thrombosis (DVT) or pulmonary embolism (PE), which can be life-threatening. The risks appear to be much higher if the patient is over 40 years old, overweight, or a smoker. Transsexual patients who smoke should be strongly encouraged to quit.

Hormone treatment must be discontinued for some time (typically 3--6 weeks) prior to any form of major surgery due to the risk of thromboembolic events. Likewise if the patient suffers an injury resulting in immobilisation, hormones should be withdrawn. In cases of minor surgery it may be safe to continue hormone treatment, but in all cases the advice of the surgeon and anaesthetist should be sought.

The manufacturer's safety data for the hormone(s) chosen should be consulted for full information; but it must be noted that the drugs companies do not acknowledge the use of these drugs in transsexual subjects and clinical data specific to TS patients is scarce.

Fluid retention and/or hypertension may result from hormone treatment. A change in the hormone regime often helps; for example several patients have experienced water retention or hypertension when taking the progestogen levonorgestrel, but have returned to normal when this was replaced by an alternative progestogen such as medroxyprogesterone acetate ('Provera').

If a particular hormone appears to be producing poor results or side-effects then a change in regime is probably wise: hormone therapy for transsexual patients is still somewhat 'hit-and-miss' although a consensus does appear to be emerging; much good research has been published by Prof. Gooren of Amsterdam. If no feminisation whatsoever is seen (not even the tender nipples that precede breast growth) after 2--3 months, or if feminisation is very limited over a longer period, then it may be beneficial to refer the patient for a serum androgen level test (testosterone and DHEAS), as some patients overproduce androgens to the extent that feminising hormones have little effect, and perhaps also refer the patient to an endocrinologist experienced in the treatment of male-to-female transsexuals.

Certain blood tests are advisable on a routine basis for patients undergoing hormonal sex reassignment. Opinions differ as to which checks are required and how often, but as guide, liver function, serum lipids and blood pressure should be checked annually at a minimum. It is advisable to check more frequently if the patient is preoperative (pre-ops require higher dosages, and hence are at greater risk of adverse effects), is also taking antiandrogens, or has any other factor predisposing her to side-effects such as being overweight, being a smoker, being over 40 years old, or having any relevant medical history (e.g. hypertension, liver problems etc).

Some practitioners also advise the checking of fasting glucose (high dose hormone/antiandrogen treatment may affect carbohydrate metabolism), thyroid function, blood clotting time and prolactin. The necessity or otherwise of checking serum prolactin has been debated recently --- some elevation of prolactin is to be expected under aggressive oestrogen treatment and would not necessarily indicate a problem, conversely there have been reports of pituitary prolactinoma in a few TS patients, which would be detectable by an excessively high serum prolactin level that fails to drop when oestrogens are temporarily discontinued.

Some practitioners also recommend monitoring the levels of sex hormones in the blood, particularly testosterone for pre-op male-to-female subjects. It is debatable whether this is necessary if the patient reports satisfactory physical development, however if the hormone treatment is producing poor results and it is proposed to prescribe an unusually high dosage of hormones or antiandrogens, then such a test might be indicated. Likewise, if prescribing antiandrogens to an agonadal subject (post-op or post-orchidectomy) is contemplated, such a test is indicated --- it is normally considered unwise to administer antiandrogens to a post-op subject.

When sex hormone levels are measured, it must be reinforced that antiandrogens that work as receptor antagonists may skew the results, since the body's response to a given serum androgen level will be depressed relative to a normal subject, even though the measured androgen level may not be much below normal. Normal testosterone levels are typically considered to be 300--1000 ng/dl for a male, 5--85 ng/dl for a female.

It should also be borne in mind that serum oestrogen levels may be misleading. With an effective dose of oestrogen being administered, there is little reason to perform this test; and the normal test for serum oestradiol is insensitive to ethinyloestradiol and certain other forms of oestrogen anyway, which may cause misleading results.

Monitoring of medications at every visit includes:

- Assess for desired and adverse effects of medication
- Check weight, blood pressure
- Review health maintenance
- Directed physical exam as needed

OESTROGENS

Oestrogens are responsible for the development of female secondary sex characteristics, so the main component of any hormone regime for a TS patient will be some form of oestrogen. Typically this is obtained either from combined oral contraceptives or oestrogen tablets intended for HRT in postmenopausal women.

The principal natural oestrogen produced by the ovaries in a natural-born premenopausal female is 17 beta-oestradiol. Numerous derivatives and metabolites exist and play specific roles in the female body. While some of the metabolites (e.g. oestrone, oestriol) may be used successfully in treating menopause symptoms in postmenopausal women, they are *not* suitable for transsexual patients; it is necessary to supply 17 beta-oestradiol or a synthetic replacement for it.

Oestrogen therapy must be continued for life in a post-operative subject, otherwise numerous problems can occur. In particular, several very severe cases of osteoporosis have been reported in post-ops who have discontinued their oestrogen treatment. 'Menopause-like' symptoms also occur if oestrogen is discontinued.

Oestradiol Valerate

This drug is equivalent to natural 17 beta-oestradiol. It is generally well-tolerated, and clinical data from postmenopausal women suggest it is safer than ethinyloestradiol for long-term use, with less risk of breast cancer, thromboembolic events or liver problems. It is not certain whether this improved safety applies in the high doses necessary for pre-op transsexuals.

This is widely regarded as the oestrogen of choice for long-term maintenance in post-op TS patients due to its good safety record; typical post-op dose would be 1--2mg daily, ideally divided into two doses.

Oestradiol valerate appears to be less effective at inducing feminisation in pre-op subjects than ethinyloestradiol, probably due to its short serum half-life --- particularly, it appears to fare poorly when 'in competition' with endogenous male hormones; adequate results have been obtained with oestradiol valerate combined with an effective antiandrogen. Typical pre-op dose would be 4--6mg daily in divided doses (1 or 2mg per dose); if 'menopause-type' symptoms appear (hot flushes, night sweats etc) this can often be a sign that the dose is not sufficient to overcome the endogenous male hormones and a switch to ethinyloestradiol would probably be advisable.

Ethinylestradiol

This drug is a synthetically-produced modification of natural 17 beta-oestradiol. The modified molecule is eliminated only slowly by the liver, giving it a far greater potency and much longer half-life than other oestrogens. It is generally well-tolerated, but appears to be less safe in very long-term use than oestradiol valerate.

Ethinylestradiol is widely regarded as the oestrogen of choice in pre-operative subjects. A dose of 100 µg daily (in two doses) is typical; this can be increased to 150 µg if necessary. Its long half-life and high potency give it excellent feminising effects.

In post-op patients, this drug may still be used, especially for patients whose feminisation has not completed by the time they have GRS. For short-term post-op use, the full pre-op dose of 100 µg may be used, this is normally reduced to 50 µg after 6--12 months. For long-term post-op use, oestradiol valerate is probably preferable.

It should be noted here that oestrogen overdosage may paradoxically cause vasomotor symptoms similar to those produced by insufficient oestrogen dosage. This is sometimes seen in post-op patients who are still on pre-op dosage, and if this effect is suspected then the oestrogen dosage should immediately be reduced to a typical post-op level. This effect is more likely with ethinylestradiol than with other oestrogens due to its high potency, and consideration may be given to an early switch to oestradiol valerate if the problem persists.

Conjugated Natural Oestrogens (Premarin)

This drug is a mixture of various oestrogenic substances extracted from the urine of pregnant mares. It lacks the potency of ethinylestradiol, and there is no evidence that it has any advantages over oestradiol valerate. Many patients dislike this drug because of ethical concerns over the manner in which it is produced. It is increasingly regarded as an outmoded treatment for TS patients. It is also more expensive than the synthetically-manufactured drugs.

A typical pre-op dose would be 5--7.5mg daily in divided doses, reducing to 1--2.5mg daily post-op.

Other Oestrogens

A number of other oestrogenic drugs exist, many of which have been tried in the past in TS patients. It has already been mentioned that metabolites such as oestrone and oestriol are not suitable for use in TS patients; other oestrogen derivatives exist but have no advantages over the three oestrogens listed above. Diethylstilboestrol has been used in the past, and while it certainly produces worthwhile feminising effects, its safety record contraindicates its use in TS subjects: many serious problems, including fatalities, have been reported.

PROGESTOGENS

Progestogens administered alone do not produce feminisation in a phenotypic male. However, progestogens are generally quite antiandrogenic and will often provide a useful degree of testosterone suppression in a pre-op patient, and more importantly when administered in conjunction with oestrogen, improve the feminisation attained compared to oestrogen-only therapy, particularly in terms of breast weight and texture.

One UK endocrinologist has claimed that progestogens have no effect in transsexual patients, however numerous studies both in the UK and elsewhere have demonstrated that this claim is false. Progestogens are now very widely used in conjunction with oestrogens in the treatment of male-to-female transsexualism.

Progestogens may also lessen the risk of cancer associated with long-term oestrogen treatment, according to some studies in natural-born females. In addition, some patients report that progestogens affect them psychologically, particularly in terms of maintaining the libido. For all these reasons, it may well be desirable to continue with a low dose of progestogen post-operatively, even though there is no absolute need for it.

No reliable data exists regarding the incidence of breast cancer in transsexuals. Many are lost to followup and conceal their transsexual past after completing their treatment, and any instances of breast cancer in this group are likely to be recorded as occurring in normal women rather than transsexuals. One researcher has claimed to find a significant excess of breast cancers among certain chromosomally-intersexed patients who have been reassigned to female.

A few patients experience androgenic effects from some progestogens, possibly including an increase in body hair. If this occurs, a different progestogen should be tried. Similarly, if fluid retention occurs, a switch to an alternative drug will probably resolve it.

Medroxyprogesterone Acetate

This progestogen (trade name Provera) is normally used for treating irregular menstrual bleeding or endometriosis, and its safety record is good.

It is widely regarded as the preferred progestogen, at least when the patient is not using combined contraceptive pills as a low-cost source of oestrogen and progestogens. Some patients, however, report slight virilising effects including, occasionally, a return of some degree of male sexual function even in post-orchidectomy subjects, which can be found disturbing; it appears that a proportion of the drug may be metabolised into testosterone in some patients. Medroxyprogesterone acetate is generally less virilising than the testosterone-derived synthetic progestogens (e.g. norethisterone and levonorgestrel), but more virilising than dydrogesterone. If a patient experiences

virilising effects with medroxyprogesterone acetate then a switch to dydrogesterone should be considered.

A typical pre-op (or early post-op) dose (to maximise feminisation) would be 10mg in two doses; post-op, 5mg or even 2.5mg may be sufficient to maintain the patient's libido.

Dydrogesterone

This progestogen (trade name Duphaston) may be used as an alternative to medroxyprogesterone acetate. It is not metabolised into testosterone within the body, and is therefore free of the virilising effects which some patients experience from other progestones. Conversely it may be less effective in maintaining libido than medroxyprogesterone acetate.

Dydrogesterone is regarded as the progestogen of choice when patients have experienced virilising effects from other progestogens.

A typical pre-op (or early post-op) dose would be 20mg in two doses, reducing to a single dose of 10mg daily post-op.

Natural Progesterone USP

This drug, which is probably unavailable in the UK, has a small but vocal group of transsexual adherents in the USA, who claim that it is superior to other progestogens. The present authors have been unable to find any clinical data to support this claim; while it appears to be free of virilising effects, first-pass effects are liable to make it relatively ineffective relative to dydrogesterone, which is also non-virilising.

The main problem with 'Natural Progesterone' is that it is largely destroyed by the digestive tract and liver upon ingestion, so very large doses (hundreds of milligrams) are used. Since the precise percentage of the drug metabolised in this way is variable and unknown, the actual serum levels obtained are unpredictable.

Synthetic Progestogens

This heading covers substances such as levonorgestrel and norethisterone, which are usually found in combined contraceptive tablets, usually with ethinyloestradiol.

Contraceptive pills provide a useful low-cost source of feminising hormones for patients who have to pay for their own medications, but of course the patient is limited to the combinations of substances available, and cannot 'mix and match' as one can with separate oestrogen and progestogen drugs.

Care should be taken with some preparations (for example, Brevinor) as they contain too high a ratio of progestogen to oestrogen, so that taking enough tablets to obtain a suitable dose of oestrogen would result in a dangerously high intake of progestogen.

One combined tablet that has been used widely in the treatment of transsexual patients is Ovrán; a typical pre-op dose of two tablets daily gives 100 µg of ethinylloestradiol and 500 µg of levonorgestrel. Most patients tolerate this well, and it generally produces satisfactory feminisation, but levonorgestrel appears (anecdotally) to give more frequent problems with water retention, hypertension and weight gain than medroxyprogesterone acetate. Safety fears have also been raised in the past about levonorgestrel-based contraceptive implants.

Some patients experience virilising effects with norethisterone or levonorgestrel, which may impair the feminising effects of oestrogen. If this is suspected then an alternative progestogen should be tried.

ANTIANDROGENS, GnRH AGONISTS AND ORCHIDECTOMY

Hormone treatment in pre-operative male-to-female subjects is normally supplemented by some form of antiandrogen treatment. While oestrogens and progestogens are to some extent antiandrogenic in themselves, a number of other methods exists to suppress the effects of androgens and make the feminising hormones more effective without having to administer the latter in unreasonably high doses.

These treatments also, of course, cause a significant reduction in male sex drive (and indeed sexual function), which is generally considered highly desirable by transsexual subjects.

There are three approaches to antiandrogen treatment:

1. Antiandrogen drugs.
2. GnRH (Gonadotropin-releasing-hormone) agonists.
3. Bilateral orchidectomy (castration).

These treatments are not applicable to patients who are post-operative, as their bodies will, by definition, be incapable of producing gonadal androgens. Adrenal androgens are produced in small amounts by both sexes, and no attempt should be made to suppress them unless a serum androgen test has indicated significant overproduction, as in cases of adrenal hyperplasia. In general it is considered unwise to administer antiandrogens to post-operative subjects (and indeed to severely hypogonadal subjects such as certain intersexed patients), as the small amount of adrenal androgens remaining in such subjects are necessary for normal functioning.

ANTIANDROGEN DRUGS

These drugs either inhibit gonadal androgen production, interfere with androgen receptor sites, or both. Most are likely to produce some side effects in effective doses; some patients cannot tolerate some or all antiandrogen drugs, in which case bilateral orchidectomy is likely to be a preferable treatment.

The effect of these drugs on fertility and male sexual function is reversible to an extent, however (like feminising hormones) irreversible infertility may ensue after some months of treatment.

All antiandrogen drugs, like feminising hormones, must be withdrawn prior to major surgery. This may lead to a degree of reversion towards masculinity, which may be pronounced and disturbing in some patients.

Cyproterone Acetate

This drug (brand names Androcur, Cyprostat) is widely regarded as the antiandrogen of choice by practitioners in Europe (it is not approved in the USA). It is an androgen receptor antagonist and weak gonadal androgen production inhibitor; normal dose is 50mg daily, which may be increased to 100 or in exceptional cases 150mg daily if required.

In these doses there are some risks associated with the drug, particularly a heightened risk of thromboembolic disease or liver damage. Carbohydrate metabolism changes are also reported; patients should receive regular blood tests (LFT and fasting glucose) and BP checks.

Possible side effects include severe lassitude, loss of concentration and depression, also weight gain and nausea. Anecdotal reports suggest that the side effects can be lessened by taking the drug after meals; opinions differ as to the best time of day to take a single dose to minimise the tiredness effect: patients are best advised to experiment for themselves, though after lunch or after the evening meal seem to be the usual choices.

Flutamide

This is a relatively new drug which has been used with success in some transsexual patients, particularly those who have experienced unacceptable side effects with cyproterone. There is relatively little clinical data available for this drug in transsexual patients.

It is a strong androgen receptor antagonist. Like cyproterone it can be hepatotoxic, it can also have significant adverse haematological effects (reduced platelet, leukocyte or erythrocyte count) or cause hypertension, and it can also produce less serious side effects such as fluid retention. Regular LFTs and blood checks are advisable when using this drug.

This drug also produces psychological side effects which can be severe in some patients. Depression, anxiety or nervousness can be extreme, and patients should be made aware of this possibility. Lassitude, insomnia and gastrointestinal disturbances have also been reported.

Typical dose is 250mg to 750mg daily (one to three 250mg tablets).

Spirolactone

This drug was originally developed as an antihypertensive/diuretic; it is also a weak androgen receptor antagonist. It is much less effective as an antiandrogen than cyproterone or flutamide, but can find use in patients who have hypertension or severe fluid retention, either pre-existing or as a result of hormone treatment.

Side effects may include lassitude, loss of concentration, and various gastrointestinal problems. There is a risk of potassium retention.

Doses range typically from 100 to 400mg daily.

Finasteride

This drug is not suitable as a general antiandrogen, but is mentioned here as it can be useful in countering male-pattern baldness in transsexual subjects. Classed as an androgen conversion inhibitor, it blocks the conversion of testosterone to DHT.

It is generally free from significant side effects, but does not appear to affect male sex drive. Typical dosage is 5mg daily.

GNRH AGONISTS

These drugs take a different approach to antiandrogens: they act on the pituitary, initially overstimulating it and then rapidly desensitising it to GnRH. The effect of this is that over a period of weeks, gonadal androgen production is greatly reduced.

Their principal advantages are that they are generally fully reversible in their effects, which makes them a useful treatment in adolescent subjects where it is desired to stall the changes of puberty but not desired to induce permanent feminisation until the subject is older; and that they do not carry the risks of thromboembolic disease associated with antiandrogens. This can be particularly useful when hormones/antiandrogens are withdrawn prior to surgery --- GnRH agonist treatment can be used to minimise the reversion to male biochemistry that many transsexual subjects find deeply disturbing.

GnRH agonists do carry risks of significant side effects and should be used with great caution. There is as yet relatively little clinical data on the use of these substances in transsexual subjects, particularly in long-term use.

Nafarelin Acetate

Normally administered as a nasal spray (typical dosage 1600 µg daily). May cause depression, insomnia, skin problems and other side effects. Being administered daily, the drug can easily be withdrawn should side effects occur.

Goserelin Acetate

Administered as a depot (i.e. time-release) injection (typically 3.6mg monthly). Reported adverse effects include heart failure, obstructive pulmonary disease and severe allergic reactions as well as more minor side effects such as lethargy and nausea. In view of the fact that it is a depot injection, this drug should be treated with caution as it cannot be rapidly withdrawn should problems occur.

Leuprorelin Acetate

Similar to Goserelin Acetate, with a typical dose of 3.75mg every 4 weeks. This drug has been used to good effect in adolescent subjects. Allergic reactions and other side effects have been reported.

BILATERAL ORCHIDECTOMY

Bilateral orchidectomy is a possible alternative to antiandrogen therapy or GnRH agonists for androgen suppression in preoperative transsexual subjects. It can be cost-effective in comparison with lengthy antiandrogen treatment; privately, orchidectomy is available for under £1000 (1997).

Orchidectomy offers several advantages over antiandrogen or GnRH-agonist therapy:

- **Safety.** The surgical procedure is simple and can be done under local anaesthesia. After orchidectomy, the patient is endocrinologically equivalent to a post-operative subject and should take the appropriate (lower) dosage of feminising hormones; there is no need for antiandrogens or GnRH agonists. This has clear safety advantages especially in patients thought to be at elevated risk of thromboembolic events. For long-term use (e.g. in patients who cannot afford GRS for a considerable time, or for whom GRS is contraindicated by other conditions), this is particularly significant.

- Immediacy. It is generally impossible for a patient to obtain GRS without living in role for at least a year. This requirement does not apply to orchidectomy, at least in Britain.
- No reversion. When hormones are withdrawn prior to surgery, or for any other reason, the patient will not revert towards male biochemistry or appearance. This is of enormous psychological benefit in many patients.
- No side effects. Some patients report transient lethargy as their body adapts to the loss of androgens, but all the side effects associated with antiandrogens or GnRH agonists are eliminated.
- Improved feminisation. In a post-orchidectomy patient, feminising hormones can act unopposed. This produces more complete and more rapid feminisation than is normally achievable with antiandrogens.
- Psychological benefits. Patients report a feeling of progress or achievement, of "asserting their true nature over a physical deformity", and of looking 'less masculine' in the genital area. For the true transsexual this can produce a significant improvement in emotional wellbeing.

There are some disadvantages to orchidectomy (aside from the obvious necessity of an additional surgical procedure), and patients should be made aware of these:

- Irreversibility. Complete loss of fertility will be irreversible. Male sex drive and sexual function can in principle be restored by administration of testosterone should the patient decide to revert to a male role. Conversely, it should be observed that hormone/antiandrogen therapy is also not truly reversible, and patients should be properly assessed by a specialist psychiatrist before any such treatment commences. With proper assessment, cases of reversion to the original gender role are extremely rare, so irreversibility is not considered to be a major issue.
- Shrinkage of scrotal tissue. If GRS is not performed for a considerable period after orchidectomy (e.g. 3 years or more), there is a risk of atrophy and shrinkage of the scrotal tissue, reducing the amount of donor material available for eventual GRS. This may or may not cause a problem, depending on the patient's anatomy and the surgeon's technique. It should be noted, however, that long-term hormone/antiandrogen use can also produce significant atrophy of penile and scrotal tissue, and surgeons normally recommend 'stretching exercises' to limit this effect; this method can equally be applied to scrotal tissue after orchidectomy.

Bilateral orchidectomy normally requires a referral from a psychiatrist; some surgeons may require a second opinion from an independent psychiatrist. Orchidectomy as a precursor to GRS is now widely regarded as a useful procedure in properly selected patients.

DRUG INTERACTIONS

Levels of Estradiol, Ethinyl Estradiol:

Increased by:	Decreased by:
Astemizole	Benzoflavone
Cimetidine	Carbamazepine
Clarithromycin	Dexamethasone
Diltiazem	Naphthoflavone
Erythromycin	Phenobarbital
Fluconazole	Phenylbutazone
Fluoxetine	Phenytoin
Fluvoxamine	Progesterone
Grapefruit	Rifampin
Isoniazid	Sulfamidine
Itrakonazole	Sulfinpyrazone
Ketoconazole	
Miconazole	
Nefazadone	
Paroxetine	
Sertraline	
Triacetyloleandomycin	
Verapamil	

Levels of Estrogen:

Increased by:	Decreased by:
Efavirenz	Nelfinavir
Indinavir	Nevirapine
Vitamin C	Ritonavir
	Smoking

Testosterone increases the hypoglycemic effect of Sulfonylureas and the anticoagulant effect of Warfarin.

REFERENCES USED:

Department of Public Health in San Francisco

Website: <http://www.dph.sf.ca.us/chn/HlthCtrDocs/Transgendprotocols.pdf>

Title of document:

Memorandum – Protocols for Hormonal Reassignment of Gender (24-7-01)

Authors: Tom Waddell Health Center Transgender Team

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The Looking Glass Society

The Looking Glass Society is a non-profit organisation dedicated to promoting understanding and acceptance of Transsexual/Gender Dysphoric people. It publishes a range of booklets concerning the condition and engages in education work, particularly aimed at people involved in caring for or working with those with Gender Dysphoria.

They are based in the South-West of England, so many of there publications reflect a UK perspective.

Website: <http://www.looking-glass.greenend.org.uk/medical.htm>

Title of Document: Transsexualism: A Medical Overview

Third Edition, March 1998

Contents last updated 27 June 2003.

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