In healthcare, as in all spheres of life, we are all meeting more trans people. While more progress needs to be made, in some societies much more than others, many of those who in the past have battled in silence feel freer to live the lives they wish to and need to. As a result, increasing numbers of trans people will present to healthcare professionals in various stages of their transition. This is illustrated by the fact that referrals to gender identity clinics in the UK have doubled every five years since the late 1960s.

Gender dysphoria is a recognised condition defined in DSM-V as a persisting difference between a person’s expressed or experienced gender and the gender others would assign to him or her, with resultant significant distress or impaired functioning. Of notable significance, the draft ICD-11 classification places ‘gender incongruence’ outside the mental health section, replacing the current ICD-10 diagnosis of ‘transexualism’.2

As practising clinicians, there are some aspects of care for trans people that may be unfamiliar. That said, the majority of general medical management for the trans population should, of course, not differ in any way from other patients.

There have already been two excellent articles on transgender issues in this publication, one looking at general support for trans people in our practice,3 and another looking at male-to-female genital reconstruction.4 While the latter touched briefly on hormonal therapy, we will explore this subject in more depth in this and a subsequent article. We aim to clearly summarise some of the important considerations relevant to providing the optimal hormonal milieu for people to commence and maintain their physical transition.

**Hormonal treatment**

For trans men and women, the aim of hormone treatment is to suppress production of the sex hormones of a person’s assigned gender, and replace them with those of the experienced gender. Thorough multidisciplinary assessment should precede the initiation of hormone treatment to evaluate an individual’s biopsychosocial health, and baseline blood tests are an integral part of this.
It is also important to identify any intersex states or medical conditions that could have a bearing on the safety of hormone prescribing. Cross-sex hormone treatment is usually continued throughout a patient’s lifetime, including after any genital reconstructive surgery, to prevent long-term complications such as heart disease or osteoporosis.

As the various national contracts in the UK stand, GPs play an invaluable role in helping their patients travel along their transition journey, as the prescribing of hormone therapy is continued in primary care. Clear shared care agreements should be made available to support this process. The General Medical Council (GMC) has published succinct guidance which can be viewed online. Its recommendations for co-operating with gender identity clinics include ‘prescribing medicines recommended by a gender specialist for the treatment of gender dysphoria’ and ‘following recommendations for safety and treatment monitoring.’ The GMC statement on prescribing for gender dysphoria is given in Box 1.

The goal of hormonal therapy in trans men is to simulate natural male puberty, a process which can take two to five years to complete. As expected, the mainstay of hormonal management here is testosterone therapy. In the majority of cases, the testosterone doses used are sufficient to suppress ovarian production, thereby achieving the dual aim of suppressing and replacing assigned-gender hormones to aid transition.

**Physical and behavioural changes**

The various physical changes seen with testosterone therapy, along with expected timeframes, are summarised in Table 1. One of the most distressing features for trans men before treatment (menstrual bleeding) will usually cease early on through negative feedback on the pituitary. This most commonly occurs within two or three cycles. There are, of course, implications for fertility. Trans men who think they may wish to have children should seek gamete storage before starting testosterone.

Uncommonly, cessation of menses may take longer. In some individuals additional therapy may be required if bleeding continues after testosterone levels are confirmed in the target ranges. Our preferred options then are to recommend either medroxyprogesterone 10mg three times daily (probably associated with less clot risk than norethisterone) or a gonadotropin-releasing hormone (GnRH) analogue, such as three-monthly injections of 11.25mg triptorelin (Decapeptyl). These medicines should be stopped if the patient undergoes hysterectomy and oophorectomy.

Another early change will be an increase in clitoral size. This is usually seen from around three to four months and stabilises around one year, reaching a typical length of 4–5cm. This is usually not sufficient for penetrative intercourse. Vaginal atrophy develops over a similar time scale. Also developing quite soon after testosterone initiation are skin changes in the form of increased oiliness and acne. This can appear within a few months and will stabilise at around one to two years. A little later, from approximately six to twelve months, deepening of the voice will become noticeable, again becoming maximal over one to two years. This move to a more masculine sound is irreversible. Some men find additional speech therapy helpful to consolidate the change.

Facial and body hair will develop in a male pattern, with changes again seen from around six months, taking four to five years to complete. In genetically susceptible trans men, male pattern baldness may develop. Over a similar time scale, a more masculine body shape can also be expected. There will be an increase in lean mass with increased strength and muscle definition, and

**Table 1. Physical effects seen with testosterone therapy, and expected timings**

<table>
<thead>
<tr>
<th>Effect</th>
<th>Onset (months)</th>
<th>Maximum (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin oiliness/acne</td>
<td>1–6</td>
<td>1–2</td>
</tr>
<tr>
<td>Cessation of menses</td>
<td>2–6</td>
<td>-</td>
</tr>
<tr>
<td>Clitoral enlargement</td>
<td>3–6</td>
<td>1–2</td>
</tr>
<tr>
<td>Vaginal atrophy</td>
<td>3–6</td>
<td>1–2</td>
</tr>
<tr>
<td>Fat redistribution</td>
<td>1–6</td>
<td>2–5</td>
</tr>
<tr>
<td>Increased muscle mass/</td>
<td>6–12</td>
<td>2–5</td>
</tr>
<tr>
<td>strength</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deepening of voice</td>
<td>6–12</td>
<td>1–2</td>
</tr>
<tr>
<td>Facial/body hair growth</td>
<td>6–12</td>
<td>4–5</td>
</tr>
<tr>
<td>Scalp hair loss</td>
<td>6–12</td>
<td>-</td>
</tr>
</tbody>
</table>

**Box 1. GMC statement on prescribing for gender dysphoria in general practice**

‘Once the patient has been discharged by a gender identity clinic or gender specialist, the prescribing and monitoring of hormone therapy can be carried out in primary care without further specialist input. From the patient’s perspective, management in primary care is far easier, and there is no specific expertise necessary to prescribe for and monitor patients on hormone therapy.’
Transgender health

Common behavioural changes include increased libido, energy levels and general drive/motivation. Some trans men will also report an increase in aggressive behaviour, though this is not usually excessive. This mirrors changes seen with testosterone therapy in cis (non-trans) men. Trans men usually describe feeling more settled as the various physical changes help to confirm their experienced gender role.

Potential adverse effects of testosterone therapy

Lipid profile and cardiovascular risk

A recent meta-analysis of 29 studies concluded that there were small but significant aberrant changes in the lipid profile with testosterone treatment in trans men, with mean changes of: LDL-cholesterol + 0.46mmol/L, HDL-cholesterol - 0.22mmol/L and triglycerides + 0.24mmol/L. It found minimal reports of myocardial infarction (MI), stroke, venous thromboembolism, and death events. It has previously been reported that MI rates in trans men are only about one third of the expected rate in cis men. However, cardiovascular risk should be assessed and managed just as it would for any other patient.

Polycythaemia

Testosterone is well known to increase haematocrit through increased levels of erythropoietin. The resultant polycythaemia is not usually significant, but must be monitored for due to the increased thrombosis risk. We recommend seeking advice if the haematocrit rises above 0.54, when testosterone therapy may need adjusting. We advise halting therapy (temporarily) with results of 0.6 or higher.

Cancer risk

There is a theoretical risk of endometrial hyperplasia and potentially subsequent cancer through the action of low levels of oestradiol (converted from testosterone via aromatase) unopposed by progesterone. While current recommendations advise on a hysterectomy after two years, or scanning every two years to assess endometrial thickness, the

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### Table 2. Testosterone therapy as used by the authors’ clinic

<table>
<thead>
<tr>
<th>Preparation</th>
<th>Dose</th>
<th>Frequency</th>
<th>Monitoring method</th>
<th>Target range, testosterone</th>
<th>Maximum dose</th>
<th>How to adjust, if needed</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Testosterone injections</strong></td>
<td><strong>(short-acting)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sustanon or testosterone enantate</td>
<td>Starting dose: 250mg (1ml vial) Dose range: 150–250mg, 0.6–1ml</td>
<td>2–4 weekly</td>
<td>Trough: just before an injection (same day) Peak: 7 days later *Bloods as in Box 2</td>
<td>Trough level: 8–12 nmol/L Peak level: less than 30 nmol/L</td>
<td>250mg every 10 days</td>
<td>Focus on trough level first and adjust dosing interval as needed to achieve target (usually by a week up or down). If trough is in range but peak is high, reduce dose in 50mg steps</td>
</tr>
<tr>
<td><strong>Longer-acting injection</strong></td>
<td>Nebido (testosterone undecanoate) (has a loading phase)</td>
<td>6–15 weekly</td>
<td>Trough: just before an injection (same day) *Bloods as in Box 2</td>
<td>15–20nmol/L</td>
<td>1000mg every 6 weeks</td>
<td>Adjust dosing interval as required (usually by a week up or down). Dose is not usually adjusted</td>
</tr>
<tr>
<td><strong>Testosterone gel</strong></td>
<td><strong>(topical)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sachets: Testogel 50mg/5g Pump: Testogel 16.2mg/20g (20mg per squirt) or Tostran (10mg per squirt)</td>
<td>Starting dose: 40–50mg Dose range: 20–100mg</td>
<td>Daily, applied in the morning</td>
<td>Bloods taken 4–6 hours after gel application (ensure no gel on arms) *Bloods as in Box 2</td>
<td>15–20nmol/L</td>
<td>100mg daily (2 sachets; 5 squirts of Testogel pump; 10 squirts of Tostran)</td>
<td>Adjust dose as required. Adjustments usually as steps of ½ sachets, or 1–2 squirts of pump</td>
</tr>
</tbody>
</table>
recent evidence in fact indicates endometrial thinning.\textsuperscript{12}

For cervical screening, the recommendation is to follow the same programme as for all those assigned as female at birth (while the cervix remains). It is important to remember that IT systems will not ‘find’ these individuals for invitation purposes once their gender is changed. Patients therefore often have to present themselves for screening, unless practices have set their own internal recalls for them.

Breast cancer risk seems to be very low, comparable to cis men.\textsuperscript{13} Self-examination is still advised, including for those who have had chest reconstruction surgery, which is often not a full mastectomy.

**Bone density**
A reassuring recent meta-analysis found no significant impact of testosterone therapy on bone mineral density at any site in trans men.\textsuperscript{14}

**Liver function**
While there have been historical concerns with high rates of liver dysfunction due to anabolic steroid use, modern protocols of testosterone therapy are associated with mild changes in liver function in only 4–7\% of patients.\textsuperscript{11}

**Testosterone therapy regimes and monitoring**
Prescribing of testosterone for trans men is, in many ways, similar to that for cis men treated for testosterone deficiency. Whilst Sustanon (a blend of four testosterone esters) is licensed for use in this transgender setting, the off-licence use of other medicines is very well established.

We will usually recommend starting trans men on Sustanon to provide a quick and reliable onset of action that can be easily reversed should the need arise. Once stabilised, other options include using gels or the longer-acting testosterone undecanoate injection (Nebido). This choice often comes down to patient preference, although the latter two options tend to give more stable levels of testosterone, avoiding the potentially symptomatic fluctuations seen with Sustanon. In addition, gels appear to be associated with lower rates of polycythaemia than injections.

It is crucial that patients are regularly monitored, both clinically and biochemically, through blood tests. This should be continued after discharge from a gender identity clinic, usually on an annual basis once stabilised. While the risk of adverse effects is low, as outlined above, it is important that ‘safety’ blood tests are included alongside monitoring of testosterone levels.

Table 2 shows the forms of testosterone therapy recommended by our clinic, with Box 2 outlining the advised monitoring.

**Conclusion**
Through a multidisciplinary approach, including a vital ongoing role for primary care practitioners, trans people can be safely and effectively medically managed through the early and later phases of their transition. Hormonal treatment for trans men will in most cases be straightforward and is often achieved with testosterone alone. There are low rates of adverse effects, provided simple monitoring is adhered to.

**Declaration of interests:** none declared.

**References**


