Premature ejaculation: A clinical review for the general physician

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Background
Premature ejaculation is one of the most common sexual dysfunctions in men. Recent epidemiological studies suggest its prevalence in Australia may range from 21–31%.

Objective
This article will discuss the current definition of premature ejaculation from a urological perspective. It will provide an understanding of the pathogenesis of premature ejaculation, as well as assessment and management options.

Discussion
Premature ejaculation can have a significant adverse effect on the quality of life for the patient and his sexual partner’s. It can potentially lead to psychological distress, diminished self-esteem, anxiety, erectile dysfunction, reduced libido and poor interpersonal relationships. Most men feel reluctant to discuss premature ejaculation with their general practitioner despite its psychological, emotional and relational effects. Effective, evidence-based treatment options are available and physicians should feel confident when exploring ways to improve the quality of life for men with sexual dysfunction.

Premature ejaculation is one of the most common sexual dysfunctions, affecting up to 21–31% of the Australian adult male population, irrespective of their age, marital status or ethnicity. This sexual condition is likely to be under-reported and under-treated because of the patients’ perceived shame and low self-esteem. This is in addition to many physicians feeling uncomfortable or uncertain about the management of premature ejaculation. The impact of premature ejaculation is mostly felt psychologically and in interpersonal relationships. Men with premature ejaculation often experience significant psychological distress, avoid physical and emotional intimacy, and become victims of false medical advertisements and unproven medical management.

Pathophysiology and associations
Psychological components often contribute to acquired premature ejaculation. However, it is likely that a complex interplay between neurophysiological factors predominantly influence premature ejaculation. In particular, genetic predisposition for impairment of inhibitory serotonergic pathways that regulate ejaculation, modulated by 5-HT2c, 5-HT1a, 5-HT1b receptors and synaptic serotonin transporters has been reported for lifelong premature ejaculation. Other conditions, such as chronic prostatitis and hyperthyroidism, may also be associated with acquired premature ejaculation.

Erectile dysfunction and premature ejaculation frequently co-exist as men with erectile dysfunction might try to
ejaculate early, before loss of erection.\textsuperscript{11,18} Thus, detection of comorbid erectile dysfunction is crucial in guiding therapeutic implementation.\textsuperscript{19}

### Assessment of premature ejaculation

Patients with premature ejaculation may present to general practice because of personal or partner-initiated reports of erectile or sexual dysfunction, and relationship difficulties. However, when the physician is unsure of the context of the presenting complaint, or uncertain about what to ask, an open-ended question, such as ‘How are things at home?’, may evoke disclosure of relevant symptoms. A full evaluation of the patient’s medical, sexual, psychological, social and drug history, along with his partner’s sexual history, is necessary to identify any factors that may be potentially reversible.

It is also important to explore the perceived degree of ejaculatory control, estimated IELT (precise timing is not necessary), previous attempts to correct premature ejaculation, and the impact on interpersonal relationships and quality of life. Various screening questionnaires such as the Premature Ejaculation Diagnostic Tool (PEDT), when combined with clinical assessment, are accurate in diagnosing premature ejaculation if it is unclear.\textsuperscript{20–22} It is particularly crucial to ascertain whether the diagnosis is lifelong or acquired, and be aware that erectile dysfunction may exacerbate the presentation. Simply inquiring about the loss of an erection before ejaculation can help to distinguish erectile dysfunction from premature ejaculation.

Physical examination of patients who experience premature ejaculation is often unremarkable. Full abdominal, neurological, lower limb and genital examinations are recommended. Although examination has a low diagnostic yield, it facilitates important reassurance for the patient that he is anatomically normal. There are no specific investigations to confirm or exclude premature ejaculation. Any additional investigations should investigate suspicion of contributory factors identified during history and examination.

### Management of premature ejaculation

Ideally, discussions about management should involve the patient and his regular sexual partner. Treatment choice requires consideration of symptom severity, reversible causes, psychosocial impact, side effects and patient preferences.\textsuperscript{23}

In clinical practice, management is complex and requires a combination

<table>
<thead>
<tr>
<th>Table 1. Summary of the four classifications of premature ejaculation</th>
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<tbody>
<tr>
<td><strong>Lifelong (primary)</strong></td>
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<tr>
<td>IELT criteria</td>
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<tr>
<td>Symptoms</td>
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<tr>
<td>Onset</td>
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<tr>
<td>Prevalence</td>
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<tr>
<td>Quality of ejaculation control</td>
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<td>Aetiology</td>
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<td></td>
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<tr>
<td>Treatment</td>
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IELT, intravaginal ejaculatory latency time
of pharmacological, psychological and behavioural treatments (Figure 1).

**Conservative management options**

**Psychological therapy**
Initially, psychological therapy was the mainstay of treatment for premature ejaculation. It is used less in current clinical practice because of time constraints, costs and requirement for strong compliance from couples.

Inconsistent, randomised evidence evaluating psychological therapy suggests its efficacy decreases over time and is inferior to pharmacotherapy. However, psychological therapy may be a suitable first-line treatment for patients with subjective premature ejaculation, or when a clear psychological aetiology is present. This can also be used to manage distress related to sexual dysfunctional, or in combination with pharmacotherapy.

**Behavioural therapy**
Various behavioural changes have been suggested in the literature. For example, pre-coital masturbation is widely thought to improve IELT, but there is a lack of data to support this practice. Alternative behavioural therapy modalities attempt to attenuate the sensory responses of PE likely

Patient/partner history
- Establish presenting complaint
- Estimate intravaginal ejaculatory time
- Perceived degree of ejaculatory control
- Degree of patient/partner distress
- Onset and duration of PE
- Psychosocial history
- Medical history
- Physical examination

Variable PE

PE unlikely

Subjective PE

Variable PE

Treatment
- Reassurance
- Education
- Psychotherapy
- Behavioural therapy
- Follow-up

Manage the primary cause

Yes

No

Acquired PE

Treatment
- Behavioural/psychotherapy
- SSRI pharmacotherapy
- Combination therapy

Follow-up
May attempt graduated withdrawal of pharmacotherapy after 6–8 weeks

Lifelong PE

Treatment
- SSRI pharmacotherapy
- Behavioural/psychotherapy
- Combination therapy

Follow-up
May attempt graduated withdrawal of pharmacotherapy after 6–8 weeks, but will often require lifelong pharmacotherapy

Figure 1. Premature ejaculation management algorithm
ejaculation by interrupting heightened arousal. These include the ‘stop-start’ (ceased genital stimulation until heightened arousal sensation subsides)\textsuperscript{28} and ‘squeeze’ (where the glans prepuce is squeezed at heightened arousal)\textsuperscript{29} techniques. These techniques are often considered intrusive, mechanical and disruptive of the normal spontaneity of coitus, and of little benefit when used alone. Other behavioural techniques include the use of multiple condoms and pelvic floor exercises. These techniques may improve premature ejaculation when combined with pharmacotherapy, but further efficacy studies are required.\textsuperscript{30}

**Complementary and alternative therapy**

There is limited evidence supporting the use of acupuncture for the treatment of premature ejaculation.\textsuperscript{31} However, complementary and alternative medicine is not a recommended form of treatment for premature ejaculation.\textsuperscript{32}

**Medical management**

**Topical anaesthetic agents**

Anaesthetic aerosols and creams containing lignocaine, lignocaine/prilocaine or herbal-derived anaesthetic agents can increase IELT and sexual satisfaction. These agents are often recommended as treatments for premature ejaculation.\textsuperscript{12,33–35} They are applied to the glans penis well ahead of sexual intercourse and should be used in conjunction with condoms to avoid numbness in the partner’s genitals.

**Serotonergic antidepressants**

Serotonin inhibits ejaculation and its effects are potentiated by tricyclic antidepressants (TCAs) and selective serotonin reuptake inhibitors (SSRIs). TCAs are effective, but infrequently used because they have prominent side effects, including nausea, dry mouth, erectile dysfunction, hot flushes and cardiotoxicity. Clomipramine is the only TCA in routine use.\textsuperscript{12,35}

The therapeutic efficacy of SSRIs for premature ejaculation is well supported by the literature.\textsuperscript{36} Daily SSRI use may improve ejaculation delay after a few days; maximal delay is usually achieved after 1–2 weeks. Paroxetine is the most effective SSRI. However, paroxetine is not suitable for on-demand use because it has a slow onset of action (5 hours) and long half-life (1–3 days), and daily dosing is required to maintain efficacy.\textsuperscript{15} Daily SSRI dosing is more effective than on-demand treatment and is often favoured by patients because spontaneity of sex is maintained; however, compliance issues can occur with long-term use.

Doses of SSRI for premature ejaculation are significantly less than those used for depression, but have a similar side effect profile. Common side effects are fatigue, nausea, diarrhoea, dry mouth and decreased libido.\textsuperscript{37} There are also anecdotal accounts of infertility.\textsuperscript{38} Serotonin syndrome may also pose a risk if the patient is on concomitant treatment with drugs that elevate serotonin levels.\textsuperscript{37}

Despite evidence supporting the use of clomipramine and traditional SSRIs (eg paroxetine, sertraline and fluoxetine) for the treatment of premature ejaculation, they are not licenced for treatment of this condition. As such, use of these agents for premature ejaculation would be off-label and incur costs to the patient, as they are not subsidised by the Pharmaceutical Benefits Scheme (PBS) for this indication.\textsuperscript{24}

In 2010, the Therapeutic Goods Administration (TGA) approved dapoxetine for the use in premature ejaculation in Australia. However, this remains unsubsidised by the PBS. Dapoxetine is a newly developed SSRI that is rapidly absorbed (1–3 hours) and provides fast-acting treatment of premature ejaculation.\textsuperscript{39} Similarly to other SSRIs, dapoxetine should be used with caution in patients with cardiac, hepatic or renal impairment. Dapoxetine has been shown to increase IELT by 2.5–3 minutes with minimal adverse effects.\textsuperscript{36,40} Patients should take 30 mg of dapoxetine at least 30 minutes before sexual intercourse. Published studies found dapoxetine to be equally effective in men with lifelong and acquired premature ejaculation. It was also found to be well tolerated in men with premature ejaculation and comorbid erectile dysfunction treated with phosphodiesterase-5 type drugs.\textsuperscript{36,40}

**Phosphodiesterase-5 inhibitors**

The precise beneficial mechanism of phosphodiesterase-5 inhibitors for premature ejaculation is unclear and its use as monotherapy is controversial.\textsuperscript{41,42} It does not affect IELT but may improve premature ejaculation in patients with comorbid erectile dysfunction by providing a perception of greater control over ejaculation.\textsuperscript{41} In this population, guidelines suggest treating erectile dysfunction and assessing the response on premature ejaculation symptomatology.\textsuperscript{12}

**Tramadol**

Tramadol is an effective, on-demand treatment for premature ejaculation, although the mechanism of action is unknown. Doses of 25–62 mg were well tolerated, compared with placebo, and were found to significantly increase IELT, heighten sexual satisfaction and improve ejaculatory control.\textsuperscript{43,44} These results were more pronounced in patients with severe premature ejaculation (baseline IELT <1 minute). Tramadol has a number of drug interactions and should be used with caution in combination with SSRIs because of the risk of serotonin syndrome. It should only be considered for monotherapy use in men with refractory premature ejaculation.\textsuperscript{12} Ongoing studies are required to evaluate drug interactions, opioid dependence issues and the underlining mechanism of action.\textsuperscript{43}

**Surgical management**

Circumcision and surgical management options for premature ejaculation are currently under investigation and not recommended. Experimental surgical
Table 2. Summary of current medical agents for premature ejaculation

<table>
<thead>
<tr>
<th>Agent</th>
<th>Recommended dose</th>
<th>Half-life (hours)</th>
<th>IELT fold increase</th>
<th>Adverse effects</th>
<th>Additional notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dapoxetine (SSRI) – short acting</td>
<td>30–60 mg, 1–3 hours before intercourse</td>
<td>1.5</td>
<td>2.5–3</td>
<td>Nausea, diarrhoea, headache, somnolence, dizziness</td>
<td>• TGA approved, not currently on PBS • No significant drug–drug interactions • Effective treatment for both acquired and lifelong PE</td>
</tr>
<tr>
<td>Paroxetine (SSRI)</td>
<td>10–40 mg/day and 20 mg, 3–4 hours prior to intercourse</td>
<td>21</td>
<td>11.6</td>
<td>Insomnia, anxiety, nausea, loss of libido, ED, anhidrosis</td>
<td>• Off-label prescriptions • Used for lifelong and acquired PE • Therapeutic effect achieved in 2–3 weeks • May hinder sperm motility • May induce mania in bipolar patients • On-demand use not as effective without daily regimen</td>
</tr>
<tr>
<td>Fluoxetine (SSRI)</td>
<td>20–40 mg/day</td>
<td>36</td>
<td>5</td>
<td>Insomnia, anxiety, nausea, loss of libido, ED, anhidrosis</td>
<td>• Possible opioid addiction • TCAs and SSRIs are contraindicated with Tramadol use • Multiple drug interactions—only indicated as monotherapy in refractory PE</td>
</tr>
<tr>
<td>Sertraline (SSRI)</td>
<td>50–200 mg/day and 50 mg, 4–8 hours prior to intercourse</td>
<td>26</td>
<td>5</td>
<td>Insomnia, anxiety, nausea, loss of libido, ED, anhidrosis</td>
<td></td>
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<tr>
<td>Clomipramine (TCA)</td>
<td>12.5–50 mg/day and 25 mg, 4–24 hours prior to intercourse</td>
<td>19–37</td>
<td>6</td>
<td>Nausea, dry mouth, ED, hot flushes, arrhythmias</td>
<td></td>
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<tr>
<td>Tramadol</td>
<td>25–50 mg, 3–5 hours prior to intercourse</td>
<td>5–7</td>
<td>4–7.3</td>
<td>Nausea, dizziness, insomnia, dyspepsia, seizures</td>
<td>• Used for concomitant ED and PE • Improved efficacy when combined with SSRI therapy • Not established monotherapy for PE</td>
</tr>
<tr>
<td>Phosphodiesterase-5 inhibitors</td>
<td>25–100 mg, 30–50 minutes prior to intercourse</td>
<td>3–6</td>
<td>Monotherapy has no effect on IELT</td>
<td>Headache, flushing, dyspepsia</td>
<td></td>
</tr>
<tr>
<td>Prilocaine-lignocaine topical cream/aerosols</td>
<td>2.5 g, applied 20–30 minutes prior to intercourse</td>
<td>1–2</td>
<td>4–6</td>
<td>ED, loss of sensation in penis and partner’s vagina, skin irritation</td>
<td>• Condom use encouraged • Used with SSRIs • Off-label prescription</td>
</tr>
</tbody>
</table>

ED, erectile dysfunction; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressants; TGA, Therapeutic Goods Administration; PBS, Pharmaceutical Benefits Scheme
therapies, such as dorsal penile nerve cryoablation, and neuromodulation and hyaluronic acid gel glans augmentation for refractory lifelong premature ejaculation have been reported to improve IELT.\textsuperscript{45–47} Botulinum toxin injections into ejaculatory muscles are currently being explored to prevent premature ejaculation.\textsuperscript{48}

Follow-up and referral
Follow-up is an essential part of premature ejaculation management. It facilitates treatment optimisation, emphasis on key features of premature ejaculation and enables additional information gathering.\textsuperscript{49} In complex or refractory cases, specialist assistance may be sought from a sexual health physician or urologist. Input from sex therapists or psychiatrists may also be beneficial.

Conclusion
Premature ejaculation is the most common cause of male sexual dysfunction. Most patients who experience premature ejaculation are likely to require multi-modal management strategies involving pharmacological, behavioural and psychological components. Patients should be monitored closely to ensure treatment and sexual satisfaction.

Key points
• Premature ejaculation is the most common cause of sexual dysfunction, especially in the younger age group.
• It is estimated that premature ejaculation affects up to 31% of Australian males.
• Premature ejaculation causes significant psychological, emotional and interpersonal distress for the patient and his partner.
• Premature ejaculation can be lifelong (primary) or acquired (secondary), and this distinction guides management.
• Management of premature ejaculation should involve the patient and his partner, and is likely to require a multi-modal approach with pharmacological, behavioural and psychological therapies.
• Currently, no premature ejaculation therapies are subsidised by the PBS.

References

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