# Fertility following spinal cord injury

Information for health professionals

AUGUST 2020



**State Spinal Cord Injury Service** 

The information is not a substitute for healthcare providers' professional judgement.

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# Introduction

Spinal cord injury (SCI) is a devastating neurological condition that can impact on every aspect of the injured person's life, including their reproductive health and fertility.

SCI causes significant disruption to male fertility and reproductive health. Although female fertility is generally not as affected, women with SCI may still face challenges during pregnancy related to selfcare and daily functioning, as well as labour and delivery.

Health professionals have a duty to educate people with SCI and their partners about the different avenues and supports available to them to have children. There have been many medical advances over the years that have helped people with SCI have children.

This document provides an overview of male and female fertility issues.

# **Fertility issues for men**

The natural fertility rate for men following SCI is severely impaired. It is estimated to be about 5-10%in those with a complete SCI lesion, so for the majority of men, medical intervention is required to father children.<sup>1</sup>

Men with SCI may be unable to achieve an erection and/or ejaculation (referred to as erectile dysfunction and ejaculatory failure). However, there are medical methods to collect semen from men with SCI.

Sperm production is usually normal, but semen quality can be poor and this may contribute to reproductive dysfunction.

#### **Semen quality**

Semen quality is reported to be normal 6–10 days after injury, however after two weeks, it deteriorates to levels approaching those observed in males with chronic SCI, typically with abnormal sperm motility and reduced viability. The majority of studies show that men with SCI have semen with a high total sperm count (commonly >100 million/ml), but poor motility (asthenozoospermia, usually <10%) and poor viability.<sup>2-4</sup>

Sperm motility tends to be higher in incomplete SCI and if the lesion is located above the spinal ejaculation centres.<sup>5</sup> Authors of one study hypothesised that the differing degrees of dysinnervation to seminal vesicles and prostate glands may result in abnormal constituents to the seminal plasma that are toxic to sperm.<sup>5</sup>

# Factors that may contribute to poor semen quality

About half of men with SCI have at least one hormonal abnormality and 86% have some hypothalamic-pituitary-testicular axis abnormality.<sup>6</sup> However, these abnormal hormonal levels do not seem to be the primary cause of infertility in men with SCI, as an equal number of studies report normal results.

Poor semen quality seems to be primarily affected by post-spermatogenic causes, such as abnormal constituents of seminal plasma, autonomic nervous dysfunction with impaired ejaculatory function, type of bladder management and sperm dysfunction, although the definitive causal mechanism is yet to be elucidated.<sup>7</sup>

There is no strong evidence to support the role of elevated scrotal temperature in affecting semen quality.

#### Table 1. Factors that may contribute to poor semen quality

Factor	Explanation
Testicular hypofunction	This can be from hypothalamic pituitary testicular axis dysfunction, hyperprolactinaemia, or testicular interstitial fibrosis.
	Nearly 65% of men with SCI have abnormal spermatogenesis on testicular biopsy, independent of the duration, level and severity of injury. However, the mean spermatid numbers per tubule met minimum standards for adequate spermatogenesis.
Epididymal function	Epididymal function is sensitive to temperature change, but there are inconsistencies amongst studies as to the correlation between scrotal temperature and quantitative semen parameters. Sympathetic nerve integrity is necessary for peristaltic contractions of the vas deferens, so if impaired, this results in abnormal transport and storage of sperm.
Seminal fluid changes	Men with SCI have elevated levels of reactive oxygen species (ROS), which inversely correlates with sperm motility.
	It has been shown that sperm motility in able-bodied men is inhibited within five minutes of contact with seminal plasma of men with SCI. Conversely, the motility of sperm from men with SCI improves when in contact with seminal plasma from able-bodied men. <sup>8</sup> Energy substrates and enzymes in seminal plasma are also altered, which may contribute
	to asthenozoospermia. Another possible causal factor is an association between antibodies and poorer quality semen from men with SCI.
	The significance of leucocytospermia remains controversial.
Prostate gland dysfunction	PSA (prostate specific antigen) levels have been found to be higher in blood, but lower in the semen of men with SCI, which may indicate a secretory dysfunction. <sup>9</sup>
Recurrent urinary tract infections (UTIs)	Although semen infection appears to have no effect on sperm counts in men with SCI or pregnancy rates of their partners, treating a UTI with antibiotics seems to improve sperm counts and pregnancy rates (10% vs 30% with sterile urine).
Sperm ultrastructure	Axonemal defects and abnormalities of flagella have been identified in the majority of men with SCI, which can add to sperm malfunction. A recent study has shown sperm parameters, nuclear maturity and DNA integrity are disturbed, leading to spermatozoa with less condensed chromatin and an increased apoptotic rate. <sup>10</sup>
Immune regulatory dysfunction (such as suppressed lymphocyte	<ul><li>Immune abnormalities in men with SCI may be caused by:</li><li>autonomic nervous system disruption to the lymphatics and spleen</li></ul>
responses to challenges that simulate cell division, reduced	<ul><li>hypothalamic-pituitary-adrenal axis</li><li>normal neurologic feedback.</li></ul>
rations of specific white blood cells and reduced natural killer cell responses)	High numbers of activated T lymphocytes that secrete elevated concentrations of cytokines can be harmful to sperm. <sup>11</sup>
Early SCI	SCI before puberty appears to interfere with spermatogenesis. In one study of seven individuals injured between 4.4 to 11.9 years of age, the three injured before the age of 9 years were azoospermic. One subject injured at age 10 years had a subnormal total sperm count, whereas in the remaining subjects injured near the age of 12 years, semen quality appears to be similar (with normal total sperm counts) to men injured as adults. <sup>12</sup>

Source: Patki et al, 2008.13

#### Improving semen quality

There is little data about treatments that improve semen quality in men with SCI. Some factors may have a positive impact.

- **Bladder management** Over time, improvements in testicular biopsies of men with SCI have been noted. This may be due to better bladder management, including an emphasis on low pressure voiding. Men using intermittent catheterisation had better sperm quality than those using high pressure reflex voiding, straining or indwelling catheterisation, but the sperm were still abnormal.<sup>14,15</sup>
- Using monoclonal antibodies against cytokines in semen – In activating specific cytokines (interleukin 6, interleukin 1beta and tumour necrosis factor alpha) in seminal plasma was shown to significantly improve sperm motility where pre-treatment sperm motility was between 11–30%.<sup>16</sup>
- **Repeated vibroejaculation** Some studies show that this improves spermatozoa morphology and forward progression to address stagnation.<sup>17</sup> It is unclear if frequency of ejaculation improves semen quality. Some have postulated that it is consistency of ejaculations over a regulated time period that is important. However, other studies showed no statistically significant improvement in sperm motility after regular ejaculation.<sup>18,19</sup>
- **Probenecid** One study has shown promising results to improve sperm motility.<sup>20</sup>

High dose antioxidants (vitamin C and E) do not have a role in improving sperm quality in ablebodied, infertile men, so are unlikely to benefit men with SCI.<sup>21</sup> However, zinc therapy improves asthenozoospermia in men without SCI, so it is hypothesised that it could also improve semen quality in men with SCI.<sup>22</sup>

#### **Ejaculatory failure**

After SCI, most men cannot ejaculate without medical assistance.

Ejaculation is dependent on spinal cord coordination of somatic input (dorsal nerve of penis), autonomic centres and somatic centres. There is also supraspinal input from the brain (cortex, thalamus, hypothalamus, midbrain and pons), which can be excitatory or inhibitory.

It is possible for supraspinal stimulation (i.e. erotic thoughts) to cause ejaculation without any peripheral stimulation, and vice versa.

Anejaculation (absence of seminal emission in the posterior urethra) after SCI results from autonomic nervous system involvement and neuromuscular dysfunction.

The ejaculation rate is strongly dependent on the number of T12–L2 segments and S2–S4 segments with complete injury. Ejaculation is often possible in incomplete injuries with masturbation and/or nonvibrostimulatory methods.

- Damage to the T12–L2 region correlates with testicular atrophy and poor ability to ejaculate.<sup>23</sup>
- Complete (upper motor neuron) lesions above T11 retain about a 5–10% chance of ejaculation during sex or masturbation.<sup>4</sup>
- Complete (lower motor neuron) lesions below L2 retain about 18% chance of emission.<sup>4</sup>
- Psychogenic emission that contains motile spermatozoa can occur if the upper limit of SCI is located below T12.

#### Freezing a new patient's sperm

After emerging from spinal shock, sperm motility and viability are maintained temporarily, then rapidly deteriorate 16 days after injury until it is similar to males with chronic SCI.<sup>24</sup> There is no relationship between duration of injury and semen quality after one year, apart from a slight decrease in sperm concentration.<sup>25</sup>

This has raised the question as to whether sperm should be cryopreserved (frozen) in the first two weeks after SCI.

Sperm motility is reduced by about 65% by the cryopreservation process and the process also negatively affects vitality, mitochondrial activity and DNA fragmentation.<sup>26</sup> In addition, it is difficult to obtain semen in the acute stage due to medical instability and the absence of an ejaculatory reflex. Fresh sperm is usually preferred over cryopreserved sperm in assisted reproductive technology (ART).

It is therefore unlikely cryopreservation will significantly improve fertility rates, especially with the improvement in ART.

#### Semen retrieval methods

Various methods can be used to collect semen from men with SCI. The most common methods are penile vibratory stimulation (PVS) and rectal probe electroejaculation (EEJ), which have cumulative success rates of 86%.<sup>27</sup> Less intrusive methods include masturbation and prostatic massage.

Men with SCI are often on multiple medications that can impact on ejaculation, such as:

- centrally acting medications (e.g. selective serotonin reuptake inhibitors (SSRIs) for depression or certain analgesics, such as Tramadol)
- adrenoceptor blockers (e.g. Tamsulosin)
- antispasmodic medications (e.g. baclofen) may affect PVS, which relies on reflex activity.

Rationalisation or delay in timing of these medications might improve the success rate of these procedures.

Intradetrusor botulinum toxin injections can have beneficial effects on ejaculation (increased vitality by reduced contamination of semen from reflux of urine into the genital tract under high detrusor pressures) but can cause retrograde ejaculation and decrease total semen volume by reducing tone of the bladder neck and strength of contraction of sexual accessory organs, smooth muscle and perineal muscles.<sup>28</sup>

To guide which sperm retrieval methods might be successful, perform a thorough clinical assessment of neurological impairment, physical health, bladder management, personal risk factors (i.e. autonomic dysreflexia) and fertility history. Female partners should also have bloodwork done.

#### Penile vibratory stimulation

Penile vibratory stimulation (PVS) is often recommended as the first line of treatment as it is safe, reliable and cost effective, yielding the highest number of total motile sperm in antegrade fractions.<sup>29</sup>

- The vibrator parameters to select from include amplitude (2.5–3.5mm), and frequency (70-100Hz). The vibrator is applied to the ventral surface of the glans for 2–3 minutes at a time. The skin should be inspected in between intervals for abrasions or oedema. Application may be repeated twice for up to 10 minutes of stimulation or until ejaculation. Pause for 1–2 minutes between applications. (For examples of Viberect and Ferticare devices, see Figures 1 and 2).
- Most patients (89%) responsive to PVS will ejaculate within two minutes of stimulation onset. In the majority of men, the ejaculation is rhythmic and forceful in nature.<sup>30</sup>

#### Figure 1: PVS device Viberect X2



Source: Australian Health Supplies

#### Figure 2: PVS device Ferticare Personal



Source: Australian Health Supplies

For more information on Ferticare or Viberect, see <u>medicalvibrator.com</u>

#### Success rate

The overall rate of ejaculation from PVS is 52.1% in patients with complete SCI.<sup>31</sup> Success is reliant on an intact reflex ejaculation pathway which involves the spinal ejaculation centres, i.e. people with injuries above T10. The more incomplete the lesion, the more successful PVS may be.<sup>31</sup>

A positive reflex hip flexion implies that the L2–S1 segments are below the level of lesion (infralesional) and increases the success rate.

Duration after SCI does not seem to impact on the success rate.

Strategies to improve success rate include the application of two vibrators, abdominal electrical stimulation and oral administration of PDE5 inhibitors or midodrine prior to PVS.

#### Risks

During PVS, there is often an accompanying rise in blood pressure in men with SCI above T6 due to autonomic dysreflexia (AD). AD is a syndrome of life-threatening hypertension, resulting from loss of central regulation of the sympathetic nervous system below the lesion.

Any noxious or strong stimulus causes reflexive sympathetic hyperactivity and vasoconstriction of the splanchnic vasculature, resulting in severe hypertension. Possible associated complications include:

- conduction abnormalities
- seizures
- posterior reversible encephalopathy syndrome
- intracranial haemorrhages
- death.

For more information, see the <u>Agency for Clinical</u> Innovation fact sheet on AD. Prophylactic antihypertensives such as Captopril 25mg sublingual can be administered and blood pressure needs to be closely monitored throughout the procedure.

First attempts of PVS should thus be in a healthcare setting. Patients must understand the management and treatment of AD before doing PVS at home.

#### Rectal probe electroejaculation (EEJ)

For a limited period in the acute phase, usually for about 6–12 days after injury, normal semen can be obtained by electroejaculation from some men with SCI.

In chronic SCI, emission of semen can be achieved in 85% of men with SCI by electrical stimulation using a trans-rectal probe over the sympathetic nerve supply in the region of the seminal vesicles.<sup>32</sup>

The electric current directly stimulates peripheral nerves over the seminal vesicles and smooth muscle fibres of the prostate and does not rely solely on the recruitment of intraspinal pathways. Sympathetic nerves cause peristalsis of the ductus deferens and closure of the internal urethral sphincter to prevent retrograde ejaculation. Parasympathetic nerves cause peristalsis of the urethral muscle and the pudendal nerve causes contraction of the bulbospongiosus to emit semen.<sup>33</sup>

The Seager Electroejaculator (Dalzell Medical Systems, USA) is the only device approved in the USA for the procedure (Figure 3). For more information, see www.dalzellusamedicalsystems.com.

- To prevent retrograde emission, an all-silicone 12Fg catheter can be passed into the bladder prior to the stimulation and the bladder drained. The bladder neck is tamponaded by applying gentle traction on the catheter with 10ml in a 5ml balloon.
- Some clinics will catheterise the patient first, remove the catheter, then perform EEJ.

- The patient is placed in the lateral decubitus position and the probe is inserted into the rectum with the electrodes facing the seminal vesicles and prostate gland. Anaesthesia is not required for the majority, but for men with preserved sensation, the procedure can cause significant discomfort and sedation or general anaesthesia may be necessary.
- Electric current is delivered for five seconds at a time, followed by rest periods of 20 seconds. The voltage is systematically increased until an antegrade emission is achieved or three stimulations have been given.
- Emission occurs in a dribbling manner and milking the urethra helps to retrieve as much semen as possible.
- If no ejaculate is obtained, recatheterisation is performed to retrieve postejaculatory urine containing retrograde ejaculated sperm.

Some clinics will also do routine proctoscopy before and after EEJ.

#### Figure 3: Seager electroejaculator



Source: Dalzell Medical Systems, USA

#### Success rate

EEJ can be successfully used in men with multiple sclerosis, diabetic neuropathy and other conditions affecting the central and/or peripheral nervous system.<sup>34</sup>

Higher spinal lesions in men, above T10, was associated with higher rates of pregnancy.<sup>35</sup>

#### Risks

Prophylactic antihypertensives may be used for those with lesions above T6 to reduce the degree of AD that occurs.

#### **Additional techniques**

Surgical sperm retrieval (SSR) may also be used, but they are often reserved for when PVS or EEJ is unsuccessful. A Cochrane review demonstrated insufficient evidence to recommend in isolation any of the newer microsurgical techniques for sperm retrieval in azoospermic men undergoing intracytoplasmic sperm injection (ICSI).<sup>36</sup>

SSR techniques include:

- percutaneous epididymal sperm aspiration (PESA)
- testicular sperm aspiration (TESA)
- testicular sperm extraction (TESE)
- micro-epididymal sperm aspiration (MESA)
- testicular biopsy.

More proximal retrieval is said to counteract the negative effects of seminal plasma factors on sperm quality.<sup>37</sup>

SSR obtains a low motile sperm count (and therefore commits the couple to ICSI), which is the most invasive and expensive of the currently available assisted reproductive technologies.<sup>30</sup>

Other methods that have been used to induce an ejaculate include intrathecal neostigmine (discontinued due to extreme risk of autonomic dysreflexia), subcutaneous physostigmine (discontinued in many units due to frequent adverse effects) and stimulation of the epididymis or hypogastric nerve.

#### **Comparison of techniques**

There are no randomised controlled trials comparing semen retrieval techniques at the time of writing.

The quality of PVS induced antegrade ejaculation has been reported to be superior to EEJ specimens, but EEJ obtains a higher total semen volume, so similar numbers of motile sperm may be obtained.<sup>38,39</sup> Brackett et al have proposed an algorithm which administers PVS first, followed by using two vibrators, followed by EEJ. The rationale is that this is less expensive, less invasive and results in a higher motile sperm count. The algorithm resulted in a sperm retrieval rate of 97%.<sup>40</sup> The same overall rate of semen retrieval was reported in a 10-year review of results from a specialised Fertility Clinic at a Spinal Unit in NSW offering a comprehensive, client-focused approach with education, fertility assessment and a range of semen retrieval and assisted reproduction options.<sup>41</sup>

	Advantages	Disadvantages
Penile vibratory stimulation	<ul> <li>At home or hospital</li> <li>Cheaper</li> <li>Suitable for higher lesions (C1–T9)</li> <li>More frequent use</li> <li>Reported higher quality antegrade ejaculation specimen.</li> </ul>	<ul> <li>Autonomic dysreflexia more severe</li> <li>Not suitable for lower lesions (below T9)</li> <li>Cannot be used during spinal shock.</li> </ul>
Electroejaculation	<ul> <li>Autonomic dysreflexia more controllable</li> <li>Suitable for lower lesions (T10–S) as well as (C1–T9)</li> <li>Can be used during spinal shock</li> <li>Reported higher semen volume.</li> </ul>	<ul> <li>At hospital only</li> <li>More staff required</li> <li>More painful</li> <li>Risk of rectal mucosal burning.</li> </ul>

#### Table 2: Comparison of main semen retrieval techniques

# **Achieving pregnancy**

A plan for assisted reproduction can now be offered to many men with SCl.  $^{\rm 41}$ 

However, going through assisted reproductive technology (ART) can cause significant stress, particularly in female partners who undergo hormonal treatments (for in vitro fertilisation).

# Assisted reproductive technology techniques

ART has a significant role in improving fertility rates in the SCI population and offers significant hope for improved reproductive capacity. The overall pregnancy rate is 51% and the live birth rate is 40%.<sup>27</sup>

Common techniques are outlined in this document. Fresh sperm is preferred over cryopreserved sperm. Detailed information is outside of the scope of this resource.

#### Intravaginal insemination

During intravaginal insemination, semen that is collected is put into a clean specimen cup and drawn into a syringe to deposit into the vagina at the time of ovulation. Fresh semen is used.

The fertility clinic usually evaluates if semen retrieval (such as PVS) was successful, then educates the couple about ovulation prediction and the optimal method for in-home insemination. It can also be done in the hospital setting.

Minimum numbers of total motile sperm have not been established for successful pregnancy using this method, but pregnancy rates of 43% have been reported, and one study reported nine pregnancies occurring among seven out of 10 couples treated.<sup>42,43</sup>

#### Intrauterine insemination

Intrauterine insemination (IUI) is when semen is collected and processed to separate the sperm, which is then placed inside the uterus, with or without fertility drugs prescribed to stimulate female ovulation. IUI is done in a hospital or clinical setting.

Cycle fecundity rate is <15% for IUI. Various studies have reported that pregnancy rates for IUI typically range between about 25% and 30%.<sup>44,45,46</sup>

#### In vitro fertilisation

In vitro fertilisation (IVF) involves placing sperm and ova in a laboratory dish, which is then placed in an incubator for up to five days. Embryos that develop to the highest quality blastocyst stage are placed into the uterus.

Intra-cytoplasmic sperm injection (ICSI) is a specialised IVF technique that involves injecting a single sperm directly into the egg, even if the sperm has little or no motility (Figure 4). ICSI is used when the number of motile sperm is too low for conventional IVF.

IVF procedures are ideally carried out on the same day as semen retrieval by PVS or EEJ, testicular sperm extraction or percutaneous epididymal sperm aspiration to obtain fresh sperm.

Cycle fecundity rate is between 25–40% for IVF. Similar pregnancy and live birth rates (up to 62.5%) have been reported in couples with SCI male partners undergoing ICSI versus couples with other aetiologies of male factor infertility.<sup>47</sup>

#### **Choice of technique**

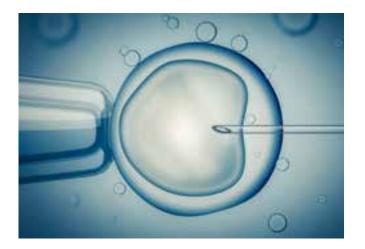
The ART technique chosen is based on the total number of motile sperm and the health of the female partner.

Intravaginal insemination is usually the first approach as it is accessible and inexpensive.

Based on a cost effectiveness estimation between IUI and IVF, it is recommended that couples attempt 3–6 cycles of IUI before proceeding to IVF, unless sperm counts are less than four million total sperm, in which case clients should proceed directly to IVF.<sup>44</sup>

Consumer preference should also be considered. Consumers should be educated about the risks associated with IVF–ICSI, such as complications resulting from superovulation, multiple gestations with associated complications to offspring, haematomas, orchitis and pain from SSR procedures.

#### Figure 4: In vitro fertilisation



Source: shutterstock.com

# **Fertility issues for women**

Although SCI has a significant impact on female reproductive physiology, women with SCI have relatively normal fertility.

There are no controlled studies comparing fertility rates with non-SCI cohorts and thus there may be unknown effects of SCI on the rate of miscarriages and live births.<sup>27</sup>

Women with SCI can still expect to have satisfying sexual relationships, bear children and experience motherhood. The multidisciplinary team and peers can provide valuable information and support for women with SCI in pregnancy and in the postpartum period.

#### Menstruation

Hormone levels are usually normal in women with chronic SCI, menarche is not delayed in preadolescent girls and the level or nature of the injury does not impact on menstruation.<sup>48</sup>

Amenorrhea (absence of menstruation) may occur immediately following injury, lasting 4–5 months on average.<sup>49,50</sup> For the majority of women, this is temporary and pre-injury patterns (and fertility) return.

Menstruation may be uncomfortable and present as increased spasticity, autonomic symptoms, more frequent bladder spasms, diarrhoea or worse premenstrual and menstrual symptoms (dysmenorrhea, cramping). Anti-inflammatories can be helpful for symptomatic relief.

While in rehabilitation, education on application of feminine hygiene products should be given. Adaptive aids such as mirrors and splinting to aid hand function may be prescribed.

#### Contraception

Women with recent SCI should be informed that they will need to consider contraception when menstruation and sexual activity resumes to prevent pregnancy.

Contraception options for women with SCI are similar to that in the able-bodied population. In general, there are rhythm methods, barrier methods (condoms, diaphragms, cervical caps, contraceptive sponges), spermicides, oral contraceptives, subdermal hormonal implants, medroxyprogesterone injections, intrauterine devices, tubal ligation, endometrial ablation and, as a last resort, hysterectomy. A detailed discussion is beyond the scope of this resource.

The method chosen should be individualised to the woman's function, mobility, risk factors and lifestyle, with adequate counselling considering the risks and success of each method. There are some special considerations for women with SCI.

- Rhythm methods using basal body temperature tracking are generally unreliable, as basal body temperature maintenance and patterns are affected in women with SCI.
- Some of the barrier methods can be difficult to apply for women who have limited hand dexterity, and the partner will need to assist.
- If a diaphragm is not fitted well, it can put pressure on the cervix, with a risk of ulceration, especially since it needs to be in place for six hours.
- Combined oestrogen-progestogen pills, medroxyprogesterone injections or subdermal implants should be prescribed with caution, as there is an increased risk of hypercoagulability and thromboembolism. Some health professionals advocate against their use within one year of injury in those who smoke, and if there is a history of cardiovascular or circulatory problems. The progestogen only pills are believed to be less of a thrombotic risk.<sup>51</sup>

- Medroxyprogesterone injections (Depo-provera) can produce oligo or amenorrhea, which can be positive for women who find menstruation a nuisance. There may be an impact on bone mineral density.
- There is an increasing trend to insert intrauterine devices. Women should be educated about the increased risks of pelvic infection or rupture especially since they are more susceptible to urinary tract infections (UTIs), which may be recognised late due to impaired sensation.
   Women with an intrauterine device need to check the length of the string after each menstrual period to check it has not moved, which may be difficult if hand function is impaired.

About 70% of sexually active women with SCI use some form of contraception, but fewer women use the oral contraceptive pill compared to before the injury.<sup>50</sup>

Women with SCI have decreased vaginal lubrication and their ability to experience orgasm is decreased.<sup>52</sup> Further information can be found on the Agency for Clinical Innovation fact sheet, <u>Sexuality After SCI.<sup>53</sup></u>

#### Pregnancy

Women with SCI can carry a child safely to term and the outcomes of pregnancy following SCI are favourable.<sup>54</sup>

There are numerous old case reports, a case series study and three systematic reviews investigating issues such as pregnancy rates, live births, complications and obstetrical management issues in women after SCI.<sup>50,55</sup> They generally show that the risks of prematurity or low birth weight babies are unclear. Rigorous, new prospective studies are required to inform practice around these issues.

There are no clear consensus or guidelines around obstetric management to achieve optimum outcomes for women with SCI.<sup>56</sup> An interdisciplinary approach with collaboration between a spinal rehabilitation physician and an experienced obstetrician in high risk pregnancy is recommended.

#### Preconception

Preconception planning and detailed discussions around anticipated difficulties can help women with SCI prepare for and address the challenges that arise during and after pregnancy. General preconception health recommendations should be discussed, such as stopping smoking and alcohol consumption, immunisation, maintaining good nutrition, weight control and exercise.

Many women with SCI are on a range of medications. The benefit to the mother versus potential risk to the foetus should be weighed up for each. Specifically, medications in the Australian categorisation system for prescribing medicines in pregnancy category C or D should be reviewed and substituted whenever possible.<sup>57</sup> Some women will decide to remain on antispasmodics due to severe spasticity interfering with their function and the risk of falls. If a woman with SCI has been taking anticonvulsants such as carbamazepine, valproate, phenytoin, or ethosuximide, an additional 4mg folate is recommended to prevent neural tube defects during preconception and pregnancy.<sup>58</sup>

Iron supplementation should be prescribed as anaemia is common, with additional aperients added to prevent constipation. Vitamin D has also been recommended to help with skin integrity, bone health and to prevent pre-eclampsia.<sup>59</sup>

#### **During pregnancy**

Frequent monitoring is important to screen for and pre-empt common medical complications experienced during pregnancy. Appointments are also an opportunity to educate women with SCI during gestation.

Some common medical issues include the following.

#### **Urinary tract infections**

Women with SCI are already at high risk of UTIs due to the neurogenic bladder and frequent catheterisation. As the uterus enlarges, it can cause ureteral compression, leading to urinary stasis and retention. This leads to a further increase in UTI occurrence, with rates of 45.5% reported and makes the pregnancy higher risk.<sup>50,60</sup>

Women with indwelling catheters (IDCs) and ileal conduits are at the highest risk, followed by those using intermittent catheterisation, and those with normal voiding. Monthly screening should be done for asymptomatic bacteriuria (ASB), as randomised control trials involving non-catheterised women have shown that eradication of ASB reduces the risk of pyelonephritis and adverse consequences of pregnancy.<sup>61</sup> There are no catheter associated-ASB treatment trials involving pregnant catheterised women. Management needs to be highly individualised, using antibiotics safe in pregnancy when indicated. Education on bladder hygiene should be reinforced.

#### **Bladder spasms**

Spasms may occur more frequently, leading to leaking, and even catheter expulsion. Catheterisation may be more difficult due to the changed angle of the urethra. Women have reported increased urination frequency and incontinence beyond what is experienced by most pregnant able-bodied women.

Although indwelling catheters are associated with higher infection rates, they may be required in the first and third trimesters to limit incontinence and AD.<sup>62</sup> Antibiotic therapy is only indicated in symptomatic bacteriuria or in symptomatic exacerbations of chronic UTI, with choice of appropriate antibiotic therapy giving consideration to possible toxic effects on the foetus.<sup>63</sup>

#### Pressure injury (skin breakdown)

Several factors can lead to an increased risk of skin breakdown including incontinence, weight gain, altered posture, anatomic changes, relative anaemia and difficulty performing pressure relieving manoeuvres and transfers. Areas at high risk are the sacrum, ischial tuberosities, back and thighs.

Patients should lie on their side and it is essential to pressure relieve more frequently and have twice daily skin checks. Clothing should be without seams, zippers or buttons.

If the woman is unable to pressure relieve effectively, consideration should be given to hiring a power wheelchair that has a tilt in space feature to 45 degrees which can be adjusted as the pregnancy progresses.

#### **Bowel complications**

Issues such as constipation and haemorrhoids are common due to further immobility and the enlarging uterus making it difficult to apply physical manoeuvres for bowel evacuation. Aperients may need to be added or dosage increased to ensure adequate bowel evacuation, as impaction can trigger AD.

#### Thrombosis and leg oedema

About 8% of pregnant women with SCI experience swelling and compression, compared to 0.1% of able bodied pregnant women.<sup>64</sup> This is due to the enlarging uterus compressing pelvic veins and immobility.

Some practical suggestions to reduce DVT risk and oedema include passive motion exercises, leg elevation, using antithrombolytic stockings and lying on the side in bed for improved venous return.

#### **Respiratory complications**

Shortness of breath from reduced respiratory volumes can result due to the enlarged uterus pushing upward on the diaphragm. This can be significant in women with tetraplegia, as the diaphragm is the primary muscle of respiration. In addition, reduced coughing and atelectasis can lead to pneumonia, a significant cause of morbidity and mortality after SCI.

Incentive spirometry and other preventive measures for pulmonary health maintenance should be considered. Vital capacity in women with high tetraplegia should be monitored, as mechanical ventilation assistance may be required if it falls below 13–15ml/kg, to avoid compromise to the mother and foetus.<sup>65</sup>

#### Autonomic disturbances

Pregnant women may become more prone to postural hypotension.

Women with an injury at or above T6 can develop AD with uterine distension and contractions, and about half report increased episodes during pregnancy.<sup>64</sup>

Antihypertensives such as Nifedipine (category C in pregnancy) or Nitroglycerine patch may be used – see the Consortium for Spinal Cord Medicine Clinical Practice Guidelines for Acute Management of Autonomic Dysreflexia.<sup>66</sup>

Thermoregulation is also affected, which can complicate intrapartum management.

#### **Functional changes**

As pregnancy progresses and the woman's centre of gravity changes, there may be increased difficulty in transferring to and propelling a wheelchair, and achieving or weight relief. Increasing spasticity can also worsen function. There may be difficulties with wheelchair fit, manoeuvrability or stability.

There is an increased risk of falls and fractures, which may lead to some women using transfer boards or limiting activities.<sup>67</sup>

Wheelchair cushions and wheelchairs (e.g. inside seat to back angle) will need to be adjusted to changing needs. There may be more equipment required to facilitate transfers and pressure relieving (e.g. rolling shower chairs, tub benches, mattresses, hospital beds), which require budgeting and planning for.

#### Pain

Lower back pain is common in pregnancy. Women with SCI may experience the same discomfort but perceive it differently. Musculoskeletal and neuropathic pain may be increased.

Physiotherapy intervention may be useful to educate the woman about keeping proper alignment of the pelvis to avoid unnecessary musculoskeletal pain.<sup>68</sup> Care should be taken when prescribing pain medications, as some are category C drugs (e.g. Duloxetine).

#### **Mental health issues**

Women with SCI may be at higher risk of depression during pregnancy.<sup>69</sup> Mental health screening should be done during appointments.

#### Labour and delivery

Preterm labour is twice as likely in pregnant women with SCI compared to able bodied pregnant women.<sup>55</sup> Premature labour may go unrecognised due to sensory impairment. Spasms of the legs or abdomen or AD may be the first symptoms of labour onset.

Women with injuries at or below T10 are likely to experience some labour pain.<sup>70</sup> Pain can also be referred to the shoulders or above the level of injury. Women should be educated about these symptoms and on uterine palpation techniques to detect contractions.

It has been recommended by some groups that after 28–32 weeks, women should be checked 1–2 times a week for effacement and dilatation and if present, they should be admitted to hospital to prevent unattended deliveries.<sup>71</sup>

AD occurs in 85–90% of women with an injury above T6 during labour and delivery.<sup>72</sup> Symptoms of AD may include:

- severe headache
- a feeling of doom or apprehension and anxiety
- sweating
- blurred vision
- nasal congestion
- bristling of hairs (piloerection)
- flushing
- bradycardia
- a rise in systolic baseline blood pressure of 20–40mmHg.

If not managed adequately, AD can result in other serious complication such as intraventricular haemorrhage and death.

AD can be differentiated from pre-eclampsia. In AD, elevated blood pressure and the associated symptoms tend to subside with uterine relaxation. Increased deep tendon reflexes, altered blood chemistry and proteinuria are symptoms of preeclampsia rather than AD, but bear in mind that the conditions can coexist and make management more difficult.<sup>73</sup> An effective approach for AD is to use epidural or spinal anaesthesia early. Some advocate routine use in the at-risk patient, with anaesthesia to be maintained until delivery of the placenta and postpartum contractions, up to 24 hours after.<sup>73</sup>

Abdominal muscle innervation is important for pushing during delivery, so the extent to which a woman can assist depends on the level and degree of impairment. Although weak abdominal muscles can make vaginal delivery more difficult, the uterus can generate intrinsic contractions in the absence of extrinsic innervation.<sup>74</sup> Various reports have quoted higher rates of caesarean sections, forceps usage, vacuum extraction and breech presentations in women with SCI. However, vaginal delivery is still viewed as the first option. Adequate pre-planning should be done to support vaginal delivery (such as insertion of an indwelling catheter for bladder management, which will require addressing any spasticity, contractures, or heterotopic ossification).

It is recommended that women with SCI consult with an obstetrician skilled in high risk pregnancies and an anaesthetist familiar with managing AD during labour.

#### **Postpartum issues**

The immediate concerns after delivery are usually healing of perineum or wound. Blood pressure should continue to be monitored and adequate pain relief prescribed, with consideration to increasing aperients as required.

As with any hospital admission, preventive measures should be implemented such as repositioning every two hours. Similarly, bladder and bowel routines should be re-established.

Although women should be encouraged to breastfeed, there can be barriers such as AD and positioning difficulties. It has also been reported that in those with SCI above T4, the 'let-down' reflex is impaired, due to decreased nipple sensation and resultant decreased feedback to the pituitary gland.<sup>75</sup> Adequate support should be given to women to address these issues.

If the patient has been taking antispasmodics such as baclofen and diazepam, this can lead to withdrawal symptoms in newborns. If the decision is made to withdraw them, it should be done slowly to avoid withdrawal seizures.<sup>71</sup> Other reviews in lactating women have found Baclofen (category B) safe, with no negative infant outcomes.<sup>76</sup> Women with SCI may be at higher risk of postpartum depression and appropriate screening should be done.<sup>69</sup>

#### Health maintenance

The recommendations for screening and preventative care in the general female population apply equally to women with SCI. This includes sexual healthcare, breast examinations and mammography and cervical cancer screening. Women with SCI should be encouraged to take an active role in health maintenance and expect health professionals to provide the same standard of care to them.

There are barriers for women with SCI, such as inaccessible facilities, lack of proper equipment, untrained staff, patient misconceptions and lack of patient and clinician information.<sup>77</sup> It can be difficult to examine women with disabilities due to lack of equipment (such as hoists or a height adjustable examination table), but pelvic examinations are particularly important, especially as sensation is impaired and symptoms may be absent or unreliable.

Yeast infections are more common after SCI, likely due to poor ventilation, excess moisture and frequent antibiotic use. Yeast infections can mimic UTI symptoms, so it is important to exclude this to avoid misdiagnosis and antibiotic over-prescription.

Similarly, women with SCI should be screened for sexually transmitted diseases. Infections can manifest with nonspecific symptoms such as increased spasticity and malaise.

#### Menopause

SCI does not impact on the age of onset of menopause or symptoms such as hot flashes, mood fluctuations, sleep disturbances, headaches, memory problems, bladder and other mucosal changes and skin dryness. However, SCI-related symptoms have been reported to increase during menopause, such as mood disorders, spasticity, AD and bladder spasms.<sup>50</sup> Greater somatic symptoms, bladder infections and diminished sexual arousal has also been reported in comparison with women without SCI.<sup>78</sup>

It is important for women to report symptoms to their doctor to exclude other causes before attributing it to menopause. Hormone replacement therapy should be considered for post-menopausal women with SCI because of the heightened risk of osteoporosis. Almost one-third of women who had menopause after injury report new long bone fractures.<sup>50</sup>

# **Parenting and child rearing**

Studies have shown that parents with SCI can provide the adequate level of care and supervision for child rearing, with no detrimental effects on the development of a child.<sup>79</sup> They can continue to offer verbal and psychological support regardless of SCI level and divide the more physical aspects of the parenting role with their partner.

For women with SCI who have babies, no increased long-term morbidity is observed.<sup>60</sup>

Planning and assistance is required to care for a newborn. Consulting an occupational therapist to assess the home environment can help address trip hazards, as well as suggest modifications for handling a baby, such as adaptive aids, slings and prams that can be attached to wheelchairs.

Connecting with peers on forums or looking up websites around disability, pregnancy and parenting can also offer valuable parenting advice. For some, the help of a nanny may be necessary. A social worker may be able to explore services and funding available as part of early pregnancy planning. Despite the challenges, people with SCI report being satisfied with their parenting role after having children.<sup>80</sup>

#### Adoption

Adoption is an option for both men and women after SCI if women do not want to or can't become pregnant, or if fertility methods fail for men. People with SCI can be positive role models and successful parents following injury regardless of a biological connection to the children with whom they develop a bond.<sup>81</sup>

### Resources

#### Consortium of Spinal Cord Medicine Clinical Practice Guidelines

- Sexuality and Reproductive Health in Adults with Spinal Cord Injury<sup>82</sup>
- Acute Management of Autonomic Dysreflexia.<sup>66</sup>

#### Agency for Clinical Innovation Spinal Cord Injury Resources

- Sexuality Following Spinal Cord Injury<sup>53</sup>
- Treatment of Autonomic Dysreflexia for Adults and Adolescents with Spinal Cord Injuries.<sup>83</sup>

#### Spinal Cord Injury Rehabilitation Evidence (SCIRE) scireproject.com

- Sexual and Reproductive Health<sup>84</sup>
- Autonomic Dysreflexia.85

## **Data and methods**

Data for this resource were drawn from a literature search and guideline review.

#### Literature search

A rapid review of PubMed was conducted in 2018, with an update in September 2019.

Key search terms included: spinal cord injuries AND fertility or reproduction.

Snowball searches were conducted from the reference lists of key articles.

#### **Guideline review**

Guidelines for spinal cord injury care are produced by different SCI services. SCIRE (Spinal Cord Injury Rehabilitation Evidence) and Consortium for Spinal Cord Medicine have developed clinical guidelines that informed this work.

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# Glossary

AD

ART Assisted reproductive technology ASB Asymptomatic bacteriuria EEJ Electroejaculation ICSI Intra-cytoplasmic sperm injection IUI Intrauterine insemination IVF In vitro fertilisation RCT Randomised controlled trial ROS Reactive oxygen species SCI Spinal cord injury SSRI Selective serotonin reuptake inhibitor PVS Penile vibratory stimulation

Autonomic dysreflexia

**UTI** Urinary tract infection

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