

Table 16. Fertility and Insemination

<b>Author Year</b> <b>Country</b> <b>Score</b> <b>Research Design</b> <b>Total Sample Size</b>	<b>Methods</b>	<b>Results</b>
<p><a href="#">Cito et al. 2020</a>                      Italy                      Case-Control                      Level 3                      N=492                      N=106 (53 couples – men with SCI)</p>	<p><b>Objective:</b> To evaluate semen characteristics and reproductive outcomes after assisted ejaculation methods with fresh in vitro fertilization/ intracytoplasmic sperm injection cycles in patients with spinal cord injury (SCI), compared to controls, affected by idiopathic male infertility (non-SCI group).  <b>Population:</b> N=386 (193 couples), Median paternal age: 38                      SCI group: N=106 (53 couples)  <b>Treatment:</b> Patients first underwent PVS, as the first-line method used to obtain ejaculation, except for medullary lesions at or below T10. Men with SCI who were “non-responders” to PVS underwent EEJ. If applying the above methods, a persistent anejaculation still occurred, testicular sperm aspiration was last proposed to retrieve autologous spermatozoa.  <b>Outcome Measures:</b> Semen characteristics</p>	<ol style="list-style-type: none"> <li>1. All patients with SCI did not have antegrade ejaculation during masturbation or coitus without the aid of medications or devices.</li> <li>2. Statistically significantly lower semen volume in SCI group (1.5mL) than non-SCI group (3.15mL) (p &lt; 0.01).</li> <li>3. Significantly higher sperm concentration (52sperm/mL), higher total sperm count (87), higher immotility (90%). In SCI group.</li> <li>4. Significantly lower progressive motility (5%) and total sperm motility AC (5% vs 80%) (p &lt; 0.01).</li> <li>5. Normal fertilization (46% vs 71%) and total fertilization (50% vs 75%) rate was significantly lower in SCI groups (p &lt; 0.01).</li> <li>6. A trend toward higher pregnancy rates per cycle was found in non-SCI (31.4% vs 21.4%), or in the live birth rate per couple, which was 27.1% in the non-SCI group and 20.0% in the SCI group.</li> <li>7. No significant differences were found in pregnancy, miscarriage and live birth rates per cycle, between the 2 groups (P = .18, .31, and .68, respectively).</li> </ol>
<p><a href="#">Kanto et al. 2009</a>                      Japan                      Case-control                      Level 3                      N=56                      N=22 men with SCI</p>	<p><b>Population:</b> 22 men with SCI (age 21-41); data on 34 men with obstructive azoospermia was obtained retrospectively for control.  <b>Treatment:</b> Testicular sperm extraction (TESE); if unsuccessful, microdissection TESE was performed, followed by intracytoplasmic injection (ICSI).  <b>Outcome Measures:</b> Fertilization; pregnancy.</p>	<ol style="list-style-type: none"> <li>1. TESE successfully retrieved sperm in 19 participants with SCI.</li> <li>2. ICSI resulted in a fertilization rate of 236 of 364 (64.8%) in SCI couples and 14/19 achieved pregnancy (73.6%).</li> <li>3. In couples with obstructive azoospermia, ICSI resulted in a fertilization rate of 435 of 567 (77%) and 29/34 achieved pregnancy.</li> </ol>

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		4. Pregnancy rate was significantly higher in couples with SCI using fresh testicular sperm-ICSI compared to frozen-thawed sperm-ICSI.
<a href="#">Kathiresan et al. 2011</a> USA Case series Level 4 N=82	<p><b>Population:</b> 82 male patients with SCI and their female partners; mean(SD) age 36.1(0.7) yrs, mean time after injury 0.8 yrs (range 0.7-34.0 yrs).</p> <p><b>Treatment:</b> 45 couples performed intravaginal insemination (IVI); intrauterine insemination (IUI) was performed in 57 couples.</p> <p><b>Outcome Measures:</b> Method of sperm retrieval, sperm quality, occurrence of pregnancy, live birth, pregnancy rate (PR), pregnancy losses, multiple gestations, total motile sperm count (TMSC).</p>	<ol style="list-style-type: none"> <li>1. Of the 45 couples who performed IVI, 17 couples had 20 pregnancies with 3 couples achieving pregnancy twice (85% - 16 through penile vibratory stimulation; 1 through electroejaculation; and 3 through masturbation)</li> <li>2. Eighteen live births occurred.</li> <li>3. Average time from male partner's first semen analysis to time of pregnancy was 6.9(1.25) mos.</li> <li>4. The mean antegrade TMSC in men achieving vs. not achieving pregnancy was not statistically significant: 90.1(30.8) million (range 2.6-425.7 million) vs. 76.5(21.0) million (range 0.3-544.5 million).</li> <li>5. 57 couples underwent IUI, where 14 couples had 19 pregnancies and 21 live births (1 twin and 1 triplet pregnancy occurred, both by IUI cycles stimulated by gonadotropins) 33% success rate, though, cycle fecundity was 7.9% (19 pregnancies of 241 cycles). Semen collected by PVS (6 pregnancies) and EEJ (13).</li> </ol>
<a href="#">Sønksen et al. 2012</a> Denmark Case series Level 4 N=140	<p><b>Population:</b> 140 SCI men with anejaculation and their healthy female partners (presenting for infertility treatment between 1988 and 2008); Age: SCI men (median 30 yrs, range 22-44), female partners (median 28 yrs, range 19-39 yrs); DOI: median 7 yrs (range 1-22), Level of lesion: C2 to T9.</p> <p><b>Treatment:</b> Men who obtained antegrade ejaculation by penile</p>	<ol style="list-style-type: none"> <li>1. Median total motile sperm count: 29 million (range 1-92 million).</li> <li>2. 60 of the 140 couples (43% pregnancy rate) achieved 82 pregnancies.</li> <li>3. 72 of the pregnancies resulted in live births with delivery of 73 healthy babies.</li> <li>4. Median time to first pregnancy was 22.8 months (range 6.0-</li> </ol>

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	vibratory stimulation (PVS) and had motile sperm in the ejaculate were offered the possibility of PVS combined with vaginal self-insemination at home. Couples were instructed to perform PVS and to instill the ejaculate intravaginally. <b>Outcome measures:</b> Pregnancy rate per couple, number of live births, total motile sperm count and time to pregnancies.	98.4). No complications were reported.
<a href="#">McGuire et al. 2011</a> Ireland Case series Level 4 N=31	<b>Population:</b> 31 men (mean age 35 yrs, range 24-49), 29 with acquired spinal cord injury (complete lesion (n=18), incomplete lesion (n=11). Injury levels: C3-C7; T1-T5; T11-L3), 2 with congenital spinal abnormality. <b>Treatment:</b> Electroejaculatory stimulation (EES) done with Seager model rectal probe – n= 27 (87%) underwent EES once, n= 4 (13%) underwent EES several times. <b>Outcome measures:</b> The Mann-Whitney U test, semen analysis (volume, density, motility, normal morphology and live sperm); pregnancy rate	<ol style="list-style-type: none"> <li>1. Of the 25 patients whose partners underwent insemination with the EES semen, 9 (36%) became pregnant. All pregnancies resulted in live births.</li> <li>2. One patient developed autonomic dysreflexia necessitating stopping EES before obtaining any ejaculate. No other side effects or complications were reported.</li> <li>3. 30 patients produced antegrade, retrograde, or both types of ejaculates.</li> </ol>
<a href="#">Hibi et al. 2008</a> Japan Case series Level 4 N=8	<b>Population:</b> 8 participants with cervical SCI and neurogenic anejaculation (age 26-46 yrs, mean 35.6). <b>Treatment:</b> Retrograde vasal sperm aspiration (ReVSA). All couples underwent intracytoplasmic sperm injection. <b>Outcome Measures:</b> Presence of motile sperm.	<ol style="list-style-type: none"> <li>1. Motile sperm was recovered in all participants who underwent ReVSA (11 procedures total).</li> <li>2. The retrieved sperm concentration was 109.4(64.7) × 10<sup>6</sup> /mL (range 31.2-156.3 × 10<sup>6</sup> /mL).</li> <li>3. The retrieved motility of sperm was 69.8% (16.8) (range 50-91%).</li> <li>4. Via intracytoplasmic sperm injection, clinical pregnancies were achieved in 8 cases.</li> </ol>
<a href="#">Shieh et al. 2003</a> Taiwan Case series Level 4 N=10	<b>Population:</b> 10 men with SCI and partner; Age: range 27-37 yrs; Injury level: C6-T12, 9 incomplete and 1 complete, 9 paraplegia & 1 tetraplegia; Time since injury: range 4-20 yrs.	<ol style="list-style-type: none"> <li>1. 7 clinical pregnancies were achieved, 2 of which ended with spontaneous abortion. 1 couple accomplished pregnancy by ICSI with cryopreserved sperm from vasal aspiration.</li> </ol>

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	<p><b>Treatment:</b> If semen sample from electroejaculation (EE) was of fair quality, then 3 cycles of intrauterine insemination (IUI) prior to intracytoplasmic sperm injection treatment (ICSI). If semen samples were poor, ICSI was suggested. If no sperm from EE, surgical retrieval of sperm was performed.</p> <p><b>Outcome Measures:</b> Pregnancy rates.</p>	<ol style="list-style-type: none"> <li>2. The fertilization and pregnancy rates of ICSI cycles using sperm from men with SCI were comparable to men without SCI.</li> <li>3. One couple attained pregnancy by using donor sperm.</li> <li>4. The cumulative successful pregnancy rate per couple was 80%.</li> </ol>
<p><a href="#">Pryor et al. 2001</a> USA Case series Level 4 N=11</p>	<p><b>Population:</b> 11 men with SCI and their partner; Injury level: tetraplegia.</p> <p><b>Treatment:</b> Electrical stimulation or vibratory stimulation followed by 1) intrauterine insemination of partner 24 hour after Luteinizing Hormone surge (n=5), 2) 50 mg clomiphene citrate &amp; hCG, followed by insemination after 32-34 hours (n=5), or 3) same as #2, except 38-40 hour delay (n=10).</p> <p><b>Outcome Measures:</b> Fertility rates, seminal parameters.</p>	<ol style="list-style-type: none"> <li>1. No pregnancies with protocol 1 or 2.</li> <li>2. 6/10 patients became pregnant with protocol 3, which has the longest delay between drug administration and insemination.</li> </ol>
<p><a href="#">Heruti et al. 2001</a> Israel Post-test Level 4 N=84</p>	<p><b>Population:</b> 84 men with SCI, 49 couples; Age: range 19-45 yrs; Injury level: cervical (34.5%), thoracic (59.5%), lumbar (5.9%); Impairment grade: AIS A (n=63), B (n=15), C (n=5), D (n=1); Time since injury: range 4 months-34 yrs.</p> <p><b>Treatment:</b> Electroejaculation followed by intrauterine insemination (IUI) for 3 trials (10million sperm/cc). If this did not result in fertilization, intracytoplasmic sperm injection (ICSI) and IVF.</p> <p><b>Outcome Measures:</b> Volume, sperm count, motility, morphology, total motile sperm count, conception.</p>	<ol style="list-style-type: none"> <li>1. Ejaculation occurred in 98.6% of patients, with sperm in 88% of patients and enough viable sperm in 54.8%.</li> <li>2. Antegrade semen parameters had significantly better sperm count, morphology, and motility than retrograde samples.</li> <li>3. No significant improvements were seen in seminal parameters after repeated ejaculations.</li> <li>4. 26 couples reached the stage of insemination. Four pregnancies were achieved after 33 cycles of In-Uterine-Insemination (pregnancy rate 28.6% per couple), and 15 after 68 cycles of In-Vitro-Fertilization (micromanipulation) (pregnancy rate of 68.75% per couple).</li> </ol>

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		5. In all, of 101 conception attempts 23 were successful, resulting in pregnancies in 18 couples, and accounting for an overall pregnancy rate of 70% per couple. 26 live births (n=12 singletons, n=5 twins, n=1 triplets) and 4 abortions.
<a href="#">Ohi et al. 2001</a> USA Post-test Level 4 N=87 men with SCI	<b>Population:</b> 121 couples (87 men with SCI and partner). <b>Treatment:</b> Electroejaculation followed by intrauterine insemination (IUI) was the route of sperm delivery. If not successful after 3-6 cycles of IUI, GIFT (gamete intrafallopian transfer) or IVF procedures were recommended. <b>Outcome Measures:</b> Pregnancy success and pregnancy outcomes.	<ol style="list-style-type: none"> <li>52/121 became pregnant (43%), 39 by IUI alone.</li> <li>All patients undergoing IVF had significantly higher cycle fecundity than did those undergoing IUI.</li> <li>The rates of spontaneous abortion and multiple gestations were 23% and 12%, respectively.</li> </ol>
<a href="#">Schatte et al. 2000</a> USA Post-test Level 4 N=17	<b>Population:</b> 10 men with SCI (7 non-SCI related anejaculation); mean age 38.9 yrs. <b>Treatment:</b> Electroejaculation and intracytoplasmic sperm injection (ICSI) and results compared to 620 ICSI cycles for non-SCI male infertility with normal ejaculation. <b>Outcome Measures:</b> Pregnancy rate.	<ol style="list-style-type: none"> <li>ICSI resulted in a median fertilization of 60%, 15% pregnancies per cycle and 29% pregnancies per couple.</li> <li>Pregnancy rates were lower for the anejaculation group compared to the severe male factor group.</li> </ol>
<a href="#">Brinsden et al. 1997</a> UK Post-test Level 4 N=35	<b>Population:</b> 35 men with SCI and their female partners; Age: (men) range 24-47 yrs, (female) range 21-43 yrs; Injury level: C5-L1; Time since injury: range 1-27 yrs. <b>Treatment:</b> Trans-rectal electroejaculation with in-vitro fertilization. 71 IVF cycles were used. <b>Outcome Measures:</b> Pregnancies, fertilization rate, motile sperm count.	<ol style="list-style-type: none"> <li>Pregnancy rates: 18 total – 51% (14 were fresh embryo transfers, 4 were frozen embryo transfers)</li> <li>Overall clinical pregnancy rate per stimulated IVF treatment was 25.4% (18/71).</li> </ol>
<a href="#">Sønksen et al. 1997</a> Denmark Case series Level 5	<b>Population:</b> 28 men with SCI and female partner; Age (men): range 24-43 yrs, (female): mean 29 yrs, range 19-39 yrs; Injury level: C2-L4; Time since injury: range 1-22 yrs.	<ol style="list-style-type: none"> <li>Ejaculation was achieved in all 28 men with SCI, either by PVS (79%) or EEJ (21%). Twenty-two of 26 men (85%) with spinal cord             </li> </ol>

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<p>N=28</p>	<p><b>Treatment:</b> Males with SCI: vibratory stimulation or electroejaculation. Female partners: assisted reproductive techniques (vaginal self-insemination at home, intrauterine insemination, in vitro fertilization with or without intracytoplasmic sperm injection).  <b>Outcome Measures:</b> Ejaculation rates, seminal parameters, pregnancy rates.</p>	<p>lesions above T10 were able to ejaculate by PVS.</p> <ol style="list-style-type: none"> <li>2. 16 couples performed at-home PVS and vaginal self-insemination and 4 achieved pregnancy and had healthy babies (25%).</li> <li>3. All couples that had children had significantly higher median motile sperm per ejaculate (105 million vs. 10 million).</li> </ol>
<p><a href="#">Hultling et al. 1997</a>  Sweden  Post-test  Level 4  N=22</p>	<p><b>Population:</b> 22 men with SCI and female partner; Age (men): range 25-51 yrs, (female): range 21-38 yrs; Injury level: C2-L3; Time since injury: range 3-33 yrs.  <b>Treatment:</b> Vibratory or electrical stimulation followed by IVF.  <b>Outcome Measures:</b> Conception.</p>	<ol style="list-style-type: none"> <li>1. Pregnancy rate: 16/25 pregnancies (64%) occurred leading to 11 deliveries.</li> <li>2. n=9 singletons, n=2 sets of twins; n=4 miscarriages during the first or second trimester (1 case of intrauterine death in week 31 of gestation).</li> <li>3. Pregnancy occurred in all groups of patients in the AIS scale A-D from injuries from C2-L2.</li> <li>4. Clinical pregnancy rate was 31% and the cumulative pregnancy rates up to four cycles were 56%.</li> </ol>
<p><a href="#">Nehra et al. 1996</a>  USA  Case Series  Level 4  N=78</p>	<p><b>Population:</b> 78 men with SCI (33 couples); Age: range 23-44 yrs; Injury level: 37 cervical, 41 thoracic.  <b>Treatment:</b> Retrospective review of electrical stimulation followed by cervical self-insemination, intrauterine insemination, in vitro fertilization, or gamete intrafallopian transfer.  <b>Outcome Measures:</b> Sperm quality, pregnancy rates.</p>	<ol style="list-style-type: none"> <li>1. Vibratory stimulation achieved ejaculation in 20/37 cervical patients, 14/26 at or above T10 and 0/15 below T10.</li> <li>2. Pregnancy rates: 17/27 achieved pregnancy (10 with vibratory stim, 7 with electroejaculation).</li> <li>3. 5/8 achieved self-home insemination with PVS.</li> <li>4. 17/27 couples (63%) were successful at conception (5 self-insemination, 5 intrauterine insemination and 7 assisted reproductive techniques).</li> <li>5. 20 live births in 14 couples.</li> </ol>
<p><a href="#">Brackett et al. 1995</a>  USA</p>	<p><b>Population:</b> 23 (21 with SCI) men and partner; Age: range 26-42 yrs; Injury level: cervical (n=7), thoracic</p>	<ol style="list-style-type: none"> <li>1. Six pregnancies (7 live births) occurred in 60 cycles of IUI (cumulative pregnancy rate</li> </ol>

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Case series Level 4 N=23	(n=12), lumbar (n=2); Time since injury: range 2-28 yrs. <b>Treatment:</b> Vibrostimulation or electro-ejaculation with ovulation induction by clomiphene citrate or gonadotropins and intrauterine insemination (IUI). <b>Outcome measures:</b> Pregnancy and live births.	26%). 2. Six couples who failed after a total of 33 IUI cycles, and 1 couple with no previous IUI cycles initiated 10 cycles of in vitro fertilization, resulting in 5 pregnancies (pregnancy rate 71%): 1 live birth, 1 ongoing pregnancy, 1 ectopic pregnancy, 2 spontaneous abortions.
<a href="#">Dahlberg et al. 1995</a> Finland Case series Level 4 N=35 men with SCI	<b>Population:</b> Men with SCI and 35 female partners; Age: range 21-42 yrs; Level of injury: C1-C5 to L1-L2. <b>Treatment:</b> Sperm was extracted through vibrator application, drug application (Nifedipine 10-30mg), and electroejaculation or sperm aspiration from the vas deferens. Sperm was then introduced by insemination or IVF. <b>Outcome Measures:</b> Live births.	1. Fertility rates: of 35 males seeking pregnancy, 29 could produce viable sperm. 2. Insemination was the primary infertility treatment used with all the couples where there was successful ejaculation. In all, 12 pregnancies resulted from home vaginal inseminations, eight from intrauterine inseminations, two from IVF with ejaculated spermatozoa, and two from IVF with spermatozoa aspirated from the vas. 3. Live births: n=24 children from 18/35 couples). Miscarriages: n=4.
<a href="#">Bechoua et al. 2013</a> France Case control Level 3 N=19	<b>Population:</b> 19 men with SCI (6 quadriplegics, 13 paraplegics, mean age=25.2±5.6 years) who underwent sperm cryopreservation from 1995 to 2011. <b>Treatment:</b> Two groups were outlined based on sperm retrieval method: antegrade ejaculation group (n=10) and surgical sperm retrieval (SSR) group (n=9). All participants underwent a sperm cryopreservation followed or not by intracytoplasmic sperm injection (ICSI). <b>Outcome Measures:</b> Samples were analyzed according to the guidelines of the World Health Organization. Pregnancy outcomes in the 8	1. Fertilization rates were 57% and 55% in the antegrade ejaculation and SSR groups respectively. 2. The embryo's cleavage rates were 90% and 93% in the antegrade ejaculation and SSR groups respectively. 3. Within the 8 couples that received ICSI, 5 couples achieved pregnancy. 4. Pregnancy rates per couple were 50% and 75% in the antegrade ejaculation and SSR groups respectively.

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	couples who chose to undergo Intra Cytoplasmic Sperm Injection (ICSI) were assessed.	
<p data-bbox="240 751 430 934"> <a href="#">Leduc 2012</a>            Canada            Case series            Level 4            N=31 (couples)         </p>	<p data-bbox="488 485 992 737"> <b>Population:</b> 31 couples with male partners with SCI and fertility disorder as result from SCI; mean(SD) age: SCI men 29.7(4.8) yrs, range 23-48, female partners 29.3(4.8) yrs, range 25-41; mean(SD) DOI: 7.6(6) yrs, range 1-29; 10 cervical, 20 thoracic, 1 lumbar.         </p> <p data-bbox="488 747 992 1066"> <b>Treatment:</b> Semen samples obtained by manual stimulation (n=10, including 6 treated by sc physostigmine), penile vibratory stimulation (PVS) (n=4), electroejaculation (EEJ) (n=5), and testicular sperm extraction (n=12). Assisted reproductive technique (ART) selected according to sperm parameters (IVI, IUI, IVF).         </p> <p data-bbox="488 1077 992 1201"> <b>Outcome measures:</b> Sperm parameters (count, motility), number of pregnancies, births, and paternities, pregnancy rate/cycle.         </p>	<ol data-bbox="1019 485 1511 1102" style="list-style-type: none"> <li>1. Among the 10 couples treated with intravaginal insemination, 9 pregnancies occurred among 7 couples.</li> <li>2. No pregnancies resulted from intrauterine insemination (2 cases).</li> <li>3. Among the 18 couples treated with IVF, 12 pregnancies were reported among 10 couples.</li> <li>4. The pregnancy rate/cycle was 43%.</li> <li>5. Following these assisted reproductive techniques (ARTs) the pregnancy rate reached 55%.</li> <li>6. Overall, 20 men with SCI (64% of the group) became fathers to at least one child.</li> </ol>