Spontaneous abortion in IVF couples—a role of male welding exposure

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BACKGROUND: Fume from welding of stainless steel contains hexavalent chromium, which in animal studies can induce paternally mediated spontaneous abortion. Human studies have shown conflicting results. The best studies include early pregnancy experience, but these are expensive to conduct. In vitro fertilization (IVF) provides new design opportunities. Our aim was to study pregnancy survival in IVF treated women with respect to paternal welding exposure.

METHODS: We mailed a questionnaire to 5879 couples from the Danish IVF register that covers all IVF treatments after 1993 (response ratio 68.2%). A subgroup of male metal workers received a second questionnaire on exposure to welding (n = 319 men, response ratio 77%). Information on outcome was collected from national health registers. Survival of the first hCG-positive pregnancy was analysed using Cox regression.

RESULTS: The proportion of pregnancies terminated by spontaneous abortion before 28 gestational weeks was 18% (n = 91 pregnancies) and 25% (n = 128) in pregnancies with paternal exposure to stainless steel welding and mild steel welding, respectively. In the reference group of 2925 pregnancies the abortion ratio was 28%. The risk ratio for pregnancies with paternal exposure to stainless steel was 0.6 (95% CI 0.4–1.0). CONCLUSIONS: We found no increased risk of spontaneous abortion in IVF treated women, who became pregnant by a man exposed to welding of any sort. Since the process of fertilization and selection of IVF pregnancies differs from natural pregnancies the negative results need not apply to other pregnancies.

Key words: IVF/miscarriage/paternal occupational exposure/pregnancy survival/welding

Introduction

Male mediated spontaneous abortion has been demonstrated in animal experimental studies (Olshan and Faustman, 1993; Marchetti et al., 1999). Fumes from welding of stainless steel contain hexavalent chromium (Knudsen et al., 1992) and chromium is absorbed by the lungs and distributed to all organs (Hyodo et al., 1980; Raithel et al., 1993; Stridsklev et al., 1993). Hexavalent chromium has mutagenic capability in somatic cells and germ cells, and hexavalent chromium administered to a male rodent may impair the viability of embryos fathered by that male (WHO working group 1988; Olshan and Faustman, 1993).

In humans ~30% of implanted embryos are lost, and ~2/3 of them are lost before the woman knows that she is pregnant (Weinberg and Wilcox, 1998). Even small, but systematic differences, in the time of pregnancy ascertainment among groups that are compared may therefore introduce bias in traditional studies that only include clinically recognised pregnancies. Several population based studies have focused on paternal welding exposure as a possible candidate for paternally mediated spontaneous abortion in humans, but results have been ambiguous (Bonde, 1993; Hjollund et al., 1995; Hjollund et al., 2000). In a study including the early phase of 280 pregnancies, an increased risk of spontaneous abortion was found if the father welded stainless steel [adjusted risk ratio (RR) 3.5; 95%CI 1.3–9.1]. However, the number of paternally exposed pregnancies was limited (n = 23). IVF treatment provides opportunities to follow a large number of pregnancies from the time of conception. The male partner is not medically treated and is less likely to alter occupational activities in the course of treatment. Consequently, IVF pregnancies constitute a possible model for research in paternal risk factors. We compared the survival of pregnancies in the Danish In Vitro Fertilization Registry with respect to paternal exposure to welding.

Materials and methods

Information on IVF treatment and pregnancy outcome

The Danish In Vitro Fertilization Register (DIVF register) was established in January 1994 and involves compulsory reporting from
both public and private clinics of all treatment cycles. For each treatment cycle the following information is available: indication for IVF treatment, origin of egg and sperm, fertilization method, date of initiation, aspiration and embryonal transfer (ET), information on the hCG analysis, and if a clinical pregnancy was detected. In 2000 there were six public and 11 private fertility clinics. From 1994 to 2000 46 614 treatments were given to 15 013 women (Danish National Board of Health, 2002). Pregnancy was defined as a positive hCG analysis. Information on pregnancy survival until clinical detection was collected from the DIVF register, while data on pregnancy outcome was collected from other registers by linkage with the woman’s personal registration number: The Danish Hospital Register, The Danish Birth Register, and the Central Population Register. Diagnoses coded as spontaneous abortion, induced abortion, ectopic pregnancy and mola (ICD-10 codes D000–D006) were classified as termination of a pregnancy.

Selection of treatment cycles
Treatment with donated eggs, fertilization with donor sperm or thawed eggs were excluded. We also excluded treatment cycles ending with ectopic pregnancies, mola or induced abortion (1.9% of pregnancies). Treatments initiated after 31 December 2000 were excluded to insure complete follow-up in the health registers. Further details are provided elsewhere (Hjollund et al., 2004).

Information on exposure
A questionnaire was mailed in October 2001 and had a part for the mother and a part for the father. The participants were asked

Table I. Register information on first pregnancy by response status

<table>
<thead>
<tr>
<th></th>
<th>Responders</th>
<th></th>
<th>Non-responders</th>
<th></th>
<th>Excluded</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>All</td>
<td>4007</td>
<td>44.2</td>
<td>1872</td>
<td>20.6</td>
<td>3192</td>
<td>35.2</td>
</tr>
<tr>
<td>Mother age</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 29</td>
<td>1059</td>
<td>49.2</td>
<td>440</td>
<td>20.4</td>
<td>654</td>
<td>30.4</td>
</tr>
<tr>
<td>30–34</td>
<td>1879</td>
<td>45.5</td>
<td>827</td>
<td>20.0</td>
<td>1428</td>
<td>34.5</td>
</tr>
<tr>
<td>35–39</td>
<td>981</td>
<td>38.9</td>
<td>539</td>
<td>21.4</td>
<td>1003</td>
<td>39.8</td>
</tr>
<tr>
<td>40+</td>
<td>88</td>
<td>33.7</td>
<td>66</td>
<td>25.3</td>
<td>107</td>
<td>41.0</td>
</tr>
<tr>
<td>Father age</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 29</td>
<td>581</td>
<td>49.2</td>
<td>260</td>
<td>22.0</td>
<td>339</td>
<td>28.7</td>
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<tr>
<td>30–34</td>
<td>1646</td>
<td>50.4</td>
<td>693</td>
<td>21.2</td>
<td>924</td>
<td>28.3</td>
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<tr>
<td>35–39</td>
<td>1183</td>
<td>47.3</td>
<td>599</td>
<td>24.0</td>
<td>719</td>
<td>28.7</td>
</tr>
<tr>
<td>40+</td>
<td>597</td>
<td>45.5</td>
<td>320</td>
<td>24.4</td>
<td>395</td>
<td>30.1</td>
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<tr>
<td>IVF center</td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Public</td>
<td>2951</td>
<td>44.4</td>
<td>1319</td>
<td>19.8</td>
<td>2383</td>
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<tr>
<td>Private</td>
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<td>553</td>
<td>22.9</td>
<td>809</td>
<td>33.5</td>
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<tr>
<td>Cause of referral</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ovulation/tubal/cervical fact</td>
<td>1668</td>
<td>36.6</td>
<td>825</td>
<td>18.1</td>
<td>2068</td>
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<td>55.4</td>
<td>503</td>
<td>23.0</td>
<td>472</td>
<td>21.6</td>
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<tr>
<td>Other causes</td>
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<td>49.8</td>
<td>48</td>
<td>20.3</td>
<td>71</td>
<td>30.0</td>
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<td>Unknown or unspecified cause</td>
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<td>48.4</td>
<td>496</td>
<td>23.8</td>
<td>581</td>
<td>27.8</td>
</tr>
<tr>
<td>Year of embryo transfer</td>
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<td></td>
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<td>1994</td>
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<td>858</td>
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<td>1995</td>
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<td>0.0</td>
<td>1126</td>
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<tr>
<td>1996</td>
<td>628</td>
<td>50.2</td>
<td>332</td>
<td>26.8</td>
<td>286</td>
<td>23.1</td>
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<tr>
<td>1997</td>
<td>274</td>
<td>55.6</td>
<td>365</td>
<td>27.2</td>
<td>232</td>
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<tr>
<td>1998</td>
<td>831</td>
<td>55.0</td>
<td>424</td>
<td>28.0</td>
<td>257</td>
<td>17.0</td>
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<tr>
<td>1999</td>
<td>909</td>
<td>58.4</td>
<td>422</td>
<td>27.1</td>
<td>226</td>
<td>14.5</td>
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<tr>
<td>2000</td>
<td>898</td>
<td>62.6</td>
<td>329</td>
<td>22.9</td>
<td>207</td>
<td>14.4</td>
</tr>
<tr>
<td>Method</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IVF</td>
<td>2652</td>
<td>40.1</td>
<td>1290</td>
<td>19.5</td>
<td>2677</td>
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<tr>
<td>ICSI</td>
<td>1181</td>
<td>55.0</td>
<td>504</td>
<td>23.5</td>
<td>464</td>
<td>21.6</td>
</tr>
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<td>IVF and ICSI</td>
<td>174</td>
<td>57.4</td>
<td>78</td>
<td>25.7</td>
<td>51</td>
<td>16.8</td>
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<tr>
<td>Embryos transferred (n)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>305</td>
<td>46.1</td>
<td>135</td>
<td>20.4</td>
<td>221</td>
<td>33.4</td>
</tr>
<tr>
<td>2</td>
<td>3303</td>
<td>49.3</td>
<td>1508</td>
<td>22.5</td>
<td>1884</td>
<td>28.1</td>
</tr>
<tr>
<td>3</td>
<td>397</td>
<td>23.3</td>
<td>228</td>
<td>13.4</td>
<td>1081</td>
<td>63.3</td>
</tr>
<tr>
<td>4+</td>
<td>2</td>
<td>22.2</td>
<td>1</td>
<td>11.1</td>
<td>6</td>
<td>66.7</td>
</tr>
</tbody>
</table>

*aSome eggs fertilized with IVF and some with the ICSI method in the same treatment cycle*
questions on reproductive history, education, job, trade, specific occupational exposures as well as smoking, drinking and other life style issues. They were also asked to indicate if actual job, trade and life style had changed during the last 5 years. Questionnaires were mailed on October 29, 2001. A response ratio of 68.2% was obtained after one reminder \( (n = 4007 \text{ usable questionnaires}) \). Characteristics of the couples are shown in Table I. Couples who had their treatment recently and couples where a male factor was identified were slightly more likely to participate.

Based on type of company, trade and job function, each father was assigned a Danish ISCO code. Fathers with ISCO codes as metal workers (7210 to 7233) were selected together with fathers who had marked ‘welding at metals’ in a list of job functions. On April 22, 2002 these 512 men were mailed a second 18 item questionnaire that focused on current welding exposure with questions about welded material [stainless steel (SS), mild steel (MS), other], welding method (manual metal arch, MIG/MAG, TIG, other), welding time (h/day, years with welding), and safety precautions (exhaust ventilation, airstream helmet). A total of 319 questionnaires were received after one reminder (response ratio 76.5%). Based on actual job situation, each man was classified as ‘SS welder’, ‘MS but not SS welder’, ‘other welder’, or ‘not welder’. In other analyses only welders who had had the same working conditions for the last 5 years were included in the exposed group. Also use of safety precautions and cumulated number of years with stainless steel welding was used as exposure indices.

**Statistical methods**

For each couple only the first pregnancy was selected for analysis \( (n = 4007 \text{ pregnancies}) \). The unexposed group were respondents who had answered ‘no’ to all specific occupational exposures in the basic questionnaire \( (n = 2925) \). We also used an alternative reference group of respondents to three other trade-specific questionnaires, who had thus been subjected to the same selection mechanisms as the metal workers (farmers, green house workers, and workers in the reinforced plastic industry, \( n = 285 \text{ pregnancies} \)).

Pregnancy survival curves were constructed by the Kaplan–Meier method (Allison, 1995). Abortions were right-censored at completion of the 28th week, and 27.9% of all hCG-detected pregnancies were terminated before that time and considered a spontaneous abortion. We used this definition of spontaneous abortion to allow comparison with previous studies, but in additional analyses we also used the current definition based upon a cut-off at 20 gestational weeks. A positive hCG test with no clinical recognised pregnancy was encountered in 14.7% of pregnancies and was assigned a survival time of 29 days \( (Hjollund et al., 2004) \). Another 5.5% became clinically pregnant but had no registered abortion or birth. A survival time of 50 days was assigned to these abortions \( (Hjollund et al., 2004) \). Abortion rate ratios were calculated by Cox regression (SAS PROC PHREG) \( (Allison, 1995) \) after taking a priori selected potential confounding factors into consideration: male and female age, smoking, coffee consumption, alcohol consumption, and number of embryos transferred (Table I). Difference between clinics, e.g. cut-off level in hCG analyses and timing of ultrasonography, was adjusted for by including clinic id number in the STRATA statement. The proportional risk assumption was evaluated by including time dependent covariates in the model \( (Allison, 1995) \).

The study was approved by the Research Ethics Committee and the Danish Data Protection Agency.

**Results**

Characteristics of exposure among the 319 metalworkers are shown in Table II. About 30% of the metal workers were actually engaged in stainless steel welding, predominantly with the tungsten inter gas welding method (TIG). The majority welded stainless steel <1 h per day. The proportion of miscarriages before the 28th gestational week was 17.6% in pregnancies where the father welded stainless steel compared to 25.0% for mild steel welding and 28.4% in the group of unexposed reference pregnancies. The survival

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Stainless steel welders</th>
<th>Mild steel welders (^a)</th>
<th>Non welding metalworkers</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( (n = 91) ) (%)</td>
<td>( (n = 128) ) (%)</td>
<td>( (n = 100) ) (%)</td>
</tr>
<tr>
<td>Welded metal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stainless steel</td>
<td>100</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Mild steel</td>
<td>86</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>36</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>Duration of stainless steel welding( \leq 1 \text{h/day} )</td>
<td>77</td>
<td>11</td>
<td>6</td>
</tr>
<tr>
<td>1–3 h/day</td>
<td>11</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 + h/day</td>
<td>6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protective measures when welding stainless steel</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Local exhaust ventilation</td>
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<td>54</td>
<td>72</td>
</tr>
<tr>
<td>Point exhaust ventilation</td>
<td>42</td>
<td>24</td>
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<td>Air stream helmet</td>
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<td>13</td>
<td>10</td>
</tr>
<tr>
<td>Any of above</td>
<td>80</td>
<td>87</td>
<td></td>
</tr>
<tr>
<td>Welded same metal 5 years ago</td>
<td>86</td>
<td>87</td>
<td></td>
</tr>
<tr>
<td>Historical stainless steel welding</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>0</td>
<td>54</td>
<td>72</td>
</tr>
<tr>
<td>&lt; 1 year</td>
<td>20</td>
<td>24</td>
<td>11</td>
</tr>
<tr>
<td>1–5 years</td>
<td>33</td>
<td>13</td>
<td>10</td>
</tr>
<tr>
<td>6+ years</td>
<td>47</td>
<td>9</td>
<td>7</td>
</tr>
</tbody>
</table>

\(^a\)No stainless steel welding.
curves of pregnancies by welding are shown in Figure 1. The pregnancy survival was consistently highest among welders compared to the reference groups.

Risk ratio was at its lowest in the exposed groups (Table III). Number of hours with stainless steel welding or number of years with stainless steel welding had little influence on the estimates. The risk estimates were similar when based upon an alternative reference group of men (data not shown), and in analyses with spontaneous abortion defined as fetal death before 20 gestational weeks (data not shown).

In supplementary analyses the following pregnancies were excluded: a self-reported IVF treatment before the first entry in the DIVF registry, a self-reported spontaneous abortion before the woman’s first IVF treatment, centres with fewer than 200 recorded pregnancies, private IVF centres, indications other than ‘tubal factor’, no indications of male factor, only one, or more than two embryos transferred, and pregnancies resulting from intracytoplasmic sperm injection. The lowest rate ratio was found in couples where ‘a male factor’ was indicated (RR 0.34; 95% CI 0.13–0.92, n = 1389 pregnancies). Unchanged estimates were found in the following presumably highly exposed pregnancies (Table II): if the father welded stainless steel at least 1 h per day, if he often used the manual metal arch welding method, or if he did not use safety precautions regularly. Pregnancies originating from men who reported to weld also 5 years earlier had the same risk estimates (data not shown).

**Discussion**

We found no increased risk of spontaneous abortion in IVF treated women who became pregnant by a man exposed to stainless steel welding. In the only previous study based on pregnancy planning couples, paternal stainless steel welding was a risk factor for spontaneous abortion (Hjollund et al., 2000). In the two studies the same methods to estimate exposure was used, and the exposure in the two studies are comparable with respect to welding intermittence, use of protective measures etc. The first study was carried out in an unselected population with respect to fertility, as only couples without previous pregnancies who were planning their first pregnancy were eligible. The participants in the present study were treated and thus selected by their reproductive problems. The data from the pregnancy planner study was collected strictly prospectively, but recall bias or other problems connected with retrospective collected data on exposure is not a very likely explanation either.

The studies differ, however, substantially with respect to the process of fertilization. In normal pregnancies only one ovum is fertilized, except in case of twinning, while in IVF pregnancies the typically two transferred embryos are usually selected from a number of candidate embryos. A Dutch study of paternal exposure to pesticides found decreased fertilization rate, but increased implantation rate in two partly overlapping groups of IVF patients (Tielemans et al., 1999; Tielemans et al., 2000). The authors suggested that ability of fertilization and successful implantation may share mechanisms. In that case an exposure (e.g. paternal exposure to pesticides or hexavalent chromium) that compromises the first step (fertilization) will result in a population of survived embryos, which may be more viable (Selevan and Lemasters, 1987). We have previously reported a borderline statistically significant protective effect of paternal exposure to pesticides and growth retardants in the same IVF material (Hjollund et al., 2004). The tendency in our data towards increased pregnancy survival in exposed pregnancies could be explained by such a biological mechanism, which may be augmented by the active selection of the (normally two) most promising embryos for transfer by the laboratory technician. Information on fertilization is not recorded in the DIVF register.

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**Figure 1.** Survival of IVF pregnancies by paternal welding exposure.

**Table III.** Risk ratio (RR) of spontaneous abortion by paternal welding exposure

<table>
<thead>
<tr>
<th>Exposure characteristic</th>
<th>N</th>
<th>N</th>
<th>%</th>
<th>RR</th>
<th>RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reference pregnancies</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>non exposed</td>
<td>2925</td>
<td>830</td>
<td>28.4</td>
<td>1</td>
<td></td>
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</tr>
<tr>
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<tr>
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</tr>
<tr>
<td>Stainless steel welding</td>
<td>91</td>
<td>16</td>
<td>17.6</td>
<td>0.60</td>
<td>0.59</td>
<td>0.36–0.98</td>
</tr>
<tr>
<td>Mild steel welding</td>
<td>128</td>
<td>32</td>
<td>25.0</td>
<td>0.86</td>
<td>0.95</td>
<td>0.66–1.36</td>
</tr>
<tr>
<td>No welding</td>
<td>100</td>
<td>32</td>
<td>32.0</td>
<td>1.14</td>
<td>1.17</td>
<td>0.82–1.67</td>
</tr>
<tr>
<td>Historical stainless steel welding</td>
<td>61</td>
<td>16</td>
<td>26.2</td>
<td>0.83</td>
<td>0.93</td>
<td>0.48–1.79</td>
</tr>
<tr>
<td>&lt;1 year</td>
<td>57</td>
<td>15</td>
<td>26.3</td>
<td>0.93</td>
<td>0.94</td>
<td>0.55–1.60</td>
</tr>
<tr>
<td>1–5 years</td>
<td>63</td>
<td>20</td>
<td>32.6</td>
<td>0.68</td>
<td>0.68</td>
<td>0.38–1.25</td>
</tr>
</tbody>
</table>

*Adjusted for centre (21 levels), male and female smoking (five levels), male and female coffee consumption (five levels), male and female alcohol consumption (five levels), male and female age (four levels), and number of transferred embryos (four levels).
Validity of the IVF model

The external validity of our results depends on comparability of IVF pregnancies and normal pregnancies with respect to causes leading to spontaneous abortion. Spontaneous abortion occurred in ~30% of reference pregnancies, similar to what has been reported in other IVF studies (Liu and Rosenwaks, 1991) as well as in non-IVF pregnancies, when early pregnancy losses are included (Weinberg and Wilcox, 1998). On the other hand, in IVF pregnancies two or more embryos are usually transferred (Danish National Board of Health, 2002). If more than one embryo is successfully implanted and results in a hCG positive pregnancy, a spontaneous abortion is only registered in case of death of all fetuses. Thus, we will overestimate the survival of the individual fetus, and although we obtained similar findings when stratified on the number of transferred embryos, it should be acknowledged that in >80% of cases more than one embryo was transferred. Little is known about physiological processes involved in human gestation in the period from implantation of the blastocyst until a pregnancy is detectable, and the initial adhesion of the blastocyst has never been observed (Robertson et al., 1985; Norwitz et al., 2001). Moreover, mechanisms responsible for early embryonal loss may be different in IVF pregnancies and natural pregnancies, and findings based upon IVF data need not be generalized to pregnant women at large. In future studies of causes for spontaneous abortion based on IVF pregnancies, information on fertilization should be included.

In conclusion, we could not corroborate our previous finding of increased risk for spontaneous abortion attributable to paternal stainless steel welding. The welding intermittence was relatively low and most participants used the prescribed protective measures. The findings are in all circumstances restricted to countries with similar standards of protection.

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References


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