Associations between andrological measures, hormones and semen quality in fertile Australian men: inverse relationship between obesity and sperm output

T.M. Stewart¹,4, D.Y. Liu¹, C. Garrett¹, N. Jørgensen², E.H. Brown³, and H.W.G. Baker¹

¹Department of Obstetrics and Gynaecology, The University of Melbourne and Melbourne IVF Reproductive Services, The Royal Women’s Hospital, Melbourne, Australia; ²Department of Growth and Reproduction, Rigshospitalet, Copenhagen, Denmark; ³School of Human Biosciences, La Trobe University, Melbourne, Australia; ⁴Correspondence address. Tel: +61-3-8345-3723; Fax: +61-3-8345-3702 E-mail: tstewart@unimelb.edu.au

BACKGROUND: The World Health Organization developed a time to pregnancy (TTP) study (number of menstrual cycles taken to conceive) to determine whether the average TTP is increasing and semen quality decreasing with time. The present study describes clinical, semen and hormone characteristics obtained from male partners of pregnant women in Melbourne, Australia, and examines the associations between these characteristics.

METHODS: Male partners (n = 225) of pregnant women (16–32 weeks) who conceived naturally had physical examination, health and lifestyle questionnaires, semen and hormone (FSH, LH, sex hormone-binding globulin, testosterone and Inhibin B) analyses.

RESULTS: Previously known associations between semen, hormone and clinical variables were confirmed as significant: sperm numbers (concentration and total sperm count) correlated positively with Inhibin B and inversely with FSH and left varicocele, while total testicular volume correlated positively with sperm numbers and Inhibin B and inversely with FSH. However, only abstinence, total testicular volume, varicocele grade and obesity (BMI ≥ 30 kg/m²) were independently significantly related to total sperm count. Compared with those with BMI < 30 (n = 188), obese subjects (n = 35) had significantly lower total sperm count (mean 324 versus 231 million, P = 0.013) and Inhibin B (187 versus 140 pg/ml, P < 0.001) but not FSH (3.4 versus 4.0 IU/l, P = 0.6).

CONCLUSIONS: Obese fertile men appear to have reduced testicular function. Whether this is cause or effect, i.e. adiposity impairing spermatogenesis or reduced testicular function promoting fat deposition, remains to be determined.

Key words: fertile men / semen quality / gonadal hormones / time to pregnancy / obesity

Introduction

Scientific controversy and public concern surrounds the claims that human fertility is declining globally because of reduced sperm production. Since the publication of the Carlsen et al.’s (1992) paper, which claimed that human sperm concentration had declined by as much as 50% over the past 50 years, there has been a continued effort worldwide to provide evidence to either support or refute this assertion (Carlsen et al., 1992). Prospective studies of andrological characteristics (clinical, semen and hormone) have been conducted in well-defined populations, specifically male partners of pregnant women in Europe, USA and Japan (Jorgensen et al., 2001; Swan et al., 2003; Iwamoto et al., 2006). The World Health Organization (WHO) Special Program of Research, Development and Research Training in Human Reproduction also responded to the controversy and developed a study ‘Sentinel Surveillance of Semen Quality and Time to Pregnancy’ to test whether human fertility is changing in different regions of the world. It was planned to be a multi-centre collaborative epidemiological study but funding was not obtained. The aim of the WHO surveillance study was to perform cross-sectional studies of currently pregnant women and their partners at 3-year time intervals to determine whether fertility and semen quality are
decreasing with time. Specifically, time to pregnancy (TTP) and factors affecting it were to be assessed by a short questionnaire administered to currently pregnant women, and in selected eligible male partners more detailed information was to be obtained by a further questionnaire, clinical examination, semen and hormone analyses. We have undertaken the baseline phase of the WHO study in Melbourne, Australia, with local funding. We describe clinical, semen and hormone characteristics obtained from 225 male partners of pregnant women and the associations between these characteristics.

Materials and Methods

Study population

Women pregnant between 16 and 32 weeks gestation who attended either the antenatal clinic at The Royal Women’s Hospital (RWH) or private obstetric practices for routine management of pregnancy and childbirth in Melbourne, Australia, between January 2000 and December 2002 were approached in the waiting areas and asked to complete the WHO TTP questionnaire. If the current pregnancy was a natural conception and if their partner was eligible (18–50 years, and both he and his mother were born in Australia), he was invited to participate in a more detailed evaluation. This included a physical examination, two semen analyses, measurement of reproductive hormones in blood and the completion of additional questionnaires. All women and men gave written informed consent. The RWH Research and Ethics Committee approved the project.

Questionnaires

The development and validation of the TTP questionnaire has been described in detail (Stewart et al. 2001). In brief, the questionnaire for women elicited information on socio-demographic factors, contraceptive, pregnancy and reproductive history, and lifestyle factors, such as smoking and illicit drug use.

Physical examination

The same experienced clinical andrologist examined each man including blood pressure by mercury sphygmomanometer, body proportions (height, arm span and leg length measured from pubis to floor), breasts for gynaecomastia (defined as any palpable breast tissue), genitalia (with the man both lying and standing), virilization (Tanner stages of pubic hair) and volume of testes using a Prader orchiometer. Stretched penile length was measured with a ruler, the end of which was pressed against the man both lying and standing), virilization (Tanner stages of pubic hair) and volume of testes using a Prader orchiometer. Stretched penile length was measured with a ruler, the end of which was pressed against the end of the penis.

Semen analysis

Two semen samples at least 2 weeks apart from each subject by masturbation after a stipulated 2–5 days abstinence were requested and the subjects recorded the number of days since last ejaculation. The majority of men produced the specimen onsite at the hospital although 20 men requested a home collection. Semen analyses were performed by two experienced clinical scientists who had good external quality control (EQC) results, and there was no significant difference between their results in this study. One scientist assessed all morphology slides. All sperm tests were performed after liquefaction of the semen at room temperature within 2 h of collection. Sperm concentration by improved Neubauer, volume by weighing the tube, motility and morphology were assessed according to the WHO (1999) manual. Sperm morphology was assessed on smears prepared from semen after washing with 10 ml of 0.9% sodium chloride to remove seminal plasma. Morphology slides were stained with the Shorr method after the smears were fixed in 90% ethanol for 30 min. Sperm morphology was assessed according to WHO (1999) using the strict method. For each sample 200 sperm from at least 10 individual fields were assessed under oil immersion with a magnification of ×1000 under bright-field illumination.

Hormone analysis

A blood sample was drawn from an antecubital vein, usually in the morning, and serum was separated by centrifugation after clotting and stored at −20°C. The frozen serum was sent on dry-ice to the Department of Growth and Reproduction, Rigshospitalet, in Copenhagen, Denmark, for a centralized analysis of the reproductive hormones: FSH, LH, Inhibin B, total testosterone and sex hormone-binding globulin (SHBG). FSH, LH and SHBG were measured by time-resolved immunofluorometric assay (Delfia, Wallac, Turku, Finland), Testosterone by a time-resolved fluoromunnoassay (Delfia, Wallac, Turku, Finland) and Inhibin B by a specific two-sided enzyme immunoassay (Serotec, UK). Intra- and inter-assay coefficients of variation (CV) for measurements of both FSH and LH were 3 and 4.5%, respectively. Both CVs for Testosterone and SHBG were <8 and <5%, respectively. The intra- and inter-assay CV for Inhibin B was 15 and 18%, respectively.

Statistical analysis

In general non-parametric tests were used because most of the data were not normally distributed. The 2.5th and 97.5th percentiles or 5th percentiles for total testicular volume (TTV), stretched penile length and semen variables (because only low values are pathological) were calculated. Distribution-free confidence limits were calculated for the percentiles. Correlations between and within clinical, semen and hormone characteristics were examined by Spearman’s rho (r) test. One-way analysis of variance was used to assess the significance of differences between categories. Multiple linear regression analysis with various end-points, such as sperm concentration, was used to determine which groups of factors were independently significantly associated, i.e. a parsimonious model was chosen including only statistically significant covariates. The problem with multiple testing because of the large number of variables and our interest in several end-points is recognized. A pragmatic approach was used as follows. Factors known, expected or reported in the literature to be related were included (e.g. age, duration of abstinence, season, smoking, alcohol consumption, urogenital diseases). The remaining variables were included but were only considered further if they were highly significant (i.e. P < 0.001, with P < 0.05 being the significance level). Time of blood sampling was related to FSH (r = 0.133, P = 0.04) and Inhibin B (r = −0.280, P = 0.001) levels and this was included as a covariate in subsequent analyses. The FSH/Inhibin B ratio was calculated as FSH multiplied by 100 divided by Inhibin B. Results of the first semen specimen were used for calculations of the relationships between semen, clinical and hormone characteristics. Sperm concentration and total sperm count (volume × concentration) were cube root transformed and FSH, LH and Testosterone log-transformed for regression analysis. The interval between semen collection and start of semen analysis was categorized as <30 min or >30 min; duration of abstinence as 1, 2, 3, 4 and >5 days; varicocele as absent (Grade 0), small cough impulse only (Grade 1), moderate sized, palpable (Grade 2) and large, visible enlargement (Grade 3); season as summer (December–February), autumn (March–May), winter (June–August) and spring (September–November); BMI as underweight <20 kg/m², normal >25 kg/m², overweight 25–30 kg/m² and obese >30 kg/m² (WHO 2000). TTV was the sum of the left and right testes.
Results

Participation and characteristics of subjects

Of the 2100 pregnant women who were approached, 2061 completed the WHO TTP questionnaire (participation rate, 98%) and 928 had eligible male partners, of whom 225 participated in the male study (participation rate, 24%). However, of the 225 men (all were Caucasian), 2 did not provide semen but underwent physical examination and hormone analysis, 2 did not have hormone analysis but underwent physical examination and semen analysis and 1 did not undergo physical examination or hormone analysis but had semen analysis. Second semen analyses were obtained from 214 men, and analysis of these produced the same results for fifth percentiles and correlations as the first sample, and are therefore not discussed further in this paper. Of the 223 couples that participated in the semen study, 183 (82%) produced planned natural pregnancies while 23 (10%) had contraceptive failures and 17 (8%) had other unplanned pregnancies. None of the pregnancies were the result of infertility treatment as this was a specific exclusion criterion for the semen study. However, 13 had been investigated for infertility and 3 had been treated for male infertility in the past.

Clinical, semen and hormone test results

The clinical, semen and hormone test results for 225 fertile men are summarized in Table I. Of the 222 men who had clinical examination, 2 had absent right testes from testicular torsion in childhood. Eunuchoid proportions, defined as arm span exceeding height by 6 cm, were evident in 30 men (14%). Mild gynaecomastia was present in 44 men (20%). The majority (95%, n = 221) had Tanner stage six pubic hair distribution. One man had slight Peyronie disease. Sixteen men had moderate to large varicoceles. The mean (median) time interval from specimen collection to start of semen analysis was 35.8 (30) min. Duration of abstinence ranged from 1 to 14 days with a mean of 3.5 (3) days: only two men abstained for <2 days and 45 for >5 days. The percentages of semen samples delivered during the different seasons were: 14.8% in summer, 29.6% in winter and 23.8% in spring. Increasing time from specimen collection to start of semen analysis has been shown to correlate with any characteristic. Other significant correlations were between sperm concentration and percentage normal morphology \( r = 0.357, P < 0.001 \) and between TTV and stretched penile length \( r = 0.332, P < 0.001 \). Year of birth was not significantly correlated with any semen variable. Other semen variables were not significantly affected by duration of abstinence. Season was not significant for any semen variable.

Correlations among the clinical, semen and hormone test results

There were strong correlations between BMI and mean arterial blood pressure \( r = 0.332, P < 0.001 \) and between TTV and stretched penile length \( r = 0.266, P < 0.001 \). Year of birth was not significantly correlated with any characteristic. Other significant correlations were between sperm concentration and percentage normal morphology \( r = 0.357, P < 0.001 \). Percentage normal morphology correlated with total sperm count \( r = 0.273, P < 0.001 \) and percentage...
progressive motility ($p = 0.359$, $P < 0.001$). Testosterone correlated positively with SHBG ($p = 0.594$, $P < 0.001$).

### Correlations between clinical, hormone and semen characteristics

Interesting correlations found in the present study are summarized in Table II. Other correlations were as follows: TTV correlated positively with sperm concentration ($p = 0.359$, $P < 0.001$), increasing varicocele grade was associated with a significant ($P < 0.001$) progressive reduction in these variables, especially for total sperm count. For example, the mean cube root total sperm count was 6.96 for men without a left varicocele, 6.46 for Grade I varicocele, 5.51 for Grade 2 and 4.84 for Grade 3 ($P < 0.001$). Inhibin B and FSH correlated significantly with sperm concentration: Inhibin B correlated positively with concentration ($p = 0.276$, $P < 0.001$) while FSH was inversely correlated ($p = -0.221$, $P < 0.001$). Interestingly, stretched penile length was correlated positively with sperm concentration ($p = 0.228$, $P < 0.001$), total sperm count ($p = 0.227$, $P < 0.001$), percentage progressive motility ($p = 0.218$, $P < 0.001$) and Inhibin B ($p = 0.223$, $P < 0.001$) and correlated inversely with FSH ($p = -0.226$, $P < 0.001$). Weight and BMI were inversely correlated with SHBG (respectively, $p = -0.268$, $P < 0.001$ and $p = -0.349$, $P < 0.001$), Inhibin B ($p = -0.278$, $P < 0.001$ and $p = -0.284$, $P < 0.001$) and testosterone ($p = -0.165$, $P < 0.05$ and $p = -0.187$, $P < 0.05$). Weight correlated negatively with sperm concentration ($p = -0.138$, $P < 0.05$).

On the basis of BMI, males were grouped as underweight ($<20$ kg/m$^2$), normal ($20–25$ kg/m$^2$), overweight ($25–30$ kg/m$^2$) and obese ($>30$ kg/m$^2$); there was a nonlinear relationship with total sperm count (Fig. 1). Fitting different curves to the total sperm count/BMI relationship revealed statistical significance ($P < 0.001$; $r^2 = 33\%$) with lower total sperm counts with both low and high BMI and a peak about BMI 25. The five men with BMI $<20$ had low total sperm counts but because of the small numbers we have not analysed this further. The total sperm count was significantly ($P < 0.05$) lower in the obese men than in those with BMI $<30$. The obese group (Table III) had significantly lower total sperm count, Inhibin B, SHBG and testosterone but not FSH. The FSH/Inhibin B ratio is significantly ($P = 0.016$) higher in the obese group (3.4 (SD 3.0), $n = 36$) than in the normal and overweight range combined (2.4 (2.1), $n = 184$).

### Multiple linear regression

Modelling of factors associated with cube root total sperm count showed only TTV, left varicocele, abstinence and the obese group were independently significant (Table IV). Omitting TTV did not alter the significance or the coefficients of the other factors greatly. Results were similar for cube root sperm concentration (not shown).

### Discussion

Previously established andrological associations of sperm output were confirmed. As ~90% of testicular volume is comprised of seminiferous tubules, it is expected that testicular size would be closely related to sperm output (Kothari and Gupta, 1974; Kaler and Neaves, 1978; van Dop et al., 1980). Similarly, the relationships between TTV, sperm number, FSH and Inhibin B are consistent with the literature (Handelsman et al., 1984; Wang et al., 1985; Plymate et al., 1992; Arã et al., 1998; Pierik et al., 1998). The presence and size of a varicocele was associated with lower sperm output also as described previously (MacLeod, 1965; Rodriguez-Rigau et al., 1981; Cheval and Purcell, 1992; WHO, 1992).

This study has also provided information on other less well-known relationships, for example, the association between stretched penile length and semen and hormone variables, and between obesity and reduced sperm count. Interestingly, stretched penile length was correlated positively with sperm concentration, total sperm count, percentage progressive motility, TTV and Inhibin B and negatively correlated with FSH. In a study such as this it is possible to find unexpected relationships between two variables that are correlated with other factors. We suspect that the penile length–sperm concentration relationship is explained by the correlations with obesity: both penile length and sperm count were lower with obesity. The smaller penile length is probably attributable to underestimation of penile length in obese subjects using a ruler to measure the distance from the pubis to the tip of the glans of the stretched penis.

When compared with the fertile Danish men from the European study (Jorgensen et al., 2001), the testosterone levels are lower in the Australian men: median (2.5–97.5 percentiles) for Australian men 17 (9–33) and 22 (11–36) for the Danish men. LH levels were slightly higher in the Australian men 3.7 (1.5–7.5) than in the

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**Table II Non-parametric (Spearman) correlation coefficients for relationships between clinical, semen, hormone test results and obese men with BMI > 30 kg/m$^2$, compared with lower BMI**

<table>
<thead>
<tr>
<th>Variable</th>
<th>TTV</th>
<th>Left varicocele</th>
<th>Obesity</th>
<th>Total sperm count</th>
<th>Inhibin B</th>
<th>FSH</th>
<th>Testosterone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left varicocele</td>
<td>−0.085</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obesity</td>
<td>0.070</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total sperm count</td>
<td>0.341$^b$</td>
<td>−0.228$^b$</td>
<td>−0.163$^a$</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inhibin B</td>
<td>0.379$^b$</td>
<td>−0.109</td>
<td>−0.247$^b$</td>
<td>0.384$^b$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FSH</td>
<td>−0.244$^a$</td>
<td>0.033</td>
<td>0.028</td>
<td>−0.207$^a$</td>
<td>−0.325$^b$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Testosterone</td>
<td>0.147$^b$</td>
<td>0.046</td>
<td>−0.103</td>
<td></td>
<td>0.128$^a$</td>
<td>0.116</td>
<td></td>
</tr>
<tr>
<td>LH</td>
<td>−0.171$^a$</td>
<td>−0.004</td>
<td>0.062</td>
<td>−0.171$^a$</td>
<td>−0.201$^a$</td>
<td>0.434$^b$</td>
<td>0.27$^b$</td>
</tr>
</tbody>
</table>

$^a P < 0.05; ^b P < 0.001$. Bold values are statistically significant.
Danish men 3.5 (1.6–6.6) while SHBG levels were similar; 29 (10–58) and 30 (11–63), respectively (Andersson et al., 2004). All serum analyses (ours and the Europeans) were assessed centrally at the same laboratory in Copenhagen. The likely explanation for the difference in the testosterone levels is different timing of the blood sampling in the two studies with respect to the diurnal variation in testosterone with its peak in the early morning (Diver, 2006). The time of sampling in the current study was 0800 to 1900, median 1133 h, and in the Danish study 0615–1245, median 0750 h.

Inverse relationship between BMI and testicular function

We confirmed that BMI and obesity had significant inverse correlations with SHBG, Inhibin B and testosterone (Seidell et al., 1990; Pasquali et al., 1991; Svartberg et al., 2003; Jensen et al., 2004; Winters et al. 2006). The lower sperm concentration in the obese men was not accompanied by significant correlations between BMI and any semen variable or TTV. Other studies have also shown an inverse relationship between obesity and semen quality (Jensen et al., 2004; Kort et al., 2006; Aggerholm et al., 2008; Hammoud et al., 2008). Hammoud et al. (2008) retrospectively examined 526 infertile patients and found that oligozoospermia and a low progressively motile sperm count (defined as $<10 \times 10^6$ progressively motile sperm) were more frequent with increasing BMI. However, the study was limited by the use of self-reported height and weight measurements (Hammoud et al., 2008). In another study, Aggerholm et al. (2008) used data derived from five separate occupational and environmental population-based semen studies to create one data base ($n = 2139$). Men who were overweight were found to have a slightly lower adjusted sperm concentration and total sperm count than men with a normal BMI (Aggerholm et al., 2008). Young Danish military conscripts ($n = 1558$) with either low or high BMI ($<20$ kg/m² or $>25$ kg/m²) had lower sperm numbers and percentage normal morphology than those with BMI in the normal range (Jensen et al., 2004). This study had 14% of subjects with BMI $<20$ whereas our

Table III  Mean (SD, n) cube root total sperm count and serum hormone concentrations in three BMI groups

<table>
<thead>
<tr>
<th>BMI (kg/m²)</th>
<th>Cube root total sperm count (×10^6)</th>
<th>FSH (IU/l)</th>
<th>Inhibin B (pg/ml)^a</th>
<th>Testosterone (nmol/l)^b</th>
<th>SHBG (nmol/l)^a</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;25</td>
<td>6.8 (2, 75)</td>
<td>3.6 (2, 75)</td>
<td>192.7 (65.7, 75)</td>
<td>19.1 (6.4, 75)</td>
<td>36.7 (14.7, 75)</td>
</tr>
<tr>
<td>25–30</td>
<td>6.9 (2, 110)</td>
<td>3.3 (2, 109)</td>
<td>182.5 (73, 109)</td>
<td>17.5 (5.3, 109)</td>
<td>29.3 (10.3, 109)</td>
</tr>
<tr>
<td>&gt;30</td>
<td>6.1 (1, 35)</td>
<td>4.0 (2, 36)</td>
<td>139.8 (47.9, 36)</td>
<td>16.7 (5.8, 36)</td>
<td>25.9 (10.8, 36)</td>
</tr>
</tbody>
</table>

One-way analysis of variance, ^aP ≤ 0.001, ^bP < 0.05.
study had only 2% with low BMI and although they had lower total sperm counts than those in the BMI 20–30 groups no strong claims can be made because of the small numbers. A BMI value of >25 kg/m² was associated with lower numbers of normal chromatin-intact-motile sperm cells per ejaculate in a study of 520 men from infertile couples (Kort et al., 2006). Other smaller studies have also shown a negative relationship between obesity and semen quality (Fejes et al., 2005; Koloszar et al., 2005; Magnusdottir et al., 2005). One study failed to find an inverse association between obesity and semen quality (Pauli et al., 2008). A few studies have also shown that male obesity is associated with an increased risk of infertility (Salmen et al., 2006; Nguyen et al., 2007; Ramlau-Hansen et al., 2007). The risk of infertility may be particularly high if the female partner is also overweight or obese (Ramlau-Hansen et al., 2007).

Concerning the cause and effect relationship of the association between obesity and reduced sperm concentrations, most authors assume that the obesity must be impairing testicular function and do not consider the alternative possibility, that defective spermatogenesis predisposes to obesity. There are many reports of hypogonadotropic hypogonadism associated with gross obesity and indications that it can be treated with aromatase inhibitors (Cohen, 2008; Loves et al., 2008; Roth et al., 2008). However, none of the subjects in this study showed features of gonadotrophin deficiency, and FSH levels are not low in the obese group. The FSH/Inhibin B ratio was significantly higher in the obese group which, together with the inverse relationship between FSH and total sperm count, is consistent with a primary testicular defect. Thus we suggest reduced testicular function may predispose to, or aggravate, obesity. It has been known from traditional animal husbandry that castration increases body fat (Hausberger and Hausberger, 1966). Studies of men having testosterone reduction therapies for prostatic cancer indicate increased fat mass and reduced muscle mass (Basaria et al., 2002; Chen et al., 2002; Smith, 2004). In light of the paucity of studies in the literature on this topic and the increasing prevalence of obesity, this association between obesity and reduced sperm counts requires further investigation.

### Table IV Linear regression of cube root total sperm count in 223 fertile men with and without TTV included as a factor

<table>
<thead>
<tr>
<th>Model</th>
<th>Factor</th>
<th>Coefficient (SE)</th>
<th>P-value</th>
<th>r²</th>
</tr>
</thead>
<tbody>
<tr>
<td>With TTV</td>
<td>Constant</td>
<td>2.34 (0.51)</td>
<td>&lt;0.001</td>
<td>37.0</td>
</tr>
<tr>
<td></td>
<td>Abstinence (days)</td>
<td>0.40 (0.06)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TTV (ml)</td>
<td>0.069 (0.009)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Left varicocele &gt;30 BMI, Obese</td>
<td>−0.39 (0.14)</td>
<td>0.006</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Obese</td>
<td>−0.77 (0.25)</td>
<td>0.002</td>
<td></td>
</tr>
<tr>
<td>Without TTV</td>
<td>Constant</td>
<td>5.77 (0.25)</td>
<td>&lt;0.001</td>
<td>21.5</td>
</tr>
<tr>
<td></td>
<td>Abstinence (days)</td>
<td>0.37 (0.06)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Left varicocele &gt;30 BMI, Obese</td>
<td>−0.55 (0.12)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Obese</td>
<td>−0.69 (0.28)</td>
<td>0.013</td>
<td></td>
</tr>
</tbody>
</table>

### Study strengths and weaknesses

A possible weakness is the inclusion of only fertile couples in the study as this may reduce or obscure a more significant relationship between obesity and other semen analyses results had infertile subjects been included. The strengths of this study were the prospective design and the blind ascertainment of results of clinical, semen and hormone data by the same clinician and scientists. Also all hormone analyses were performed centrally in a facility in Copenhagen which also participated in the European and US studies of partners of pregnant women (Jorgensen et al., 2001; Swan et al., 2003). Our laboratory participated in two EQC programs, the Australian External Quality Assurance Schemes for Reproductive Medicine and an International EQC program conducted by Dr Niels Jørgensen. Obtaining a representative sample of the general male population is a near impossibility since few men volunteer, and previous experience indicates that volunteers disproportionately represent those who are concerned about their fertility, either because of previous testicular disorders or suspected infertility (Bonde, 1990; Handelsman, 1997; Larsen et al., 1998; Cohn et al., 2002). The design of this study allowed assessment of this type of selection bias and this will be reported separately. The semen analysis results provide useful normative data for our geographic region. They have been included in a WHO-sponsored report (Cooper et al., in preparation) and the reference values for the 5th Edition of the WHO Semen Analysis Manual (date of publication is unknown at this stage).

### Conclusion

In conclusion, this study has provided useful normative data for fertile Australian men. As well as confirming many well-established andrological associations, there was a lower sperm concentration in obese men with BMI >30. Whether this is cause or effect, in terms of adiposity reducing spermatogenesis or reduced testicular function promoting fat deposition, remains to be determined.

### Acknowledgements

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