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Occupational heat exposure and male fertility: a review

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In humans, as in most mammals, spermatogenesis is temperature dependent. This temperature dependence has been clearly demonstrated by several experimental studies showing that artificial increases in scrotum or testicle temperature in fertile men reduce both sperm output and quality. Our knowledge of the effects of occupational heat exposure on male fertility comes mostly from a small number of epidemiological studies. We conducted an extensive review of these published reports, focusing on methodology and design (retrospective or prospective; reference group; number of subjects) and principal results (using several indicators such as the time taken to obtain a pregnancy or sperm characteristics). We concluded that occupational heat exposure is a significant risk factor for male infertility, affecting sperm morphology and resulting in delayed conception. The limits and biases involved in this type of research are also discussed.

Key words: heat exposure/male infertility/occupational exposure/semen analysis

Introduction

In humans, as in most mammals, testicular function is temperature dependent. Normal testicular function requires a temperature 2–4°C below body temperature. There is therefore a temperature difference between the body core and the testicles, as first reported by Badenoch in 1945 and subsequently confirmed by various other authors (Harrison and Weiner, 1949; Kitayama, 1965; Mieusset and Bujan, 1995). Testicular temperature is regulated by two mechanisms. The scrotum is responsible for the first level of regulation: it has no subcutaneous fat, and the total surface area of its skin changes with temperature. It can therefore dissipate heat to the exterior as appropriate. The second thermoregulatory system is located in the spermatic cord where there is a counter-current heat exchange between incoming arterial blood and outgoing venous blood, the temperature of which is lower than that of arterial blood due to loss of heat through the skin of the scrotum. Thus this heat exchange system results in the pre-cooling of arterial blood arriving at the testis (Glad Sörensen *et al*., 1991).

Numerous external factors (for example, posture, clothing, lifestyle, and season) can affect the temperature difference between the body core and the scrotum. Experimental studies in animals and humans have demonstrated the role of exogenous heat exposure in male infertility (MacLeod and Hotchkiss, 1941; Watanabe, 1959; Waites, 1973; Zorgniotti *et al*., 1982; Jegou *et al*., 1983; Byers and Glover, 1984; Oldereid *et al*., 1992; Rojansky *et al*., 1992; Mieusset and Bujan, 1995; Parazzini *et al*., 1995). Indeed, numerous epidemiological studies have indicated the possible effects of various types of occupational exposure on male fertility.

Two case reports in the literature describe reduced fertility due to occupational heat exposure: one in a baker and another in a mechanic who took regular hot baths (Brun and Clavert, 1977; Rubben *et al*., 1988).

Sas and Szöllosi (1979) found that 291 (9.4%) of the 2984 patients consulting for infertility in Szeged (Hungary) were professsional drivers, whereas this occupation accounted for only 3.8% of the general population in the same catchment area. The incidence of the most severe sperm anomalies (oligoasthenozoospermia and azoospermia) was correlated with the number of years of driving and with the use of agricultural and industrial heavy machinery with high levels of vibration.

In a case–control study of data from medical records and mailed questionnaires from 1977 to 1980, Rachootin and Olsen (1983) found an association between infertility and occupational exposure to heat (with heat exposure being deduced from the job description). Comparing 1069 infertile couples with 4305 fertile control couples, the heat exposure odds ratios for men with sperm abnormalities was 1.8 (1.2–2.6), while that for men with idiopathic infertility was 1.6 (0.9–2.7). Using time to conception (within and after 1 year) as a reproductive indicator, an odds ratio of 1.8 (1.4–2.4) was found for delayed conception (up to 1 year) for couples of which the male partner had been occupationally exposed to heat.

Brindley (1982) showed that 23 paraplegic men in wheelchairs (rehabilitated apyrexial men with spinal injuries) had deep scrotal temperatures (measured by invagination thermometry) which were about 0.9°C higher on average than that of 13 normal men in a sitting position. There was a significant correlation between higher deep scrotal temperature (>36.3°C) and low motile sperm counts for the 28 paraplegic men with successful electroejaculation.

In a case–control study in 1981 in Italy, Buiatti *et al*. (1984) compared 112 azoospermic or oligozoospermic males attending an outpatient clinic with 127 control patients. The controls resided in the same area, attended the same clinic, but had normal routine examination results, and a sperm count of

Table I. Male fertility factors reported by the main studies of heat exposure due to occupational or lifestyle

Study	Type of study and no. of subjects	Outcome and main results Odds ratio (OR) (95% confidence interval)
Sas and Szöllosi (1979)	Retrospective study 2984 infertile patients	9.4% of infertile patients were drivers compared to 3.8% of the general population in the same area
Rachootin and Olsen (1981)	Case–control study 1069 cases, 4305 controls	OR = 1.8 (1.2–2.6) for men with sperm abnormalities OR = 1.8 (1.4–2.4) for couples with delayed conception
Brindley (1982)	Descriptive survey 44 men	Higher deep scrotal temperature for paraplegic men in wheelchairs Significant lack of motile spermatozoa in men with higher scrotal temperature
Buiatti *et al*. (1984)	Case–control study 112 cases, 127 controls	OR = 0.8 (0.4–1.5) for men who usually sit at work
Figa-Talamanca *et al*. (1992)	Retrospective study 92 exposed, 87 non-exposed	Childless: 7.6% of exposed subjects, 1.1% of controls; $P = 0.05$ Normal sperm motility: 7% for exposed subjects, 28% for controls; $P = 0.05$
Bonde (1992)	Prospective study 17 exposed, 73 non-exposed	No difference in sperm count and motile sperm count
Thonneau *et al*. (1997)	Retrospective study 402 fertile couples	Time to pregnancy was significantly longer for subgroups ‘exposed to heat’ and ‘seated in a vehicle more than 3 h/day’
Figa-Talamanca *et al*. (1996)	Retrospective study 72 exposed, 50 non-exposed	Lower prevalence of normal spermatozoa in exposed group: 46% versus 64% in control group (taxi drivers)
Velez de la Calle (personal communication)	Case–control study 307 cases, 172 controls	OR = 3.0 (1.4–6.7) for men in an occupation involving exposure to heat

$>20\times10^6$/ml. The sitting posture at work or the wearing of tight trousers was not found to be related to azoospermia or oligozoospermia.

Figa-Talamanca *et al*. (1992) compared the reproductive indicators and semen characteristics of 92 healthy ceramic oven operators with long-term exposure to high temperature, to those of 87 non-exposed workers in the shipment department of the same company. They observed a significant difference between the percentages of childless men in the exposed and non-exposed groups (7.6 compared with 1.1, $P = 0.05$). Twice as many of the heat-exposed workers reported difficulties in their partner conceiving (23% compared with 12%). Semen analyses (of one sample from each of the 46 exposed and 14 non-exposed workers) did not indicate a difference in mean sperm concentration and morphology, but showed a lower percentage of normal sperm motility for the exposed workers (7% compared with 28%, $P = 0.05$).

In Denmark, Bonde (1992) compared 17 manual arc alloyed steel welders, moderately exposed to radiant heat (with semen samples being obtained before, during and after heat exposure) with 54 non-welding metalworkers and 19 flexoprinters (non-heat-exposed reference groups). Sperm count and motile sperm count were not significantly lower for the welders than for the two reference groups. However, for the welders, the proportion of spermatozoa with normal shape declined significantly after 6 weeks of heat exposure, and increased after a break in exposure to heat.

Figa-Talamanca *et al*. (1996) studied 72 taxi drivers and 50 control subjects (of similar age and smoking habits) in Rome. They compared salivary testosterone concentrations, sperm quality (concentration, morphology and motility), and time taken to obtain conception. The taxi drivers had a significantly lower prevalence of normal sperm forms (45.8% compared with 64.0%) than the control group. This observation was more pronounced in those who had been working as drivers for a long time. A significant association between smoking and poor sperm morphology was also observed.

In France, the relationship between male occcupational heat exposure and time to obtain a pregnancy was studied in a retrospective survey of 402 fertile couples (Thonneau *et al*., 1997). The time (in months) to obtain a pregnancy for the subgroups ‘exposed to heat’ (median = 4.0; mean = 11.8; SD = 13.3) and ‘seated in a vehicle for more than 3 h/day for occupational reasons’ (median = 4.5; mean = 14.4; SD = 28.5) was significantly longer ($P < 0.05$ for both groups) than that for the controls (median = 2.8; mean = 7.8; SD = 13.3). The results obtained from focusing on two specific male professions, baking and welding, were consistent with our overall results: 14% of the bakers’ partners obtained a pregnancy within 3 months compared with 55% among the controls ($P < 0.05$) while 29% of their partners became pregnant within 6 months compared with 74% among the controls ($P < 0.02$).

More recently, in an unpublished case–control study in a French town, J.-P. Velez de la Calle (France, personal communication) compared all couples who had sought medical advice for infertility lasting longer than 12 months with fertile couples (defined as couples who had a successful delivery during the period of the study). The adjusted odds ratio was 3.0 (1.4–6.7) for male occupational exposure to heat. The main occupations of men reporting such heat exposure were: bakers, submariners, welders and metallurgy workers (J.-P. Velez de la Calle, personal communication).

In published studies, the assessment of heat exposure has been unsatisfactory: either self-reported or deduced from occupational title. However, it is possible to evaluate scrotum temperature precisely using a digital portable register (Jockenhövel, 1990). Future research should focus on accurate heat exposure assessment to determine if men really have been exposed to heat and to investigate possible dose effects. However, possible associations with other risk factors for male infertility, such as lead exposure in some drivers (Gennart *et al.*, 1992) should also be taken into account.

The time taken by the couple to conceive (also called the time to pregnancy, TTP) has already been successfully used as a reproductive output indicator in retrospective studies (Baird *et al.*, 1986; Joffe, 1989; Boldsen and Schaumburg, 1990). In a retrospective survey conducted through the Oxford Family Planning Association, Joffe *et al*. (1995) found that the TTP is a sensitive measure of reproductive function, and that valid data can be derived retrospectively, even with a long duration of recall. In this and in a similar study (Zielhuis *et al*., 1992) the feasibility, validity and reliability of questionnaires using the TTP have been demonstrated.

The most readily available indicator of male fertility is semen evaluation: concentration, motility and morphology of spermatozoa. There are large differences in the characteristics of spermatozoa from a particular individual, with the duration of abstinence and the season both having a significant effect. Thus longitudinal series with two sperm analyses (at a time interval of 2 weeks, and with a duration of abstinence of between 2 and 4 days) are required.

The availability of substantial numbers of semen samples from non-exposed individuals with lifestyles similar to those of the exposed men would also improve the power of comparisons between the two groups (exposed and non-exposed) and strengthen conclusions (Baird and Wilcox, 1986; Bonde and Giwercman, 1995).

As observed by Handelsman (1997), the voluntary aspect of the donation of spermatozoa by exposed and non-exposed men is a major potential source of bias, making it necessary to interpret the results obtained in such studies with great caution. It is still not possible to match the groups of men in terms of age, lifestyle and social position. However, even if it were, some men probably have personal reasons (linked with fertility status or with the type of exposure being studied) for wanting to donate spermatozoa for this type of research. An alternative approach involves the use of exhaustive lists of people potentially exposed or not exposed, such as a list of employees of a large company. The order of names on the list should be randomized and the men should then be approached for inclusion in the study according to their position in the new randomized list. Unfortunately, such a procedure is likely to generate so many refusals that it would lead to another form of 'volunteer' selection.

To conclude this review, male heat exposure seems to have a deleterious effect on male fertility and must be considered as a significant risk factor for male infertility. In men under normal healthy environmental conditions, the testicular thermoregulation system is certainly able to maintain the 'normal' scrotal hypothermy. In men repeatedly subjected to abnormal situations (such as drivers or workers exposed to high temperatures) and perhaps also in men with impaired arterio-venous testicular systems, there may be chronic thermo-dysregulation which may, in time, result in substantial changes in sperm characteristics (such as motility and morphology) as has been reported in animal models (Mieusset *et al*., 1992).

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