

## How the fertility of males and females is affected by stress, lifestyle and pharmaceutical agents

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### Abstract

**Background:** Infertility in men is the most discussed issue among couples. It is generally believed that about half of infertility in couples is due to the men side, mainly due to frustrations in the process of spermatogenesis. Currently it has been found that lifestyle modifications are vital to improve infertility and interest in this area has increased. Examples include maturation, mental stress, diet, active work, high temperature of scrotum, hot water, caffeine, and mobile phone use. This review will examine the effects of personal satisfaction (a modifiable lifestyle factor) and mental stress on infertility in male. It will also show the effects of high scrotal temperature and unhealthy views of exercise on infertility in male.

**Materials and Methods:** Forty of the 118 (34%) men patients who underwent IVF agreed to participate in this review. Only patients having IVF for the first time were recalled for re-examination to reduce the adjustments to the sperms sample screening process that would occur in men with some experience of IVF. Of these, 31 completed the retest and eight decided not to proceed after the initial testing period; one patient's cycle was cancelled prior to ovulation.

**Conclusion:** Our study found that IVF patients had significantly lower sperm quality when they collected their eggs, which suggests a link between sperm quality and psychological stress. Whether physical (frozen reserve sperm samples) or psychological (evacuation preparation, targeted morphology, treatment groups) interventions are effective in reducing stress in male IVF patients and controlling stress-related changes in sperm quality is still unknown. Further studies are awaited to light some further developments.

**Keywords:** Fertility of male; Spermatozoa; Stress; Nutrition; Physical exercise; Natality; Spermatogenesis

### 1. Introduction

In developed countries, reducing the number of people suffering from infertility is a major concern for muchhealth organisations. In Europe, several studies have shown that population fertility may be declining [1]. The net effect, as recommended by some studies, is a 7% reduction in fertility [2]; if the pattern observed for 15 years continues for 45 years, the reduction in fertility can be multiplied by the ridiculous theory of halving [3].

Infertility affects everyone. In half of couples who become automatically childless, factors related with infertility in men are identified, as well as abnormal sperms boundaries. In these cases, the fertile partner compensates for the problem

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of infertility in men and then, assuming that the reproductive capacity of both partners is reduced, infertility in principle results [4].

Thus, lifestyle changes can have a more enriching and controlling impact. Regenerative medicine can be critically or critically affected by several factors such as paternity time, supplements, actual exercise, obesity, caffeine, scrotal temperature, clothing, boiling water, mobile phones that can sway personal satisfaction of the sperms boundary and DNA damage operated by the sensitive forms of oxygen (ROS) along these lines. is negatively affected [5]. Likewise, the coordinated harmony between cellular improvement frameworks [7] and oxidative stress can determine crippling treatment early growth, pregnancy misfortune, birth deformities and childhood illness [8-10]. In this control, through an organized program of educational exercises, ecological, dietary/actual exercises and spiritual help, with the additional use of cellular enhancement nutritional supplements, lifestyle adjustments prevent infertility and consequently better improve individual satisfaction and the likelihood of envisioning the unexpected and increase the likelihood of origin and mates. Presenting evidence that proves it can help.

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## 2. Job of stress on fertility of male

Infertility is generally stressful in itself, with difficulties, tests, analyses, treatment, frustration, unfulfilled desires and a huge financial burden [11]. Spermatogenic potential is thought to be related to stress and the presence of stress impairs luteinizing chemicals (LH) and testosterone beats, resulting in a decrease in spermatogenesis and quality of sperms [12, 13].

Preclinical studies have shown that severe stress reduces testicles capacity. Testicles tissues from stressed rats showed high levels of cortisol and apoptosis of microbial and Leydig cells [14, 15]. On the other hand, the net effect of stress still persists, as shown by the continued presence of glucocorticoid receptors (GR) in Leydig cells, [16], Sertoli cells [17] and microbial cells [15]. Throughout the year, significant levels of glucocorticoids function in all cell types that are tolerant to apoptotic activation [15-17]. Leydig cells are an important target for glucocorticoid induction in the testis. Currently, our understanding of glucocorticoid induction in relation to the physiology of azoospermia is restricted. Stress induces various neuroendocrine, immune and social responses. Currently, new evidence for the NR3C1 polymorphism of a nucleotide that promotes GR responses to glucocorticoids has been recommended in the Sertoli and Leydig cell fitness guidelines [18]. Thus, the quality of this mutation (in a super dominant manner with heterozygotes) is certainly related with better motility of sperms and superior testicles work. This is closely related to occupation [18].

In people, GR polymorphisms may represent a variable response to stress [19]. Hidden stresses such as work, life events, excessive stress or two stressful life events at the same time can negatively affect quality of sperms [11]. Apparent stress on sperm sample supply is said to be inversely related to quality of sperms, with a 38.5% decrease in sperm stability and a 46.38% decrease in motility during oocyte retrieval, despite no change in volume or morphology and unfortunately a higher sperm threshold [20, 21].

Second, Natural disasters, war and "stressful life" are important determinants whose effect on fertility cannot be assessed, so that the true problem of stress is not properly appreciated. This stress can be inferred from the persistence of high stress in daily life, even without apparent outbursts.

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## 3. Cancer prevention agents

Another emerging project in the treatment of infertility in men is the use of cell enhancers [71]. These are atoms such as eggs white, kerloplasmin and ferritin, ascorbic acid, alpha-tocopherol, beta-carotene, reduced glutathione, uric acid cleavage and bilirubin or the proteins superoxide dismutase, catalase and glutathione peroxidase, among various small particles [71]. These serve to eliminate the abundance of ROS in the initial release and help to convert ROS to intensities that are more unfavorable to the cell [71]. When ROS are present to such an extent that surrounding cancer prevention agents cannot eliminate them, they cause increased oxidative stress, thereby destroying sperms proteins, lipids and DNA and inhibiting sperms dysfunction [71]. Ascorbic acid (nutrient C) is a true cancer prevention agent present in the testes with the proper function to protect the last choice from oxidative damage [72]. It also contributes to assisting spermatogenesis, to some extent, through its ability to maintain this cancer prevention factor in a functional state [72]. Nutrient C itself is maintained in a reduced state by dehydroascorbate reductase, a GSH-coordinated enzyme that is abundant in the testes [72]. The task of production is assigned to myoinositol, the second precursor carrier of Ins(1,4,5)P3 [73, 74]. Myoinositol balances protein phosphorylation processes and intracellular Ca<sup>++</sup> concentrations and may be beneficial for motility of sperms through the spermatozoa pore Ca<sup>++</sup> channels (CatSper) in the plasma layer of the long flagellar fibers [75,79]. N-acetylcysteine (NAC) is also an amino-degrading agent that may shows cell-

enhancing properties upon its conversion to cysteine, a glutathione precursor [80] In vitro studies have shown the beneficial work of NAC on microbial cell resistance [81] through the reduction of ROS levels, which consequently further enhances motility of sperms [82]. However, the results of clinical studies using any cancer prevention agent have been questioned. A double-blind, placebo-controlled, randomized review examined the effects of selenium and log N-acetylcysteine in 468 infertile men with idiopathic oligoasthenospermia and recommended a favorable effect [83].

Although there is a positive relation between nutrient D levels and quality of semen (motility of sperm), there is no evidence between nutrient D levels and quality of semen (motility of sperm).

Although there was a positive correlation between nutrient levels and the quality of spermatozoa, there was a positive correlation between nutrient levels and the quality of spermatozoa.

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#### 4. Antidepressants Medications

There are a lot of antidepressants medications which can cause infertility in men, as the incidence of depression in a person lifetime is 16% which leads to high number of prescriptions containing antidepressants medications like escitalopram, in the USA almost more than 250 million prescriptions were having antidepressants medications in thrm. Although the exact origin of depression is still unknown, it is believed that ventral limbic regions involved in processing emotions are overactive, whereas the dorsal prefrontal cortex is underactive [52,53,54,55,56].

Individuals with depression are currently treated of choice with antidepressant drugs, particularly (SSRIs) called selective serotonin reuptake inhibitors [41,42,43]. MFI has been linked to SSRIs as a cause. However, few studies have examined the impact of SSRIs on MFI due to the rise in SSRI use in recent years. The fact that certain studies have connected depression on its own, without the use of pharmaceuticals, to changed testosterone levels, which may potentially contribute to MFI [20, 26], further complicates the situation. Nevertheless, numerous additional researches have fallen short of proving such a correlation.

##### 4.1. Calcium Channel Blockers and Alpha 2 adrenergic receptor agonists

Calcium channel blockers are calcium ion antagonists. These drugs inhibit the movement of free calcium ions, usually these calcium ions act as important secondary messengers, between ion channels and ionophores. Calcium channel blockers usually act on heart muscle, vascular smooth muscle, skeletal muscles and nerve cells [23, 24, 27]. Calcium channel blockers drugs are normally indicated to treat several health conditions including hypertension and congestive heart failure [26, 28].

There are also clinical trials suggesting an association between Calcium channel blockers, in addition to the in-vitro type of studies described above. These are not enough studies and a small study of sperm from men taking Calcium channel blockers did not show a reduction in oocyte fertilisation rates in in vitro fertilisation (IVF) without intra-cytoplasmic injection of sperms [36]. However, the pregnancy rate per transfer in embryos derived from men taking Calcium channel blockers was only 18% [33]. The authors were unable to identify a large prospective trial evaluating fertility outcomes in men taking Calcium channel blockers, although there is significant data to suggest that Calcium channel blockers may contribute to MFI.

Some drugs of adrenergic systems like Alpha 1 adrenergic antagonists/ blockers are a class of drugs that are most commonly used to treat lower urinary tract symptoms associated with benign-prostatic-hyperplasia [33]. such drugs have a high affinity for alpha-adrenergic receptors especially alpha 1 receptors and somehow alpha 2 also on lower urinary tract smooth muscle cells and blood vessels. AABs also have a strong affinity for binding to a number of other receptors, including those for dopamine and serotonin [31].

However, no detrimental effects on ejaculation or some deteriorated semen parameters have been demonstrated in other trials using AABs other than tamsulosin, such as alfuzosin [34]. While there is significant data to suggest that Alpha adrenergic blockers, particularly tamsulosin, may contribute to MFI, the authors could not identify a large prospective study assessing fertility outcomes in men taking Alpha adrenergic blockers.

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#### 5. Materials and Methods

Forty of the 118 (34%) men patients who underwent IVF agreed to participate in this review. Only patients having IVF for the first time were recalled for re-examination to reduce the adjustments to the sperms sample screening process

that would occur in men with some experience of IVF. Of these, 31 completed the retest and eight decided not to proceed after the initial testing period; one patient's cycle was cancelled prior to ovulation.

All review participants noted the consent form approved by the clinic's Human Research Committee. In addition, semen samples were collected and a single questionnaire form was completed to investigate stress levels in the accompanying circumstance. 4.5 months before the IVF cycle (measurement sample: T1) and at the time of eggs retrieval (IVF sample: T2).

Sperms assessment and handling of Semen samples were collected by masturbation in a controlled temperature clinical environment. We asked men to adhere to a time limit of 46.38-72 hours. Samples were collected in clean cups and concentrated at room temperature for 30-45 minutes before handling the samples.

Volume of semen was estimated to the nearest 0.1 ml using an adjustable pipette. The sample was further evaluated externally for shading, consistency and bedding and any abnormalities were noted. Undiluted semen (5  $\mu$ l) was placed in the McClure chamber and integrated into a robotic semen analyzer (Hamilton-Thorn, Danvers, MA, USA). The number and nature of foci and motility of sperms were assessed. The complete motility of sperms (motile sperms concentration x volume) was determined for each sample. The subjective rates of motility of sperms tested were: average mode, and moderately fast, average straight arching, and average horizontal headed rooting (LHD). In cases where sperms foci were  $<10 \times 10^6$ , manual assessment was used to investigate sperms quality. In this case, 10  $\mu$ l of attenuated semen (1:20 in F-10 Ham's F-10 + 0.4% bovine serum eggs white as cow's milk) was placed in the haematometer to ensure absolute spermatozoa focus, fixation of motile spermatozoa and forward movement. Another quantity of attenuated semen was used to investigate semen morphology according to the principles of the World Health Organization (WHO, 1980).

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## 6. Stress Questionnaire

Semen samples were collected by masturbation in a clinical controlled temperature environment. We asked men to adhere to a time limit of 46.38-72 hours. Samples were collected in a clean cup and pooled at room temperature for 30-45 minutes before sample handling.

The volume of semen was estimated to the nearest 0.1 ml using an adjustable pipette. The sample was further evaluated externally for shading, consistency and bedding and any abnormalities were recorded. Undiluted semen (5  $\mu$ l) was placed in a McClure chamber and loaded into a robotic semen analyzer (Hamilton-Thorn, Danvers, MA, USA). The number and nature of foci and motility of sperms were assessed. The complete motility of sperms (mobile sperms concentration x volume) was determined for each sample. The subjective motility of sperms velocities examined were the mean mode and average velocity, mean straight curvilinear and mean horizontal head root (LHD). Manual assessment was used to investigate sperms quality when the sperms focus was less than  $10 \times 10^6$ . In this case, 10  $\mu$ l of attenuated semen (1:20 in Ham's F-10 + 0.4% bovine-serum eggs white as milk) was placed in a haematometer to check absolute semen focus, fixation and propulsion of motile spermatozoa. Another volume of attenuated semen was used to investigate the morphology of the semen according to the principles of the World Health Organization (WHO, 1980).

### 6.1. Statistical Analysis

Stress and sperm threshold from T1 to T2 were assessed by the Wilcoxon signed rank test (Glantz, 1981). Spearman's correlation with nonparametric data to investigate the relationship between stress and sperm threshold growth during two trials. Additionally, ch2 tests to eliminate individual correlation of sperm-related changes over a long period of time, establishing a robustness test of the same yates. Gage (patient T1 scores were separated by Spearman's correlation test. Patients classified as men with normal propensity and normal azoospermia were examined. According to the endpoint of this study, male patients with variability were classified as having a total motile sperm count of less than  $20 \times 10^6$  in the fluid collected by the test sample. Spearman's conjugation test was also used in cases where there was a significant relationship between stress and sperm limit.

Declining male fertility is an important public health issue in the current century, particularly because it is related with aging, unhealthy lifestyles, and environmental variables that significantly affect fertility. shows and affects the future of humanity. Thus, lifestyle adaptations through organized programs of education, environment, diet, practical exercise, and spiritual support, along with additional use of nutrients that diminish cells, can prevent infertility. leading to greater personal satisfaction and complete well-being for couples. possibilities and progress. perhaps helping them rationalize the possibility of conception.

## 7. Discussion

The results showed that men having IVF had lower quality of sperms at the time of egg retrieval, providing key evidence for a link between mood and quality of sperms. Total sperm attachment rate, motility of sperms rate, and quantitative and subjective motility of sperms rate were completely reduced during oocyte retrieval compared to before IVF; Individual examination of quality of semen over both study periods also showed that this specificity occurred at a higher rate among examiners. Other researchers have detailed a comparable, less dramatic decrease in quality of sperms related with IVF; Harrison et al. (Harrison et al.) found that sperm attachment, total sperm count, and motility were slightly decreased in 500 semen samples subjected to IVF and produced before IVF. In a study of similar design, Kentenich et al., 1992, contrary to previous assessments, found that 36% of IVF men had significantly reduced sperm foci during oocyte retrieval. These studies did not limit their subjects to patients having IVF for the first time and did not specifically measure nervousness.

Although psychological stress is generally expected to influence quality of sperms, few attempts have been made to assess the level and type of stress in male IVF patients. It is used to identify pleasant and unpleasant sensations experienced by men in response to various IVF-related situations; but no attempt has been made to link these feelings to changes in sperm boundaries. In this study, specific psychological factors were assessed using cognitive and situational intensity tests after sperm retrieval during the baseline control phase and after sperm retrieval during the egg retrieval phase. This method was used to examine changes in mental state and quality of sperms over two test periods, and it was possible to establish a boundary between stress and quality of sperms.

The men in this study experienced significantly higher stress levels before treatment and during ovulatory sperm collection, and although situational stress levels did not increase significantly between the two-year trial, the sample mean score T1 (41.1) showed that T2 (42.2). Higher than Dziegielewski and Tyler, he showed higher scores on strength and quality of sperms of the men tested.

Regarding this study, it should be noted that patients with male variability show a specific response compared to patients with normal azoospermia. The value of sperm donation from patients with male variability was clear, but there was no decrease in quality of sperms at the time of oocyte collection, as observed in patients without male variability. This can be explained by the fact that the significance of the male group increases at T1 and remains high at T2. It was impressive that patients with male variability clearly recognized sample significance, even during the standard examination period, when apparent significance remained high and the semen cut-off point was low. Assuming that the apparent significance is related to quality of semen, this relationship is expected: slightly improved quality of semen at T2 in some male component patients may reflect a degree of instability in their semen samples. Perhaps the results of this study are more reliable than Boivy's recent findings; in which male patients who underwent ICSI and IVF reported higher intensity than normal azoospermic men before IVF, but intensity was equally high in both encounters during actual treatment. The border has not been measured.

The physical distractions related with the semen collection room, such as the presence of other people, distractions, and the emergency room environment, often lead to patient frustration. This level of frustration does not increase at the time of egg retrieval, nor do these variables fully transfer or amplify the negative changes related with sperm restriction. Therefore, changing the format of semen collection centers should focus on optimal compliance, but may apply less to the nature of the semen supplied.

The mechanism by which psychological stress affects quality of sperms is not yet known. The cycle of human spermatogenesis lasts about 70 days (the time that undifferentiated spermatozoa transform and develop into motile spermatozoa). Given the 30-45 days period (T1-T2) considered in this review, the increased stress experienced during the oocyte retrieval approach is unlikely to directly affect spermatogenesis. Instead, the effect of stress can be indirect, through the hormonal part of spermatogenesis. It has been shown that this specificity could be linked to the hormonal changes observed in men during stress. Testicles biopsies from prisoners awaiting execution showed complete inhibition of spermatogenesis in all cases, despite being under severe stress (Steves, 1952). Mild types of stress, such as stress from combat or medical procedures, have been shown to cause non-local conditions.

testosterone concentrations in affected men. This may be the result of chemical activation of the hypothalamic-pituitary-adrenal node, which is known to be reinforced by stress. Social stress in the body has been shown to be related with decreased testicles size due to changes in luteinization (LH) and testosterone chemistry. We found that in a group of marmoset monkeys exposed to constant stress, volume of semen and sperm stabilization rate were significantly

reduced. This effect was related with a decrease in the convergence of LH and testosterone (decreased LH and testosterone in the face of stress). This development, for all intents and purposes, appears to be disrupted by drugs endogenous to the hypothalamic-pituitary-adrenal junction. Unlike the agonist naloxone, there is evidence that the drug interferes with the inhibitory effects of stress on LH and testosterone; Additionally, changes in LH and testosterone directly affect testicles capacity and quality of sperms in high stress situations, both ideal and parasympathetic.

The results of this review are somewhat restricted due to the small sample size. In addition, 23% of members withdrew from the exam during the study. This may be because male IVF patients perceive this as an anxiety issue. Additionally, much did not complete the questionnaire, seen as an attempt to limit the effects of IVF-related stress. This raises concerns about the need to enroll subjects and obtain physiological recordings of mental stress in the future. Integrating the assessment of specific hormones, such as urinary cortisol and plasma testosterone, into current studies of stress and quality of sperms would clearly be beneficial.

The results of this review are somewhat restricted due to the small sample size. In addition, 23% of members withdrew from the exam during the study. This may be because male IVF patients perceive this as an anxiety issue.

In this study, IVF patients were shown to have significantly lower quality of sperms at the time of egg retrieval, suggesting a relationship between quality of sperms and psychological stress. Whether physical (frozen reserve sperm samples) or psychological (evacuation preparation, targeted morphology, treatment groups) interventions are effective in reducing stress in male IVF patients and controlling stress-induced changes in quality of sperms remains. Further studies are awaited.

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## 8. Conclusions

Male infertility is the most discussed topic among couples. It is generally believed that around half of infertility in couples is caused by the man, mainly due to frustration in the process of spermatogenesis. And there are a lot of factors which can affect the male infertility among them main two factors are life style and some medications those medications can be some anticancer medications, antidepressants, calcium channel blocker and alpha2 adrenergic agonist. Several studies have been performed and which showed somehow showed some direct and indirect relations with this kind of medication and somehow lifestyle also.

Our study found that IVF patients had significantly lower sperm quality when they collected their eggs, which suggests a link between sperm quality and psychological stress. Whether physical (frozen reserve sperm samples) or psychological (evacuation preparation, targeted morphology, treatment groups) interventions are effective in reducing stress in male IVF patients and controlling stress-related changes in sperm quality is still unknown. Further studies are awaited to light some further developments.

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## Compliance with ethical standards

### *Disclosure of conflict of interest*

No conflict of interest to be disclosed.

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