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**Impact of anabolic steroids on male fertility and the role of post-cycle therapy in recovery**

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**Abstract**

**Introduction:** AAS are a group of hormones that greatly influence the strength and size of muscle. They are widely used by athletes and bodybuilders. Yet research indicates that the use of these compounds has significant implications for male reproductive health as well.

**The aim of the study:** This study was intended to analyze systematically the relationship between AAS use and men's reproductive health; looking at both what influence AAS has on semen quality and male hormone levels and how post-cycle treatment (PCT) might help in the restoration of any adverse effects caused by AS.

**Methods:** This review was based on available data collected in the PubMed database and Google Scholar web search engine using anabolic-androgenic steroids, male fertility, hypogonadism, post-cycle therapy, and reproductive health.

**Results:** Results suggest that AAS use can lead to testicular atrophy, while research shows that anabolic steroid abuse impairs normal sperm production. These findings include aspermia, oligospermia, or aspermatogenesis. The time period for recovery of sperm quality is also different after use of anabolic steroids, and all cases are expected to have a profound impact on spermatogenesis over the long term. Anabolic steroids may suppress the HPG axis and decrease the male's fertility hormone, testosterone. If PCT is combined with hCG or SERMs, a person's own regular hormone levels return after 10 weeks with good prospects for recovery from low testosterone.

**Conclusion:** Studies show that the use of AAS seriously affects the male reproductive system and may even have long-term consequences for this function. PCT seems to offer a reasonable method for re-establishing the hormonal equilibrium and hence proving fertile offspring, which reinforces the need for careful AAS use and monitoring. Further research will be needed before any moves can be taken towards optimizing PCT regimes, in addition to the as-yet-determined long-term consequences for male fertility.

**Keywords:** anabolic-androgenic steroids, male fertility, hypogonadism, post-cycle therapy, reproductive health.

**Introduction**

Anabolic-androgenic steroids (AAS) are derivatives of testosterone that are synthetically manufactured. They are principally used by athletes and bodybuilders to improve performance [1]. In young athletes, the use of AAS has now been estimated at 14%, while among professional or amateur body builders it is up to 70% [1] [2]. These substances are widely recognized for their ability to increase muscle mass, improve physical strength and generally improve performance in sports. Anabolic steroids are now being used to try to improve athletic performance in a wide range of sports, including bodybuilding, weightlifting, powerlifting, football, baseball, track-and-field games, cycling sports, wrestling matches and mixed martial arts. The adverse effects of long-term use of anabolic steroids occur not only in terms of performance enhancement but also for health and well-being, especially male reproductive health. By binding to intracellular androgen receptors, AAS mimics the effects of testosterone, thus inhibiting the normal functioning of the hypothalamic-pituitary-gonadal axis as if exogenous testosterone were present [1].

AAS abuse can have numerous adverse effects on organs, such as the genital system. However, the physio-pathological mechanisms responsible for AAS abuse-related genital system diseases in humans are still not fully understood [1]. Studies have reported a positive correlation between AAS abuse in athletes and morphologically abnormal spermatozoa [1] [2]. Anabolic steroid-induced infertility is characterized by oligo or azoosspermia and abnormalities in sperm motility and morphology [1] [2]. The aim of this study is to evaluate the complex relationship between anabolic-androgenic steroids and male sexual function, based on many studies.

**A Closer Look at the Positive Impacts of Anabolic-Androgenic Use**

Anabolic-androgenic steroids (AAS) do have a number of positive effects and are frequently used in sports or bodybuilding as a result. AAS can lead to a dramatic increase in muscle mass, one of its most prominent features. They can even make cells amino acid production capacity more efficient [2]. The development of cellular tissue within muscles is largely due to these substances, which increase protein synthesis throughout cells. Athletes can get an extra sprint or workout in every day because endurance and strength are both increased [3]. AAS can help reduce the recovery time needed after intense physical exertion. They can alleviate muscle damage and fatigue, leading to quicker recovery and the ability to endure more frequent and intensive training sessions [4]. AAS are occasionally prescribed clinically to treat conditions that lead to muscle loss, such as cancer and AIDS. They are also used in hormone therapy for transgender men and to treat delayed puberty or loss of testicular function in males. AAS stimulates the production of red blood cells, which enhances oxygen delivery to tissues, including muscles. This improved oxygenation can enhance endurance and physical stamina [5]. Some AAS serve to burn fat, which is useful for athletes and bodybuilders alike as they try to reduce the percentage of body fat on their frames while increasing lean muscle mass. As athletes and bodybuilders use certain AAS, they often report a sense of increasing aggressiveness. This is a positive feature in any competitive sports situation [6]. Users' confidence and self-esteem may increase as well after they suddenly find their own ability to perform changed by such obvious alterations. Users willing to take on these risks in order to gain the benefits may find it essential to give careful thought to how best they can steer clear of AAS misuse and its long-term consequences for their health.

**The role of testosterone in male fertility**

Male fertility requires testosterone production. The most important functions of this hormone are to determine the development of primary sex characteristics, including genitalia and reproductive organs (secondary sex characteristics as well, such as hair distribution patterns; in adult men this hormone produces body hair.) Testosterone is made by Leydig cells in the testicles and regulated via the hypothalamus-pituitary axis. The hypothalamus secretes gonadotropin-releasing hormone (GnRH). This hormone causes the anterior pituitary to create luteinizing hormone (LH) and follicle-stimulating hormone (FSH). LH turns Leydig cells into testosterone factories as well as, meanwhile, FSH stimulates Sertoli cells toward more rapid growth for sperm-cell offspring (that is to say spermatogenesis). Conversely, in the testis, testosterone inhibits its own production of new sperm. It also turns off the hypothalamic-pituitary-gonadal axis that controls this entire process: at the hypothalamic level, the pituitary gland, and lastly, the testis itself. The low level of testosterone results in less sperm production and a lower chance of having children. However, high levels of this hormone also have hazards for fertility. [7] [8]

**Anabolic-androgenic steroids impact on the hypothalamic-pituitary-gonadal axis**

The use of testosterone supplements can have significant effects on the activity of the hypothamespituitary-gonadal (HPG) axis. AAS acts on this axis in many ways, and these encompass the following mechanisms. Initially, the HPG axis functions in a negative feedback loop fashion. The hypothalamus releases gonadotropin-releasing hormone (GnRH), directing the pituitary gland to release luteinizing hormone (LH) and follicle-stimulating hormone (FSH). LH then induces the testes to secrete testosterone, while FSH is necessary for sperm production. The concentration of testosterone in the blood provides feedback to both the hypothalamus and pituitary to govern any further production of hormones [9]. Next, after ingesting additional testosterone from their supplements, the amount of testosterone in the bloodstream will be higher. This can then be detected by the hypothalamus and acted upon accordingly. Third, high levels of testosterone cause the hypothalamus to release less GnRH. This is an important factor, because glandular balance should be maintained and overproduction avoided [10]. Lower levels of GnRH stimulation result in a decrease of both LH and FSH production, downstream from the pituitary [11]. As LH is responsible for instructing the testes to manufacture testosterone, lower levels will mean that the body now has to rely more on external sources of testosterone. But even more important than this, with declining FSH, there will naturally also be a decrease in spermatogenesis.Accordingly, this has many profound implications concerning people’s prospects for fertility: reduced FSH production can mean large reductions in both the amount of sperm and their quality. Eventually, such complete male sterility may become a common hazard of testosterone supplements. It is especially true for men who use testosterone without medical supervision to increase athletic performance. [11].

In an extensive meta-analysis, AAS consumers had statistically lower levels of luteinizing hormone, follicle-stimulating hormone, and endogenous testosterone than non-users. It was also noted that while serum gonadotropin levels returned to baseline within 13-24 weeks post-AAS use, serum testosterone levels remained lower than baseline, suggesting long-term impacts on the reproductive system and potential fertility issues. [12]

In another study, data from 6,033 patients who sought treatment for hypogonadism between 2005 and 2010 was analyzed. It found that profound hypogonadism, defined as testosterone levels of 50 ng/dL or less, was identified in 1.6% of the patients, with prior anabolic androgenic steroid exposure being the most common cause (43%). In a further survey of 382 men who already had hypogonadism, 20.9% had previously used anabolic steroids. The study substantiated that prior anabolic steroid use is a common practice among young men seeking treatment for symptomatic hypogonadism and is the most frequent cause of profound hypogonadism. [13]

The purpose of another analysis was to determine whether hypogonadism produced by anabolic-androgenic steroid abuse can be altered. In the study, 179 cases of AAS users were examined. It was found that hypogonadism was clearly diagnosed and linked selectively with AAS abuse in 168 cases. Still, of those, only 4 cases showed complete reversibility of hypogonadism with HPG axis recovery. The review concludes that AAS-induced hypogonadism is a seriously underestimated problem and that full recovery is difficult. [14]

**Post-cycle therapy and fertility**

It's possible that the HPG axis "fall" could persist for some time after a long course of testosterone supplementation. It could be a long time before the full complement of recovery from this is accomplished, and during this period, the whole thing for the patient is disrupted because there are no normal hormones being produced in their body at all. Many patients in this state will suffer irreversible or semi-fixed fertility changes due to standing still. The time it takes for PCT to be completed varies from person to person. It’s possible that some individuals may need 4-6 weeks before they’re completely done with the recovery process, while others may need 8-10 weeks before they’re fully recovered from anabolic steroid use. [15] [16] According to a study at ENDO 2023, men who stop using anabolic-androgenic steroids may be able to restore their testosterone with the use of post-cycle therapy drugs such as hCG (human chorionic gonadotropin) and selective estrogen receptor modulators (SERMs). [17] SERMs like Tamoxifen and Clomiphene Citrate are typically involved in PCT regimes. They can potently stimulate the hypothalamic-pituitary-gonadal (HPG) axis, which is often suppressed after AAS induction. These medications help stimulate natural testosterone production and keep seminiferous tubule mass in shape by reducing estrogenic negative feedback on the HPG axis. [18] Human Chorionic Gonadotropin (hCG) is used as a substitute for LH, stimulating the testes to produce testosterone and preventing testicular atrophy.

In a study that included 29 men, the research team was blind to all the measures taken. The purposes of the study were to determine whether hCG can preserve fertility and intratesticular T levels in patients taking replacement testosterone for their low T levels. Exogenous testosterone replacement therapy was given in an intramuscular injection of 200 milligrams per week. At the same time, hCG (human chorionic gonadotropin) was administered to groups of men at doses of 125 IU or 500 IU every other day, or alternatively with a placebo. It was discovered that the intra-testicular testosterone levels among the groups were significantly different. With placebo, there was a 94% drop in intratesticular testosterone. With 125 IU of hCG the reduction was only 25%. In the group receiving 250 IU of hCG, intratesticular testosterone dropped by only 7%. Interestingly, the 500 IU group showed an increase of 26%. Furthermore, it was found that the joint use of hCG and testosterone therapy could help preserve normal spermatogenesis. This result was important because it suggests that small doses of hCG may counteract the harmful consequences seen at high doses of human chorionic gonadotropin on sperm production in mammals. It is suggested by this latest research that small doses of hCG might even increase fertility among men throughout reproductive age who need testosterone replacement therapy. This line of investigation implies that such an approach will preserve, if not improve, the quantity and quality of sperm produced. [19]

The observational, prospective study was conducted at clinical sites, involving male AAS users with clinical symptoms of hypogonadic and functioning parameters such as luteotrope hormone (LH), follicle stimulating hormone (FSH), total testosterone (Tt), etc. The investigation's purpose was to examine the process of HPG axis recovery in male AAS users after 3 months off, somewhat longer, and until PCT. The study was carried out from January to August 2019. A total of 44 men were recruited, with an average age of 29 years and an average usage period reaching 6 months. Three months after cessation and PCT had passed, LH and Tt had significantly improved in most participants. However, 20.5% still had a poor recovery. It was also found that there was a clear correlation between both the duration of AAS use and the intake dose taken, as well as the type, and one's own testosterone recovery level. The level of inhibin B was suggested as a potential marker for the recovery of spermatogenic epithelium. [20]

Another study was conducted with a group of 520 patients with a confirmed history of AAS intake within 1 year of presentation. The purpose of this study was to confirm the deleterious effects of AAS abuse, monitor spontaneous recovery, and demonstrate the effects of treatment regimens on recovery. Patients were monitored for spontaneous recovery in the first 3 months; if they showed no recovery, they were randomized to undergo either continued observation or the commencement of medications. Results showed that treated patients showed faster improvement compared to non-treated patients. The study used International Index of Erectile Function (IIEF) values, hormone levels, testicular size, and semen parameters to measure recovery. 94 patients presented with infertility (18%). 61 had oligospermia and 33 had azoospermia. After treatment, only 14 (15%) patients achieved a successful pregnancy at 12 months, while all azoospermic's patients continued to have infertility at the end of the follow-up period [21].

 **Conclusion**

AAS are popular among many athletes and bodybuilders, with young people in amateur sports using them for up to 15 years. They are also common in professional sports. The consequences of AAS abuse can have systemically deleterious effects on several organs, especially the genital system. The precise mechanism that produces these effects is still not entirely clear. AAS use has been associated with serious reproductive health issues, including testicular atrophy, azoospermia and hypogonadism induced by anabolic steroids. These conditions result in oligospermia or azoospermia, and abnormalities of sperm motility and morphology. There is a variation in recovery time under these conditions. Generally, sperm quality can be expected to improve for individuals within a few months. However, a complete recovery might take as long as three years. PCT, which involves drugs such as hCG and SERMs, is used to counteract the negative effects of AAS and reestablish hormonal normalcy. Studies suggest that PCT may be effective in recovering the HPG axis as well as improving fertility outcomes. However, the efficacy of PCT varies from individual to individual, and further research is needed.

**Author Contributions**

Dorobek W.-concept, original draft preparation; Dorobek W.,Walczak D., Szerej K., Stankiewicz K., Świeczkowski- Feiz J. -writing, review and editing. All authors have read and agreed to the published version of the manuscript.

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Publicly available datasets were analyzed in this study. This data can be found here:<https://www.ncbi.nlm.nih.gov/>.

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**Conflicts of Interest**

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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