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ANABOLIC ANDROGENIC STEROIDS

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ABSTRACT

Steroids are the compounds belonging to family terpenoid lipids. Anabolic steroids are the synthetic derivatives of male hormone testosterone. The introduction of anabolic steroids has demonstrated a substantial effect on physical strength, endurance, and muscle tissue synthesis and athletic performance since the beginning of the 20th century. Anabolic steroids are more than thirty types. They promote protein anabolism. Because of their potential to enhance muscle strength and athleticism, they are traditionally abused in sports to gain an advantage over opponents. Athletes still use them to increase their physical and athletic performance and bodybuilders use them to bulk and increase in size. Anabolic steroids have been well-documented as having adverse side effects on primary and secondary sex characteristics. Females are given male attributes by steroids, while males experience sterility and erectile dysfunction. They may also lead to an increase in cholesterol and triglyceride levels, both of which are associated with a high chance of cardiovascular disease. Researches have indicated an indirect link between anabolic steroids and cardiovascular disease. Androgenic anabolic steroids have shown to alter the immune reaction by influencing lymphocyte differentiation and proliferation, natural killer cytotoxic activity, antibody production and production of certain cytokines. Anabolic steroids are also abused amongst adults who are not involved in sports for physical appearance and muscle mass. The use of anabolic steroids is a significant problem in the adolescent population, according to the National Institute of Drug Abuse. Sport's governing bodies prohibit the use of performance-enhancing drugs (PEDs) in competition and penalize athletes who test positive. Individuals who possess knowledge about the half-lives of particular drugs, dosages and cycles try to avoid detection. The procedures for screening anabolic androgenic steroids (AAS) in laboratories accredited by the World Anti-Doping Agency are comprehensive and sensitive, and are primarily based on gas chromatography- mass spectrometry, liquid chromatography -mass spectrometry. The detection of natural testosterone administration, especially in men, is increasingly being detected using carbon isotope mass spectroscopy. This present work reviews steroids in general to create awareness among adolescents so that they can improve their knowledge and follow safe practices regarding anabolic steroids.

KEYWORDS

Steroids, Anabolic steroids, Athletic performance, cardiovascular disease, sports, testosterone.

INTRODUCTION

The term "steroid" originates from cholesterol, which can be either natural or synthetic and acts as a chemically active hormone-like compound. Steroids comprise medications for reducing swelling and inflammation, like prednisone and cortisone, as well as vitamin D, and certain sex hormones such as testosterone and estradiol. Steroidal medications such as cortisone and prednisone reduce inflammation and can relieve pain.[1] Steroids form a distinct class of compounds found abundantly across all organisms, ranging from lower species in the evolutionary hierarchy to higher mammals, including humans. A specific subset of steroids plays a pivotal role in determining sex in organisms and is synthesized by the gonads in humans. The action of steroids as artificial strengtheners has been known since the early 1930s. During that period, it was discovered that testosterone was the hormone responsible for male sex characteristics and played a role in sexual maturation in young individuals. They were utilized in conditions such as "the Eunuch syndrome," sexual impotence, starvation, cryptorchidism, and for treating extensive burns.[2] Testosterone (C-19 steroid hormone), the primary androgen circulating in the testes, functions as both an active hormone and a precursor for the production of the more potent androgen, dihydrotestosterone (DHT), through 5 alphareduction (figure 1).[3] During embryonic life, androgens cause the formation of the male urogenital tract and hence are responsible for development of the tissues that serve as the major sites of androgen action in postnatal life.[4] Dihydrotestosterone (DTH) formation acts both as a general amplifier of androgen action and conveys specific function to the androgen-AR complex. The mechanism by which this specific function is mediated is unknown. The enzyme aromatase regulates the balance between androgens and estrogens by converting testosterone into estradiol (E2). Consequently, the control of E2 production by aromatase is considered crucial in the sexual development and differentiation.[5] In 1935, Ruckzika synthesized the first synthetic version of testosterone from cholesterol. Testosterone is produced by the interstitial Leydig cells located in the testes, primarily regulated by the gonadotropins secreted by the pituitary gland.[6] After secretion, testosterone is conveyed through the bloodstream to target organs and specific receptor sites. Functions directly influenced by testosterone and pertinent to athletes can be categorized into two main groups i.e. androgenic functions (related to male characteristics) and anabolic functions (constructive or muscle-building effects). Structural modifications of testosterone have been done to dissociate the anabolic from the androgenic effects and to maximize the anabolic effect and minimise the androgenic activity.[7] In the late 1930s, initial experiments conducted in Nazi Germany confirmed that steroids indeed influenced muscle development and endurance, contributing to the formation of muscle tissue and the enhancement of physical endurance.[8] Subsequently, steroids gained popularity due to their anabolic effects.[9] The use of steroids in athletic events had been steadily rising, leading to their prohibition at the 1976 Olympics and subsequent competitions. [10-12] Engaging in sports is a widely favoured activity globally. Success is frequently defined by victory, which can drive athletes to resort to performance-enhancing drugs (PEDs) in the pursuit of gaining an edge over their competitors.[13] According to the American Academy of Pediatrics (AAP), performanceenhancing drugs are substances consumed in non-pharmacological quantities with the explicit goal of enhancing athletic performance, strength, speed, endurance or altering body weight or composition. Performance-enhancing drugs encompass an array of substances such as AAS, hormone precursors, stimulants, human growth hormone (HGH), agents enhancing oxygen-carrying capacity, agents for weight control and gain.[14] Anabolic-Androgenic Steroids (AAS) are a group of synthetic compounds similar in chemical structure to the natural anabolic steroid testosterone. [15-17] "Anabolic" refers to muscle building, and "androgenic" refers to masculine characteristics. Their duration of action is typically longer than that of physiological androgens.[18] They are either produced endogenously or exogenously. Their initial development was in the late 1930s in an effort to treat hypogonadism and chronic wasting.[19] There are more than thirty types of anabolic steroids.[20] These drugs are only legally accessible through prescription to treat conditions caused by abnormally low testosterone production, which include delayed puberty and some types of impotence. They are also prescribed in the treatment of weight loss in patients with HIV infection.[21] The illegal use of anabolic steroids may involve doses that are 10 to 100 times higher than the usual prescribed dose. [22]

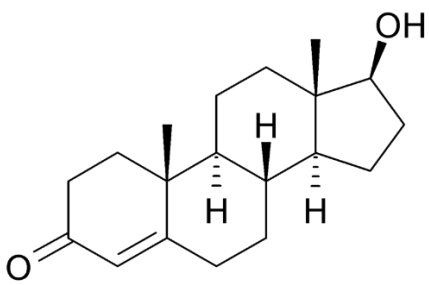

fig 1. structure of testosterone

AAS STRUCTURE

Steroids are compounds that belong to the family terpenoid lipids. They are characterised by carbonfour ring structure. Acetylo-CoA is the precursor of steroids which is also the precursor of isopentenyl pyrophosphate (IPP) and dimethylallyl pyrophosphate (DMAPP).[23] Anabolic androgenic steroids can be classified mainly into two groups ie. those with alkylation of the 17-α position with the methyl or ethyl groups or those with esterification of the 17-β-hydroxyl group.[24] Some structural modifications have been made to testosterone, In order to maximize the anabolic effect and reduce the androgenic effect (figure 2).

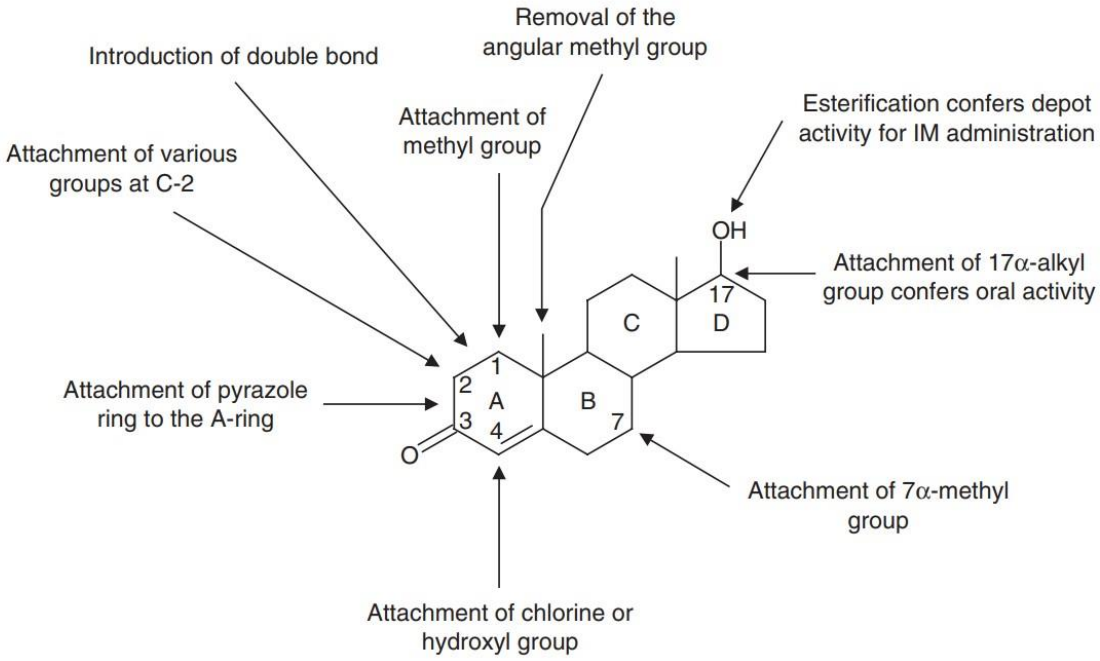

fig 2. The structure of testosterone, and structural modifications to the A- and B-rings of this steroid that increase anabolic activity; substitution at C-17 confers oral or depot activity (reproduced from Kicman and Gower,[17] with permission from the Royal Society of –Medicine). IM = intramuscular

The 17a-alkylated anabolic steroids can be made orally active by substituting the 17a-H on the steroid nucleus with a methyl or ethyl group.Alkyl substitution prevents deactivation of the steroid by first-pass metabolism by sterically hindering oxidation of the 17b-hydroxyl group. Oral action can also be conferred via a methyl group bonded to C-1. Eg: methenolone. The 17b-hydroxyl group is typically esterified with an acid moiety in parenteral formulations.[25] The parenteral preparations are esterified in order to prevent rapid absorption from the oily vehicle, usually arachis oil plus a small amount of benzyl alcohol (α-cresol). The esters include cyclohexylpropionate, decanoate, laurate and phenylpropionate for nandrolone; acetate, cypionate, decanoate, enanthate, isocaproate, phenylpropionate, propionate and undecanoate for testosterone, undecylenate for boldenone and acetate for trenbolone.[26] The mode of administration of the 17-α- is by oral route whereas 17-β is usually through injection (table 1).[27] Among the most well-known and widely used anabolic steroids are 19-Norandrostenedione, Boldenone, Stanozole, Androstenedione, and Androstenediole. 19-Dihydro-epiandrosterone and its agonists, or β2-Agonists, include clenbuterole, formoterole, salvutamole, salmeterole, tervultaline, and so forth.[28] The examples of structures of common ASS are shown in figure 3.

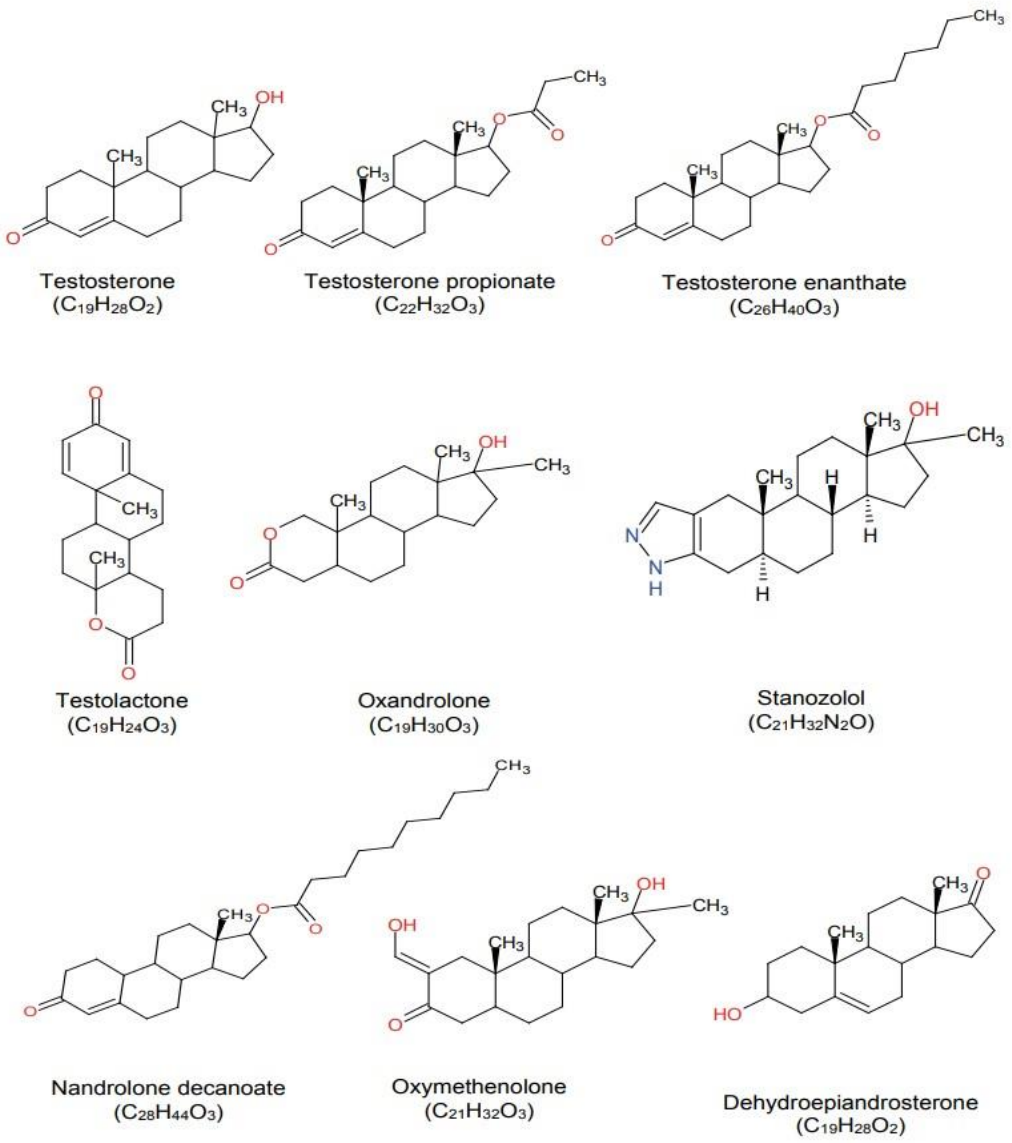

fig 3. chemical structure of testosterone and its common derivates adapted from [27]

+MECHANISM OF ACTION

AAS, being fat-soluble hormones, have the ability to permeate cell membranes and directly affect the cell nucleus. The pharmacodynamic effect of AAS initiates as the exogenous hormone penetrates the membrane of the target cell and binds to an androgen receptor (AR) located in the cytoplasm of that cell.[29] They interact with ARs across various tissues, including muscle, bone, and reproductive systems.[30] AAS are thought to exert their actions by different mechanisms. They include modifying the androgenic receptor expression as a result of a. directly affecting the topology of androgen receptor and thus subsequent interaction with co-activators and transcriptional activity and b. intracellular mechanism. Other mechanism of actions includes c. an anti-catabolic effect by interfering with glucocorticoid receptor expression and d. by genomic as well as non-genomic pathways in the CNS which results in changes in behaviour. [31-33] It forms an androgen receptor complex in the cell nucleus.[34] After binding to the androgen receptors, anabolic steroids trigger a translocation of the hormone-receptor complex to the cell nucleus, where they either alter gene expression or activate cellular signalling pathways.[35] There are two main ways that AAS affects muscle mass.[36] First, by increasing the synthesis of proteins; second, by blocking the effects of the stress hormone cortisol on muscle tissue, they shorten the recovery period and significantly lower muscle catabolism. It has been claimed that the AAS may prevent the activity of glucocorticoids, another class of steroid hormones that accelerate muscle breakdown, which would explain the decrease in muscle breakdown.[37] Anabolic steroids influence cellular differentiation, promoting the growth of muscle cells over fat-storing cells.[38] AAS show anabolic effects, such as increased appetite, greater synthesis of protein from amino acids, accelerated remodelling and growth of bone, and stimulation of bone marrow, which increases red blood cell production. AAS promotes the growth of muscle cells through a variety of processes, which increases the size of skeletal muscles and increases strength. [39-41] The molecular mechanism of androgenic anabolic steroid (figure 4).[42]

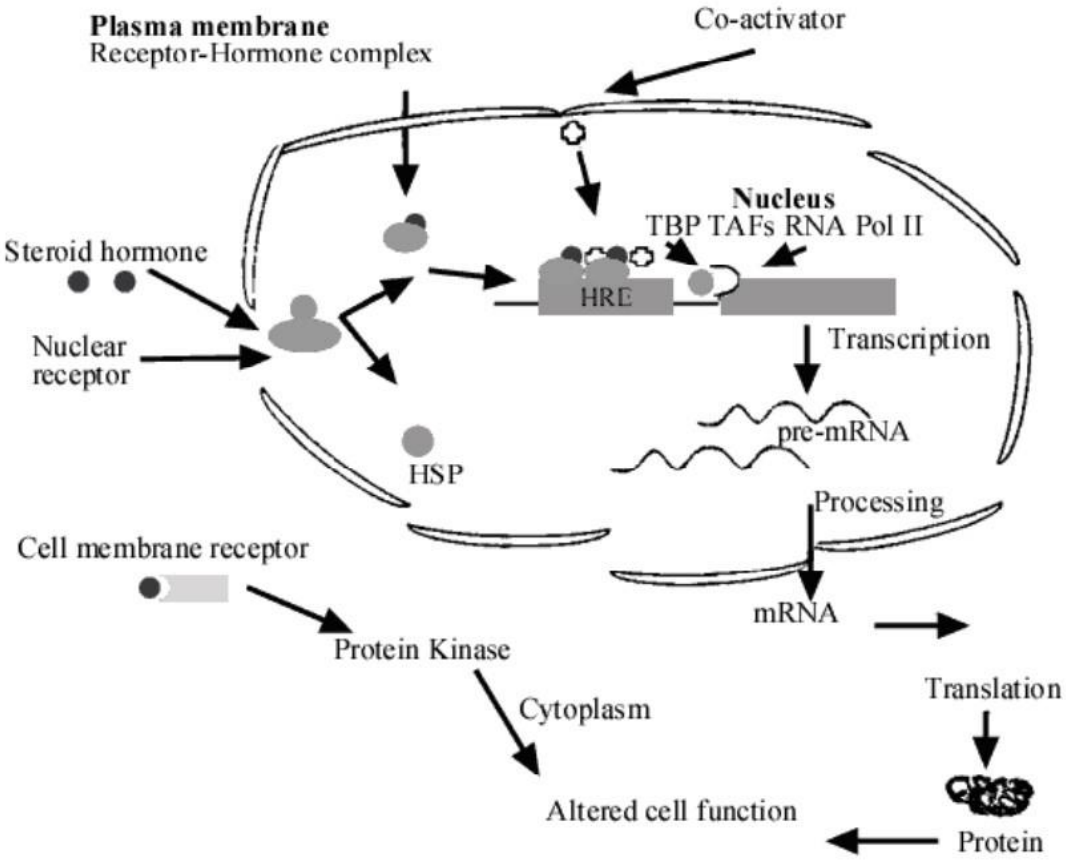

fig 4. molecular mechanism of androgenic anabolic steroids.[42]

table 1. commonly used anabolic steroids

Oral agents: drug
C-17 alkylated agents
Ethylesterenol
Fluvoxymesterone
Fluvoxymesterone
Methyltestosterone
Metandienone
Oxymetholone
Oxandrolone
Stanozolol
Injectable agents: drug
Testosterone salts: cypionate, ecanoate, enanthate, propionate, phenpropionate, isocaparoate, testosterone propionate, phenpropionate, isocaproate, decanoate
Nortestosterone
Nandrolone decanoate
Nandrolone phenpropionate
Boldenone undecylenate
Methenolone enanthate

ADVERSE EFFECTS

The broad categories of adverse medication effects associated with AS are: hepatic, cardiovascular, reproductive/endocrine, dermatological and psychiatric (table 2).

HEPATIC EFFECTS

Many factors, including the drug's formulation, route of administration, dosage, the duration of use, and idiosyncratic reactions, might cause hepatic adverse effects from AAS.[43] The C-17 alkylated anabolic steroids are more frequently linked to liver toxicity among the anabolic steroids.[44] The 17α-alkylation modification makes their use desirable for oral intake.[45] Use of AS has been linked to elevations in alkaline phosphatase, lactate dehydrogenase, alanine transaminase, and aspartate transaminase. A higher chance of increased LFT is experienced by those who use anabolic steroids.[46] Elevated liver transaminases have been linked to hepatotoxic events, which can result in acute cholestatic syndrome.[47] Abuse or usage of anabolic steroids is frequently linked to an increased risk of liver damage, tumors, hepatocellular adenomas, and peliosis hepatitis. Moreover, studies have indicated that the incidence of liver cancers is typically higher in men than in women.[48] Fatty liver diseases, chronic vascular injury etc. linked with toxicants like alcohol, and significant lipoprotein alterations have been observed with the use of AAS.[49] Hepatotoxicity caused by AAS is characterized by disruption of antioxidative components, bile acid production upregulation, and hepatocyte hyperplasia induction.[50] Although a lot of changes can be reversed by stopping, there are some effects that can worsen to the point of being extremely dangerous.

Cardiovascular effects

The adverse effects associated with AAS use are generally Myocardial infarction, cardiomyopathy and fatal arrhythmias.[51] AAS-induced cardiomyopathy can be triggered by increased heart chamber diameters, modifications to diastolic function that affect ventricular relaxation, and subclinical changes to left ventricular contractility. [51-53] The pathophysiology of ventricular arrhythmias triggered by the use of AAS has been found to involve an increase in Tp-e interval, Tp-e/QT ratio, and Tp-e/QTc ratio, with reports of sudden death.[54] The use of anabolic steroids may promote platelet aggregation, potentially by causing a reduction in prostaglandin PgI2 production by platelets or an increase in thromboxane A2 generation by them, leading to a hypercoagulable state. Additional data pointing to left ventricular dysfunction has been documented in rodent models. Eight weeks of testosterone treatment increased left ventricular stiffness and decreased cardiac function and stroke volume, according to a rat study.[55] Atherosclerosis and hypertension can also arise as a result of the altered lipid metabolism, as was previously mentioned.[56] The kind, amount, and duration of anabolic steroids taken can all affect how strong these effects are. Adverse effects seem to be reversible when the medication is stopped. [57-58] When anabolic steroids are used excessively or for extended periods of time, such as in "abuse," the risk of cardiovascular disease may rise.[59]

Reproductive effects

Administration of anabolic steroids in men causes a predictable, dose-dependent depression of luteinising hormone (LH), and follicle-stimulating hormone (FSH) via the negative feedback loop of the hypothalamic pituitary-gonadal (HPG) axis. [60-62] Administration of AS can result in hypogonadotropic hypogonadism since spermatogenesis requires LH and FSH. These physiological alterations have the following consequences: decrease in sperm density, sperm count, decreased sperm motility, abnormal sperm morphology and testicular atrophy. [63-66] This ultimately manifests as reduced libido, aggressive behaviours, and erectile dysfunction.[67]

Bodybuilders typically utilize hormones like chorionic gonadotropin (hCG) to increase the production of testicular testosterone and LH since they are aware of these effects.[68] Gynaecomastia and elevated vocal pitch are two typical complaints made by AS users. In an effort to counteract these effects, a lot of AS users self-administer tamoxifen, an antiestrogenic drug. Anabolic steroids use in women can lead to deepening of the voice, hirsutism, acne, clitoral hypertrophy, decreased breast mass, decreased menstruation, increased appetite and male pattern baldness. Despite discontinuing the causative agents, these effects may remain irreversible.[69] For men who have taken AAS excessively for less than a year, quitting use can be sufficient to bring their testosterone levels back to normal. To reestablish spermatogenesis, additional therapy with clomiphene or gonadotropin may be needed if the abuse has persisted for more than a year.[70]

ADDITIONAL ADVERSE EFFECTS

In case reports, animal studies, and controlled clinical trials, the use of AS has been associated with aggressive behaviour and mood swings. [71-72] Anabolic steroid use has been linked to increases in irritability, aggression, and arousal. This could have both positive and negative effects. Research indicates that approximately 60% of individuals using anabolic steroids report elevated levels of irritation and hostility. [73-74] Alopecia, sebaceous cysts, enlargement of the sebaceous glands, greasy hair and skin, and acne are among the skin abnormalities that are known to be brought on by AS. The alterations in the skin caused by high dosages of AS include a rise in Propionibacteria acnes, cholesterol, and free fatty acids.[75] One typical side effect of using anabolic steroids is gynecomastia. Studies have revealed a 37% incidence rate for anabolic steroid users. A benign growth of the male breast caused by an imbalance between the hormones estrogen and testosterone is known as gynecomastia. Elevated sensitivity of the breast to the level of circulating estrogen. The primary cause of men's increases in estrogen production is the aromatization of circulating testosterone. Anti-estrogens (selective estrogen receptor modulators) like tamoxifen, clomiphene, or anastrozole, a nonsteroidal aromatase inhibitor, are commonly used by anabolic steroid users to reduce the negative effects of estrogen and increase the synthesis of testosterone. When gynecomastia is identified, treatment frequently involves cosmetic surgery to address the issue. One of the more prevalent adverse effects of using anabolic steroids is acne. According to one research, 43% of users incurred acne as a result of using androgens. Approximately 61% of users report changes in libido as the most frequent adverse event in a small sample of anabolic steroid users.[76]

System	Effects
Cardiovascular	Increased total cholesterol
	Increased low-density lipoprotein
	Decreased high-density lipoprotein
	Hypertension
	Myocardial ischemia
	Cerebrovascular accidents
Male reproductive	Abnormal spermatogenesis
	Impotence
	Testicular atrophy
	Gynecomastia
	Priapism
	Prostatic hypertrophy
	Prostate cancer
Female reproductive	Menstrual irregularities
	Hirsutism
	Clitoromegaly (irreversible)
	Deepening voice (irreversible)
	Male-pattern baldness
	Uterine atrophy
	Breast atrophy
Musculoskeletal	Premature physeal arrest
	Increased risk of tendon or muscle injury
Liver	Elevated liver function tests
	Hepatocellular carcinoma
	Hepatoadenoma
Skin	Acne
	Striae
Psychological	Mood swings
	Aggressive behavior
	Depression
	Addiction
	Withdrawal

table 2. adverse effects of anabolic- androgenic steroids. [77-78]

CONCLUSION

Results from research involving both humans and animals indicate that supratherapeutic doses of AAS not only cause discernible improvements in performance but also able to cause negative side effects on the immune system as well as a number of other body systems. Depending on the severity and length of AAS usage, these effects could be severe and protracted. It would be ideal to utilize a double-blind, placebo-controlled experimental model to assess the effects of AAS misuse. Nevertheless, participants would be exposed to supratherapeutic amounts of different AAS, which could be harmful to their health. The adverse effects of anabolic steroids can be quite harmful to the body and the mind. Because they can halt growth and create lasting changes to a woman's voice and genitalia in females, they may be more hazardous in young adults. People who quit using these medicines may experience extreme melancholy and irritability. Anabolic steroids are testosterone derivatives that have stronger anabolic and less virilizing effects. These effects include muscular growth and androgenic, or masculinizing, effects. It is well established that anabolics and corticosteroids affect numerous physiological systems in different ways. These impacts have a wealth of evidence; however, the precise mechanics are yet unclear. We have evaluated the current body of knowledge regarding the effects of anabolics on the musculoskeletal and cardiovascular systems in this work. It is commonly known that while the recipient may benefit from short-term effects, longterm impacts can have a wide range of negative side effects and can be harmful. The dual nature of the respective receptors that regulate gene expression is primarily responsible for the problematic nature of steroids.

Physicians should emphasize to their patients that even while athletes take AS more frequently than others, the long-term implications are not well-established, thus caution is advised. This means that the clinician must read as much as they can about AS by looking through both medical and popular media sources. Doctors must advise patients who use AS to stay away from these agents in order to reduce any potential health hazards and advise them that the effects of these agents on general health have not been thoroughly researched.

Adults use them for muscle building even if they are aware of their detrimental effects because adults don't know enough about anabolic steroids, hence public health campaigns are needed to raise awareness about steroid use is safe. This review was not meant to encourage or endorse the usage of anabolic steroids. Instead, the goal was to talk about relevant medical topics and offer another viewpoint given that many users of anabolic steroids don't seem to prioritize the risks to their health and safety or the possibility of unfavourable medical outcomes.

REFERENCES

1. Hill, J. A., Suker, J. R., Sachs, K., & Brigham, C. The athletic po1ydrug abuse phenomenon. American Journal of Sports Medicine, 2007:; 8(4): 269-271.
2. Strauss RH, et al. Anabolic steroids in the athlete. Annual review of medicine 1991;42:449-57.
3. Wilson JD, Leihy MW, Shaw G, et al. Androgen physiology: unsolved problems at the millennium. Mol Cell Endocrinol 2002; 198: 1-5
4. Bruchovsky N, Wilson JD. The conversion of testosterone to 5-alpha-androstan-17-beta-ol-3-one by rat prostate in vivo and in vitro. J Biol Chem 1968; 243: 2012-21
5. Kroon FJ, Munday PL, Westcott DA, et al. Aromatase pathway mediates sex change in each direction. Proc Biol Sci 2005; 272: 1399-405
6. Ruckzika L, Wettstein A, Kaegi H, et al. Sexual hormone VIII Darstellung von Testosterone unter Anwendung gemischter Ester. Helv Chim Acta 1935; 18: 1478
7. Di Pasquale MG. Anabolic steroid side-effects: facts, fiction and treatment. Warkworth (ON): MGD Press, 1990
8. Sullivan ML, et al. The cardiac toxicity of anabolic steroids. Progress in cardiovascular diseases 1998;41(1):1-15.
9. Landry GL, et al. Anabolic steroid abuse. Advances in pediatrics 1990;37:185-205.
10. Beckett AH, et al. Misuse of drugs in sport. British journal of sports medicine 1978;12(4):185-94.
11. Loughton SJ, et al. Human strength and endurance responses to anabolic steroid and training. The Journal of sports medicine and physical fitness 1977;17(3):285-96.
12. Wilson JD. Androgen abuse by athletes. Endocrine reviews 1988;9(2):181-99.
13. Castillo EM, Comstock RD. Prevalence of use of performance-enhancing substances among United States adolescents. Pediatr Clin North Am. 2007;54(4):663–675.
14. Gomez J; American Academy of Pediatrics Committee on Sports Medicine and Fitness. Use of performance-enhancing substances. Pediatrics.
15. Haupt HA, Rovere GD. Anabolic steroids: a review of the literature. Am J Sports Med 1984; 12: 469-84 [121]
16. Shahidi NT. A review of the chemistry, biological action, and clinical applications of anabolicandrogenic steroids. ClinTher 2001; 23: 1355-90
17. Kicman AT, Gower DB. Anabolic steroids in sport: bio-chemical, clinical and analytical perspectives. Ann Clin Bio-chem 2003; 40: 321-56
18. No authors listed. Adolescents and anabolic steroids: a subject review. American Academy of Pediatrics. Committee on Sports Medicine and Fitness. Pediatrics 1997; 99(6): 904-8.
19. Hoberman J., Yesalis C., The history of synthetic testosterone, Scientific American 1995, 272, 7681
20. Shodganga. Introduction to anabolic steroids. [Internet].2015[cited 2017 february10]. Available from shodganga inflibnet.ac.in/bitstream/10603/32011/10/5%/20introduction .pdf.

21. Wilson JD. Androgen abuse by athletes. Endoc Rev 1988; 181-99.

22. FNP Davis Kathleen. Anabolic steroids: what you should know [internet]. 2016 [cited 2018 April 22]. Available from https://www.medical news today.com/article/246373.php.

23. Grochowski LL, et al. Methanocaldococcus jannaschii uses a modified mevalonate pathway for biosynthesis of isopentenyl diphosphate. Journal of bacteriology 2006;188(9):3192-8.

24. Hameed A., Brothwood T., Bouloux P., Delivery of testosterone replacement therapy, Curr. Opin. Invest. Drugs, 2003, 4, 1213-1219

25. van der Vies J (1993). Pharmacokinetics of anabolic steroids. WienMed Wochenschr 143: 366368.

26. Coert A, Geelen J, de Visser J, van der Vies J (1975). The pharmacology and metabolism of testosterone undecanoate (TU), a new orally active androgen. Acta Endocrinol (Copenh) 79:789–800.

27.Kuhn C.M., Anabolic Steroids, Recent. Prog. Horm. Res., 2002, 57, 411-434

28. Brodsky IG, et al. Effects of testosterone replacement on muscle mass and muscle protein synthesis in hypogonadal men--a clinical research center study. The Journal of clinical endocrinology and metabolism 1996;81(10):3469-75

29. Lavery DN, McEwan IJ (November 2005). "Structure and function of steroid receptor AF1 transactivation domains: induction of active conformations". The Biochemical Journal. 391 (Pt 3): 449–464. doi:10.1042/BJ20050872. PMC 1276946. PMID 16238547.

30. Heinlein CA, Chang C (April 2004). "Androgen receptor in prostate cancer". Endocrine Reviews. 25 (2): 276–308. doi:10.1210/er.2002-0032. PMID 15082523. S2CID 24665772.

31. Cato AC, Nestl A, Mink S (2002). Rapid actions of steroid receptors in cellular signaling pathways. Sci STKE 2002: RE9.

32. Heinlein CA, Chang C (2002a). The roles of androgen receptors and androgen-binding proteins in nongenomic androgen actions. Mol Endocrinol 16: 2181–2187.

33. Losel RM, Falkenstein E, Feuring M, Schultz A, Tillmann HC, Rossol-Haseroth K et al. (2003). Nongenomic steroid action: controversies, questions, and answers. Physiol Rev 83: 965–1016.

34. Horton R., Markers of peripheral androgen action in vivo and in vitro, Clin. Dermatol., 1988, 6, 46 51

35. Riggs BL, Khosla S, Melton LJ (June 2002). "Sex steroids and the construction and conservation of the adult skeleton". Endocrine Reviews. 23 (3): 279–302. doi:10.1210/edrv.23.3.0465. PMID 12050121. S2CID 28160750.

36. Brodsky IG, Balagopal P, Nair KS (October 1996). "Effects of testosterone replacement on muscle mass and muscle protein synthesis in hypogonadal men--a clinical research center study". The Journal of Clinical Endocrinology and Metabolism. 81 (10): 3469–3475.
doi:10.1210/jcem.81.10.8855787. PMID 8855787.

37. Hickson RC, Czerwinski SM, Falduto MT, Young AP (June 1990). "Glucocorticoid antagonism by exercise and androgenic-anabolic steroids". Medicine and Science in Sports and Exercise. 22 (3): 331– 340. doi:10.1249/00005768-199006000-00010. PMID 2199753.

38. Azziz R, Carmina E, Dewailly D, Diamanti-Kandarakis E, Escobar-Morreale HF, Futterweit W, et al. (February 2009). "The Androgen Excess and PCOS Society criteria for the polycystic ovary syndrome: the complete task force report". Fertility and Sterility. 91 (2): 456–488. doi:10.1016/j.fertnstert.2008.06.035. PMID 18950759.

39. Schroeder ET, Vallejo AF, Zheng L, Stewart Y, Flores C, Nakao S, et al. (December 2005). "Six-week improvements in muscle mass and strength during androgen therapy in older men". The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences. 60 (12): 1586–1592.
doi:10.1093/gerona/60.12.1586. PMID 16424293.

40.Grunfeld C, Kotler DP, Dobs A, Glesby M, Bhasin S (March 2006). "Oxandrolone in the treatment of HIV-associated weight loss in men: a randomized, double-blind, placebo-controlled study". Journal of Acquired Immune Deficiency Syndromes. 41 (3): 304–314.
doi:10.1097/01.qai.0000197546.56131.40. PMID 16540931. S2CID 25911263

41. Giorgi A, Weatherby RP, Murphy PW (December 1999). "Muscular strength, body composition and health responses to the use of testosterone enanthate: a double blind study". Journal of Science and Medicine in Sport. 2 (4): 341–355. doi:10.1016/S1440-2440(99)80007-3. PMID 10710012. 42. Kicman A.T., Pharmacology of anabolic steroids, Br. J. Pharmacol., 2008, 154, 502-521

43. Zheng E, Sandhu N, Navarro V. Drug-induced liver injury secondary to herbal and dietary supplements. Clin Liver Dis. 2020;24(1):141–155. doi:10.1016/j.cld.2019.09.009

44. Ishak KG, Zimmerman HJ. Hepatotoxic effects of the anabolic/androgenic steroids. Semin Liver Dis 1987; 7: 230-6

45. Park J, Mcllvain V, Rosenberg J, Donovan L, Desai P, Kim JY. The mechanisms of anabolic steroids, selective androgen receptor modulators and myostatin inhibitors. Korean J Sports Med. 2022;40(2):67–85. doi:10.5763/kjsm.2022.40.2.67

46. Haupt HA, Rovere GD. Anabolic steroids: a review of the literature. Am J Sports Med 1984; 12: 469-84

47. Wu S, Daston G, Rose J, et al. Identifying chemicals based on receptor binding/bioactivation/mechanistic explanation associated with potential to elicit hepatotoxicity and to support structure activity relationship-based read-across. Curr Res Toxicol. 2023;5:100108. doi:10.1016/j. crtox.2023.100108

48. El-Serag, H.B. (2004) Hepatocellular carcinoma: recent trends in the United States. Gastroenterology 127,S27-S34.

49. Kafrouni MI, Anders RA, Verma S. Hepatotoxicity associated with dietary supplements containing anabolic steroids. Clin Gastroenterol Hepatol. 2007;5(7):809–812. doi:10.1016/j.cgh.2007.02.036

50. Albano GD, Amico F, Cocimano G, et al. Adverse effects of anabolic-androgenic steroids: a literature review. In: Healthcare. Vol. 9. MDPI; 2021:97

51. Kennedy MC, Lawrence C. Anabolic steroid abuse and cardiac death. Med J Aust. 1993;158(5):346–348. doi:10.5694/j.1326-5377.1993. tb121797.x

52. Fadah K, Gopi G, Lingireddy A, Blumer V, Dewald T, Mentz RJ. Anabolic androgenic steroids and cardiomyopathy: an update. Front Cardiovasc Med. 2023;2023:10.

53. Torrisi M, Pennisi G, Russo I, et al. Sudden cardiac death in anabolic-androgenic steroid users: a literature review. Medicina. 2020;56(11):587. doi:10.3390/medicina56110587

54. Elitok A, Öz F, Panc C, et al. Acute effects of Red Bull energy drink on ventricular repolarization in healthy young volunteers: a prospective study. Anatol J Cardiol. 2015;15(11):919. doi:10.5152/akd.2015.5791

55. LeGros, T., McConnell, D., Murry, T., Edavettal, M., Racey-Burns, L.A., Shepherd, R.E. and Burns,

A.H. (2000) The effects of 17 α-methyltestosterone on myocardial function in vitro. Medicine and Science in Sports and

Exercise 32, 897-903.

56. Novák J, Bienertová-Vašků J, Kára T, Novák M. MicroRNAs involved in the lipid metabolism and their possible implications for atherosclerosis development and treatment. Mediators Inflamm. 2014;2014:1–14. doi:10.1155/2014/275867

57. Dhar, R., Stout, C.W., Link, M.S., Homoud, M.K., Weinstock, J. and Estes, N.A. III. (2005)

Cardiovascular toxicities of performance-enhancing substances in sports. Mayo Clinic

Proceedings 80, 1308-1315.

58. Parssinen, M. and Seppala, T. (2002) Steroid use and long-term health risks in former athletes. Sports Medicine 32,

83-94.

59. Tikkanen, H.O., Hamalainen, E., Sarna, S., Adlercreutz, H. and Harkonen M. (1998) Associations between skeletal muscle properties, physical fitness, physical activity and coronary heart disease risk factors in men. Atherosclerosis 137, 377-389. Tikkanen, H.O., Harkonen, M. and Naveri, H. (1991) Relationship of skeletal muscle fiber type to serum high density lipoprotein cholesterol and apolipoprotein A-I levels. Atherosclerosis 90, 48-57.

60. Gill GV. Anabolic steroid induced hypogonadism treated with human chorionic gonadotropin. Postgrad Med J 1998; 74:45-6

61. Jarow JP, Lipshultz LI. Anabolic steroid-induced hypogonadotropic hypogonadism. Am J Sports Med 1990; 18: 429-31

62. MacIndoe JH, Perry PJ, Yates WR, et al. Testosterone suppression of the HPT axis. J Invest Med 1997; 45: 441-7

63. Yesalis CE, Bahrke MS. Anabolic-androgenic steroids: currenttissues. Sports Med 1995; 19: 326-40

64. Hickson RC, Ball KL, Falduto MT. Adverse effects of anabolic steroids. Med Toxicol Adverse Drug Exp 1989; 4: 254-71

65. Holma PK. Effects of an anabolic steroid (metandienone) on spermatogenesis. Contraception 1977; 15: 151-62

66. Yates WR, Perry PJ, MacIndoe J, et al. Psychosexual effects of three doses of testosterone cycling in normal men. Biol Psy- chiatry 1999; 45: 254-60

67. Rahnema CD, Lipshultz LI, Crosnoe LE, Kovac JR, Kim ED. Anabolic steroid–induced hypogonadism: diagnosis and treatment. Fertil Steril. 2014;101(5):1271–1279.
doi:doi:10.1016/j.fertnstert.2014.02.002

68. Duchaine D. Underground steroid handbook II. Venice (CA): HLR Technical Books, 1989

69. Straus RH, Liggett MT, Lanese RR. Anabolic steroid use and perceived effects in ten weight-trained women athletes. JAMA 1985; 253: 2871-3

70. Mullen C, Whalley BJ, Schifano F, Baker JS. Anabolic androgenic steroid abuse in the United Kingdom: an update. Br J Pharmacol. 2020;177 (10):2180–2198. doi:10.1111/bph.14995

71. Conacher GN, Workman DG. Violent crime possibly associated with anabolic steroid use. Am J Psychiatry 1989; 146: 67944.

72. Pope Jr HG, Katz DL. Affective and psychotic symptoms associated with anabolic steroid use. Am J Psychiatry 1988; 145:487-90

73. Pope, H.G., Kouri, E.M. and Hudson, J.I. (2000) Effects of supraphysiologic doses of testosterone on mood and aggression in normal men. Archives of General Psychiatry 57, 133-140.

74. Silvester, L.J. (1995) Self-perceptions of the acute and long-range effects of anabolic-androgenic steroids. Journal of Strength and Conditioning Research 9, 95-98.

75. Blue JG, Lombardo JA. Steroids and steroid-like compounds. Clin Sports Med 1999; 18: 667-89

76. O'Sullivan, A.J., Kennedy, M.C., Casey, J.H., Day, R.O.,

Corrigan, B. and Wodak, A.D. (2000) Anabolic androgenic steroids: Medical assessment of present, past and potential

users. Medical Journal of Australia 173, 323-327.

77. Silver MD. Use of ergogenic aids by athletes. J Am Acad Orthop Surg.

2001;9(1):61–70.

78. Henderson LP, Penatti CA, Jones BL, Yang P, Clark AS. Anabolic androgenic steroids and forebrain GABAergic transmission. Neuroscience 2006;138(3):793–799.