Equine Communications

A digest of clinical notes and letters.

Letters may include preliminary communications discussing recent developments, first observations of a new disease, a new pathological finding, or any other brief article or case history of outstanding importance or general interest.

Practical review articles and case histories should be written to provide instructive information on a particular technique, disease, or condition that will be relevant for the equine veterinarian in practice.

"Equine Communications" is intended to complement the Journal's editorial and to open the lines of communication among the equine practitioners. Your frequent participation is encouraged. All contributions will be promptly acknowledged.

Pharmacology Review: The Anabolic Steroid Androgen Group of Drugs—Tom Tobin, D.V.M., Ph.D., Kentucky Equine Drug Research Program, Department of Veterinary Science, University of Kentucky, Lexington, KY

Everyone is familiar with the marked changes which occur in the human male at about the time of puberty. During this period the male increases in height, shows increased muscle development, thickening of bones, and the changes in voice, hair pattern, and aggressiveness which are associated with the adult male. All these effects are due to increased secretion by the testis of the androgenic[a] or "male-making" hormones.

The androgens, of which testosterone is the primary example, produce both the increase in bone and muscle mass (the anabolic effect) and changes in the secondary sexual characteristics, such as changes in voice, crest, biting, and aggressiveness of the stallion. These changes in secondary sexual characteristics are known as the androgenic actions.[1]

Because the anabolic effect, as a simple increase in muscle mass, was relatively easy to measure and it appeared that there might be a good market for a pure anabolic drug, research chemists working in various drug companies modified the natural testosterone molecule in attempts to produce such a pure anabolic drug. Various groups succeeded to varying degrees in separating the body building from the androgenic effects, but none was completely successful. Therefore, all the anabolic steroids on the market today retain some of the androgenic action of the original testosterone molecule, and it is this residual androgenic action which gives rise to many of the side effects of this group of drugs. It is also appropriate to mention at this point that very little work has been done on anabolic steroids in the horse and that most of the work reported here is derived from experience in humans or experimental animals.[1]

The most clear-cut and easily demonstrated action of the androgens is to increase an animal's production of red blood cells and thus its hematocrit.[4] In most species the entire male usually has a higher hematocrit than the female, and the hematocrit of the castrated male is lowest of all. Testosterone injection in the castrated male can produce up to a 20% increase in the red blood cell count. This effect also occurs in the female, and to a lesser extent in the entire male, which, of course, already has considerable circulating testosterone. Nevertheless, the effect of the androgen-anabolic steroid group on erythropoesis is sufficiently clear-cut to render them the drugs of choice in most forms of anemia, and in human medicine they are considered the most useful nonspecific stimulants of red blood cell formation.[4,7]

The anabolic steroids also have very clear-cut effects on bone growth but must be used with care. They act to increase the retention of calcium in bones,[1,2] giving rise to thicker bone and greater growth if the epiphyseal plates have not closed.[2] However, large quantities of testosterone or anabolic steroids early in life can hasten closure of the epiphyseal plates at which growth occurs and thus prevent further growth in length of these bones. In the human, eunuchs[b] always grow somewhat taller than the normal male because their lack of testosterone delays closure of their epiphyseal plates.[7] Therefore, any use of the androgen-anabolic steroid group in young horses before closure of the epiphyseal plates carries with it the danger of accelerating closure of these plates and preventing further growth.

The effects of the androgen-anabolic steroid group of drugs on muscle mass and athletic performance is also a hotly argued area. The simplest and perhaps the purest use of the anabolic or muscle building action of these drugs is in the body building field. At a recent "Mr. America" contest in Detroit, one of the former Mr. America's, Mr. John Grimek, estimated that somewhere between 99% and 100% of the entrants in the contest had experimented with this group of drugs, and that a high proportion of the competitors were using these drugs in massive doses. Other estimates suggest that 80-90% of weight lifters use these drugs, about 75% of football players, and about 33% of athletes in general.[8] It seems that the body builders at least know exactly what they are doing, for most of the scientific work to date supports their conviction that the anabolic steroids produce considerable increases in muscle mass and body weight.[1]

[a] From the Greek, *andros* = man + *gen* = make

[b] Eunuch — male castrates, traditionally caretakers in a Sultan's harem

While the anabolic drugs may produce clear-cut increases in muscle mass, whether or not this increase in muscle mass is accompanied by increased or improved performance has been questioned. Some scientists hold that the increased muscle mass is simply due to increased fluid retention and that no increase in muscle power occurs.[1] Other studies have shown that when the anabolic steroids are combined with a high protein diet and vigorous training, an increase in muscle strength does occur. The weight of the reports and the experience (and conviction) of the athletes who use them seem to suggest that athletes who use the anabolic steroids and who train and diet accordingly may expect to increase their body weight up to 5% and their muscle strength up to 18%.[11]

Very closely interwoven with the effects of the androgen-anabolic steroids on body mass and performance are their psychological effects. Thus, the androgen-anabolic steroid group act to produce a marked feeling of well-being and confidence, and they also increase appetite and are important in the development of characteristic male aggressive behavior. The relationship of testosterone to aggressiveness had long been suspected, and one of the first reported uses of androgens to improve performance occurred during W.W. II, when German troops were supposedly given testosterone injections before battle to enhance their aggressiveness.[8] How much these psychological effects on mood, aggressiveness, and confidence influence athletic performance is not clear, but a strong feeling exists among athletes and trainers that anabolic steroids are a great help to the mediocre performer, giving him "winner's" confidence along with the will to win. There is no reason to suppose that these psychological effects do not occur in animals and that they are not equally significant.

The side effects of the anabolic steroids largely depend on the fact that none of these compounds is a pure anabolic agent and are related to their residual androgenic action. Thus, in young, growing horses premature epiphyseal closure would seem to be the most serious problem. In this regard, oxandrolone has been reported to favor bone growth over epiphyseal maturation. Another somewhat less serious problem would be the tendency of the increased body weight to produce epiphysitis. Rooney[9] has outlined how muscular young Quarter Horses are predisposed to this problem, and the anabolic steroids could presumably produce the same effect simply by increasing the body mass of young horses above that which their forming bones can carry. For mature horses, a possible problem suggested by some authors is that the increase in muscle mass may occur without a corresponding increase in bone strength. Since the weakest point in any tendon is its point of insertion into bone, an increased risk of bone:tendon rupture appears to be a possibility. Other possible problems in fillies involve overt masculinization and interference with future breeding performance due to the androgenic action remaining in most anabolic steroids. However, none of the data from human females suggests the likelihood of irreversible effects on the fertility of fillies.

A paradoxical effect of the androgen-anabolic steroid group of drugs in the male is that they act to reduce sex drive, potency (the ability to maintain an erection), testicle size, and sperm count.[3] Thus the animal or the athlete on anabolic steroids possesses all the muscle mass and secondary sexual characteristic of a super male, except that his sexual performance is likely reduced. The reason for this paradoxical effect is that testosterone produced in the testicle is the signal that tells the brain that all is well and functioning in the testicle and surrounding areas. Thus, when high levels of the anabolic steroids come in the blood to the brain, the brain assumes that the testicle is overproducing testosterone and commands (through the gonadotrophins) the testicle and associated departments to cease and desist for a while. The upshot of this is that if the dosage of the androgen-anabolic steroid is maintained the testicle shrinks and sex drive, potency, and fertility are lost.

This effect of high doses of androgen-anabolic steroids has been a problem for some human athletes on the anabolic steroids, and what may be a related condition has been seen in horses. Since 1970, in the Kentucky area, there has been a large increase in the number of immature germ cells seen in stallion semen samples submitted to our department for analysis. Recently, the accidental death of one of these stallions gave a colleague[10] the opportunity to microscopically examine the testes of one of these horses. In this particular animal the testes showed focal areas of degeneration and loss of ability to form normal spermatozoa. This condition has existed for at least 3 years in the particular horse in question. The cause of this irreversible effect on the testicles and spermatogenesis in these stallions is not known, but the anabolic steroids must be prominent among the possible causes.

The only group of anabolic steroids with toxic effects not directly related to their androgenic action are the methyl-substituted anabolic steroids. These methylated derivatives were introduced to prolong their action in the body but have wound up producing a number of slowly developing and quite serious liver toxicities. The simplest of these include mild hepatitis and an inability of the liver to eliminate bile. A more serious effect associated with this group of drugs is the induction of precancerous liver changes, which return to normal if their administration is stopped. If administration continues, liver cancer can appear after a number of years.[5] Because non-methylated anabolic steroids apparently do not produce these hepatic effects, use of the methylated steroids should be avoided in all species.

A more satisfactory mechanism of prolonging the action of this group of drugs is to esterify the compound and suspend it in oil, and this is the type of anabolic steroid now in use. The

nature of the ester group determines the duration of action. Some of these derivatives are quite long acting and may only require administration at intervals of up to 1 month.[1,6]

At the moment, to my knowledge, no racing jurisdiction in the United States is testing for anabolic steroids, but in the spring of 1976, testing started in England, and disciplinary action was taken against a number of trainers. The basis for the screening test against the anabolic steroids is called a "radioimmunoassay" (R.I.A) and depends on binding of the anabolic steroid in urine to a specific antibody. While these tests are highly sensitive, they are not specific. Any anabolic steroid, metabolite of an anabolic steroid, or even testosterone itself could give rise to a positive test. For this reason, RIA assays in no way identify the drug administered, and RIA data alone should not be taken as evidence of anabolic steroid administration. The International Olympic Committee requires definitive identification of all drugs before invoking disciplinary action, and for this gas chromatographic-mass spectrometric analysis is required. The absolute sensitivity of the mass spectrometer is not clear, but the Race Course Security Services Laboratory in England reports being able to detect nor-testosterone in urine by radioimmunoassay for up to 44 days after the administration of 200 mg of 19 nor-testosterone laureate intramuscularly.[6] This is a very long time to be able to detect the effects of a relatively small dose of drug, and the only question which remains is how long after administration its presence can be confirmed by mass spectrometry.

The length of time for which the presence of an anabolic steroid can be confirmed in urine is critical. For instance, it is possible for a horse or other athlete to be on steroids until 2 to 3 weeks before an event. The anabolic steroids can then be discontinued, but the horse will still have the increased bone and muscle mass for the competitive event. The critical question then becomes which declines more rapidly, the drug's anabolic effect or the chemist's ability to identify and confirm the drug? At the moment, we do not have the answer to this question.

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Hoof Wall Repair Using 10X—William Moyer, D.V.M., Willowdale Veterinary Centre, Kennett Square, PA

Introduction

Hoof wall cracks and defects are common occurrences in equine practice. Fortunately, for most horses (for a variety of reasons) the degree of damage is such that the defect is of questionable significance. For those horses, however, with deep and/or painful hoof wall problems or for those being asked to compete regularly, the importance is greater. The therapeutic measures vary with the nature of the damage and the type and timing of the work the patient is being asked to perform. In those cases requiring a hoof wall restoration, a multitude of available products exist (fiberglass, methylmethacrylates, rubber, metallic implants, etc.). Each of the above has certain drawbacks which limit its use, such as difficulty in use, poor bonding with the hoof wall, volumetric shrinkage during cure, poor strength, slow cure, possible tissue damage, and being generally nonphysiological.

A recently introduced product, known as 10X,[a] answers all of the previously mentioned shortcomings. The product was a spin off of research, still in process, on "glue-on" horseshoes. It has, to date, been applied to a variety of problems (quarter, heel, and toe cracks; major and minor hoof wall avulsions; as a follow up to "seedy toe" repair on patients with chronic third phalanx rotation) and has been tested on horses under a variety of circumstances and weather conditions. We have employed it with success on horses performing various types of work: flat and harness racing, steeple chasing, 3-day eventing, show jumping and hunting, endurance riding, and various pleasure pursuits.

[a] 10X, produced and distributed by Farriers Inc., Unionville, PA 19375.