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Topic: Breeding, Drugs, and Breakdown: The State of Thoroughbred Horse Racing and the Welfare of Thoroughbred Racehorse

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Regulation of Anabolic Steroids and Androgenic Steroids in Racing Horses in the State of Pennsylvania

Introduction and Background

Anabolic steroids are synthetic derivatives of the male hormone, testosterone, that have been modified for promoting protein synthesis, muscle growth, alter fat/muscle ratio and increase red blood cell numbers [1]. These agents can exert strong effects on the body that may be beneficial for athletic performance [2]. Androgenic steroids, on the other hand, are naturally occurring steroids, such as testosterone and nandrolone, that are produced by the non-castrated male horse (stallions) and estrogen by the female horse. Published information is available on human subjects that suggest improvement in the strength skills following the administration of anabolic steroids [3-7]. The lack of well structured double-blind studies have led some to concluded that anabolic steroids do not increase muscle size or strength in males with normal hormonal function and have discounted positive results as unduly influenced by biased expectations of athletes, inferior experimental design, poor data analysis, or at best, inconclusive results [4,8,9]. On the other hand, the perception of the public and anecdotal information on dramatic changes in athletic performance have led the public to view the administration of anabolic steroids as cheating and enhancing performance beyond the athletes' natural ability. This perception is in all sports, including horse racing, and the administration of anabolic steroids to some horses violates the concept of a level playing field and risks the health and welfare of the horse.

Effects of Anabolic Steroids

Anabolic steroids have been extensively employed in equine racing over the past 25 years. Many practicing veterinarians attest to the gains in physical strength, stamina, and mental attitude when anabolic steroids are used in performance horses that have gone off-feed, and have a "stale" or "sour" attitude. This may be a substitute for more comprehensive veterinary care. Many may feel that the horse may be at a competitive disadvantage and thus, are administered steroids because others in racing do so. The improvement in athletic performance may be the result of change in behavior and aggressiveness more so than any specific effects on the

physiological parameters that affect performance. Behavioral effects following the administration of anabolic and androgenic steroids have been supported by a number of studies. In female horses, the injection of the male hormone, testosterone, eventually caused total suppression of all reproductive activity and the development of stallion-like behavior and aggression [10]. Following the administration of anabolic steroids to geldings and mares, components of stallion behavior have been described, characterized by teasing, mounting and aggressive behavior toward other horses [11-13]. The administration of testosterone to the gelded horse will dramatically alter its behavior. Current veterinary pharmacology text books do not discuss anabolic steroids from a therapeutic point of view, but only from the legal control aspects [14].

Studies Conducted on Anabolic Steroids in the Commonwealth of Pennsylvania

The impetus for the study of anabolic and androgenic steroids in racing horse in the Commonwealth of Pennsylvania was the common knowledge of their use and the observations by the Commission Veterinarians of pre-race aggressive behavioral problems in many horses coming to the paddock. Analytical methods were developed for the detection, quantification and confirmation of anabolic and androgenic steroids in plasma, and the methods was published in 2005 and 2006 [15,16]. Results from the analysis of plasma samples from winning horses in 2003 confirmed the extensive use of anabolic and androgenic steroids in that better than 60% of the horses racing in PA at that time were competing with a plasma concentration of an anabolic steroid and, in some cases, more than one steroid. The 3 most commonly found steroids in that study were boldenone, stanozolol, and testosterone. Studies were also conducted on the pharmacokinetics (elimination from the body) of 2 of the most commonly used anabolic steroids boldenone and stanozolol [17].

To date, the United States and Canada appear to be the only countries with horse racing that historically have not sanctioned the presence of anabolic steroids in racehorses during competition, compared to European and Asian counterparts that monitor and issue stiff penalties for the use of anabolic steroids in equine athletes. Anabolic steroids were added to the list of controlled substances in 1991 under the Anabolic Steroids Control Act. Certain veterinary products fall under this act and have been reclassified as Schedule III drugs by the Drug Enforcement Agency (DEA). The drugs under the DEA Schedule III include boldenone, mibolerone, stanozolol, testosterone, and trenbolone and their esters and isomers [14]. Despite

these restrictions, anabolic steroids are easily obtained through internet and other clandestine sources. The stigma and penalties imposed on human athletes who have used or have apparently used anabolic steroids and related compounds are now cascading into the racing industry in the USA and today there is a higher level of awareness of the use of these drugs in the racing industry.

Regulation of Anabolic Steroids in the Commonwealth of Pennsylvania

The Commonwealth of Pennsylvania started regulating the use of anabolic and androgenic steroids on April 1, 2008. Prior to April 1, Pennsylvania horsemen and those in the surrounding states who were likely to race their horse in Pennsylvania were notified of the new policy as early as October of 2007.

The Commonwealth of Pennsylvania is regulating the use of anabolic and androgenic steroids by analyzing plasma samples obtained from equine athletes post competition. Plasma samples were chosen over urine because the pharmacological action of any drug is generally based on plasma concentration of the parent or active metabolite of the compound and not its concentration in urine. Thus, to determine if the drug had any pharmacological effect as to influence the performance of the horse at the time the horse was competing, the right place to look for the presence of the drug or in this case, anabolic steroid, is in blood/plasma. Furthermore, the complex excretion pattern of anabolic and androgenic steroids makes urine a more difficult and less meaningful medium to use in regulating the use of any drug. The use of plasma in screening for the presence of anabolic steroids allows its quantification. The use of plasma allows pharmacokinetics studies to be performed which can suggest some guidelines for veterinarians and horsemen, as the time periods for the steroids to be cleared from plasma.

Transition period

Anabolic and androgenic steroids are eliminated from the body very slowly. As the result of this problem, the Pennsylvania Racing Commissions in concert with the various Horsemen's Associations agreed on a transition period using the plasma concentrations of anabolic and androgenic steroids as guideposts (see appendix 1 for transition policy). The transition period would allow the horses to compete during this period as the blood (plasma) concentrations of previously administered anabolic steroid(s) progressively decreased below the level of quantification and confirmation. As part of this transition period, pre-race sampling of anabolic and androgenic steroids was offered to those horsemen who were concerned that the

concentration of a previously administered steroid in the horse was above a concentration that would trigger a violation. During the month of May of 2008, there has been a progressive reduction in the number of horses with a quantifiable plasma concentration of steroids and as of June 10, 2008 most of the samples are free of quantifiable plasma concentrations of anabolic steroids. By "free of", is meant undetected at the level of picograms – trillionths of a gram – per milliliter of plasma.

Intact Male Horses (Stallions).

The androgenic steroids, testosterone and nandrolone, are naturally produced in measurable concentrations in the intact male horse; therefore, the proposed regulation requires that a tolerance threshold be suggested for the intact male horse above which concentration during competition would suggest that commercially purchased testosterone or nandrolone had been administered. To accomplish this, studies sponsored by the Pennsylvania Horse and Harness Racing Commissions are in progress.

Nandrolone, naturally present in the intact male horse was not detected in non-race track geldings or mares, and therefore, its presence in racing geldings or mares was due to exogenous administration. Both genders have low plasma concentrations of the opposite male or female hormone. Low plasma concentrations of testosterone can be detected in some female horses. These drugs, if detected, are usually at plasma concentrations below the level of quantification and so are considered inconsequential; similarly low concentrations of estrogen can be found in the male.

Background Information on Exercise-Induced Pulmonary Hemorrhage (EIPH, Bleeding) and Furosemide (Lasix™, Salix™).

Introduction

Small amounts of blood in the nose of the horse following vigorous exercise have been noted for many years. Initially, the origin of the bleeding was thought to be from the head or nasal cavity, or basically a bloody nose. When this was observed, the horse was commonly referred to as a "bleeder". It was Cook in 1974 that suggested that the source of blood in the nose of a horse following vigorous exercise was from the trachea and lungs [1]. With the development of a fiberoptic endoscope long enough to examine the deeper portions of the horse trachea (windpipe) and lungs, Pascoe in 1981 confirmed the source of the hemorrhage as the lungs and termed the condition as Exercise-induced Pulmonary Hemorrhage [2]. Exercise-induced pulmonary hemorrhage (EIPH) or "bleeding" has been observed in Thoroughbred, Standardbred, Quarter Horses, and in all competing horses. Until recently many were convinced that the Thoroughbred horse bled more frequently than the Standardbred horse. However, the result of a recent study showed that the incidence is virtually identical between these 2 breeds of horses [3]. The hemorrhage was related to the intensity of exercise and not the duration and is a condition that is prevalent in all horses worldwide [4]. A relationship between severity of bleeding and racing success has not been established [2,4,5]. This is counter-intuitive to the assumption that if a horse bleeds its performance will be impacted; on the contrary horses that bleed still win big races.

Diagnosis of EIPH

There are a number of ways in which EIPH can be diagnosed. Occasionally horses will show evidence of bleeding by a small quantities of blood appearing at the nostrils following or up to 1 to 2 hours after the race. Most often the horse will swallow the small amount of blood and the diagnosis is made by endoscopic examination of the lung 1 to 2 hours after the race by looking for blood in the trachea or a tracheal wash to examine the number of red blood cells.

Mechanism of Exercise-Induced Pulmonary Hemorrhage (EIPH).

The mechanism of EIPH in the horse was suggested by West in 1993 as "stress related failure of pulmonary capillaries", which means that the smaller vessels (capillaries) in the lung can rupture when exposed to high blood and lung pressures [6-9]. This concept was confirmed in the horse when it was shown that very high pressure could produce rupture of small capillaries in the lungs leading to hemorrhage [10]. Following this break in the integrity of the small and very thin pulmonary capillaries, some red blood cells would become trapped within interstitium of the lungs and some will leak into the air sacs (alveoli) of the lungs. Red blood cells in the air spaces of the lungs will work their way upwards into the trachea and be eventually cleared from the lungs and airways by the ciliary escalator. The cells that appear in the airways and the trachea from are used as markers to confirm that the horse had bled.

Pressures of over 100 mmHg in the lungs arteries are realistic in the exercising horses especially when rapid swings in breathing pressures are also taken into account [9,11-13]. Compared to other species, including man, the horse has high lung arterial pressures during exercise. When lung arterial pressure exceeded 90 mmHg there was an increase in red blood cell counts from materials washed from the trachea indicating pulmonary hemorrhage had occurred. These pressures within the lungs can be achieved at treadmill speeds of 33 mi/h. Most horses exceed these speeds during a race. It is speculated that the arterial pressures may be higher in the horse competing on a track surface with a rider on its back.

Furosemide and the Reduction of Pressures in the Lung

Furosemide is used as a pre-race medication with the expectation of reducing arterial lung pressures, thereby reducing or eliminating EIPH. The reductions in pulmonary pressures produced by the administration of furosemide have been reported to be in the range of ~10 to 15 mmHg [14-17]. With estimated transmural pressures of over 100 mmHg created during exercise in horse, the pressure changes produced by the administration of furosemide are not of sufficient magnitude to reduce pressure within the capillaries to a level where hemorrhage resulting from rupture of the capillaries would be prevented. From a physiological prospective, the reduction of pressure produced by the administration of furosemide is not of sufficient magnitude to prevent or markedly reduce EIPH.

Effect of Furosemide on EIPH

Furosemide has been used empirically and has been approved for many years by the racing industry for the control of exercise-induced pulmonary hemorrhage (EIPH) or "bleeding" in racehorses. Its use in horses for this purpose has been controversial and has been criticized by organizations outside and inside of the racing industry. Despite the use of furosemide, horses continue to present blood in the trachea after exercise. No studies have shown a complete absence of blood from the trachea, in horses diagnosed with EIPH post-race or exercise, as a result of furosemide administration [3,17-22]. One study did, however, report that 64% of Thoroughbred horses administered furosemide before exercise had a decrease in blood in the trachea, although the report has not been verified by others investigators [23]. The majority of reports indicate that furosemide does not prevent EIPH in horses.

Furosemide and Performance

Literature available on this subject suggests that furosemide has the potential of increasing performance in horses without significantly changing the bleeding status. In a race track study conducted on Thoroughbred horses, there was an improvement in racing times in many horses after the administration of furosemide with similar observation in Standardbred horses [24,25]. One study examined the records of 22,589 Thoroughbred horses racing in US and Canada with and without the pre-race administration of furosemide. The conclusion of this study was similar to those of less extensive studies; horses that were administered furosemide raced faster, earned more money, and were more likely to win or finish in the top 3 positions than horses that did not [26]. A study which examined the effects of furosemide on the racing times of horses without EIPH under racing conditions showed and increase in racing times in many of the horse. The difficulty in the conduction of this study was based on the fact that it is difficult to find a population of horses that do not bleed following exercise, but the overall conclusions were similar to those of other studies [20].

Results from very elegant treadmill studies indicated that the increase in speed was due to significant weight loss produced by the administration of furosemide and not by any specific stimulatory or direct ergogenic effects on the horse. Based on the reduction in weight, the accumulated oxygen deficit was less during the 2-minute run as was the production of lactates. Thus, the sudden weight loss due to water loss (diuresis) induced by furosemide allowed the horse to run faster. This effect was reversed by the addition of an average of 16.1 kg of added

weight to the horse which was the estimated weight loss due to the diuresis produced by furosemide administration 4 hour before exercise [27,28]. Others have also concluded that the reason for the increase in speed of the horse was the loss of weight due to the loss of body fluids produced by the administration of furosemide [29]. Replacing this weight loss negates the effect of its administration.

Administration of Furosemide (Lasix™) and Detection of Drugs in Urine.

Furosemide (Lasix™, Salix™) is a rapidly acting diuretic [30] and its intravenous administration results in a number of changes. The most visual effect is the increase in urine volume. This increase in the production of urine which starts in about 10 minutes following intravenous administration produced a decrease in urine specific gravity; this results in reduction of the kidneys ability to concentrate drugs in urine. The main concern with the administration of furosemide is the reduction in post-race specific gravity produced by the extensive urination, and the possible influence that this dilution might have on the detection of therapeutic medications and drugs in urine [31-36]. It is important that a sufficient period of time be allowed for the specific gravity of urine to return to normal, and that the dose of furosemide administered pre-race is compatible with this concern.

Most equine analytical chemists use the specific gravity of 1.010 as a cut-off point below which the detection of drugs in urine may be compromised. In most racing jurisdictions a 3½ to 4-hour rule exists for the race-day administration of furosemide, with dose of 100 to 500 milligrams allowed by intravenous administration.

Methods of detection have improved since these studies were conducted and more sensitive methods are currently being used by most laboratories which reduce the impact of dilute urine on the detection of drugs, but it does not eliminate the impact of very dilute urine on drug detection. The use of plasma is becoming more prevalent in the detection of drugs and furosemide administration has little effect on the plasma concentration of drugs.

Comments on the Health and Welfare of Horses

A very basic element in the health and welfare of the horse is the living and training environment of race tracks. Well ventilated barns are essential in reducing dust in the environment that horses are exposed to on a daily basis, and reducing the transfer of communicable diseases when outbreaks occur. Dusty and poorly ventilated barn conditions contribute to pharyngitis, bronchitis and other respiratory disorders that can sideline a horse from competition. Track surfaces on which the horse train and compete is an issue that will be discussed by others on this panel.

Funding for research in horse health and welfare is limited to non-existent and yet the horse carries the burden and the responsibility of keeping us in the business of racing. The total annual economic impact of the horses and horse racing in many states is large, yet the research on the health issues of one player upon which the weight of the industry rests is generally neglected. Other viable industries have vigorous research and development programs.

There are many health issues that can be addressed, but the ones outlined below can have the greatest short-term and long term economic impact on the racing industry.

An area of greatest concern for short-time economic loss in the competing horse, are muscle and skeletal injuries and respiratory and airway diseases. Many of these conditions impact the well-being and prevent the horse from competing on a short time basis.

Conditions that result in catastrophic economic loss and death in horse are laminitis, gastro-intestinal emergencies, and catastrophic track injuries. Other areas of concern for maintaining the health and well-being of the horse are lack of good pain management in injured horses and the growing concern of antibiotic-resistant infections, as well as equine nutrition, reproduction, growth, and nutrient management. Maintaining the strength of the gene pool requires investigations into improvement of the longevity of breeding female and male horses and research into foal losses and sustaining pregnancy to term. Others can add to this list of the many conditions were research funds would contribute to the health of the horse. Veterinarians are the primary advocates for the health and welfare of the horse and it is essential that these concerns are actively addressed.

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Appendix 1

Steroid Policy: see Pennsylvania Department of Agriculture, Commissions and Councils, Horse Racing Commission for March 24, 2008, announced a policy for the use of steroids in Thoroughbred racing.