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DRUGS IN SPORTS

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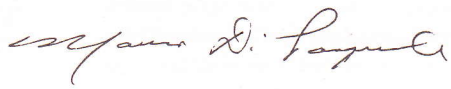
Foreword

I am gratified by the enthusiastic response to the premier issue of *Drugs in Sports*. The newsletter's content and format were received favorably by all levels of sports, including researchers, government agencies, sporting federations, sports physicians, chiropractors, coaches and trainers, and athletes.

As well, we received several helpful recommendations for the newsletter and ideas for future topics. We have considered these recommendations carefully and plan to implement some of these in upcoming issues.

I am grateful for this feedback and urge readers to write to me care of Decker Periodicals Inc., One James Street South, P.O. Box 620, L.C.D. 1, Hamilton, Ontario, L8N 3K7.



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Inside This Issue

Editorial: Why Athletes Use Drugs

Although most people are aware of the use of drugs by competitive athletes, many are not aware that substances such as anabolic steroids are widely used by recreational athletes. The use of these compounds by competitive athletes differs in some respects from their use by recreational or social athletes. Certainly some of the moral issues are different, as are the methods of enforcement — with an attempt (however inconsistent and flawed) by sporting bodies to eliminate use of performance-enhancing drugs by amateur athletes.

In many ways, however, the use of these drugs by both types of athletes has many similarities, including the reasons that they are used, their side-effects, the source of the drugs, and the implications and repercussions of increased legislation against performance-enhancing compounds, especially the anabolic hormones.

Both groups of athletes use drugs to achieve specific ends. For competitive athletes that end is winning and all that winning brings — fame, power, and money. Noncompetitive athletes use anabolic steroids to improve their physical and emotional states. When these athletes look better they feel more confident at work and play and are more successful in dealing with the opposite sex. Anabolic steroids help both types of athletes to cope with the stress and competition of modern life.

In competitive sports, doping gives an athlete a competitive edge. Today, however, the use of drugs in sports is so pervasive that most athletes must use drugs if they wish to remain competitive.

In order to make sports competitions fairer, sporting federations, led by the International Olympic Committee (IOC), have instituted drug testing programs. Unfortunately, all that has been accomplished so far, and the doping control programs can hope for no more regardless of how sophisticated testing becomes, is a decrease in the use of *some* drugs by *some* athletes. Certainly doping control has decreased the use of drugs at the novice and intermediate level. It has also decreased the use of what I call "drugs of the moment" such as amphetamines and narcotic analgesics at all levels.

Most elite athletes, however, have merely shifted the emphasis on the drugs they use and when they use them. Some drugs such as nandrolone (an anabolic steroid) are no longer used because they can be detected for such long periods of time. Oral medications are used more frequently than injectables, and other compounds are substituted for the ones that can be detected easily. Sometimes the alternate drugs are potentially more dangerous, since less is known about their use and side-effects than the more established, but easily detectable drugs. Contrary to popular belief, since drug testing will not make competition drug-free, legislating against the use of anabolic steroids will not help those athletes who now feel coerced into using performance-enhancing drugs in order to stay competitive.

The intensive media coverage and sensationalism surrounding the use of drugs by athletes have spawned much indignation on the part of government, sporting bodies, and the general public. These agencies and individuals are outraged that the purity of sports has been soiled by the use of drugs. Most athletes, however, have a more realistic view — their acceptance of performance-enhancing drugs is based on the reality of competition.

It seems that the very people who are outraged by the use of drugs by athletes are the ones who liberally use an arsenal of "accepted" drugs such as alcohol, caffeine, nicotine, aspirin, oral contraceptives, cold medications, antihistamines, herbal products, homeopathic preparations, megadoses of vitamins and minerals, and even illicit recreational drugs. Many of them smoke, drink, refuse to exercise, and are grossly overweight. The anti-drug stance taken by these individuals is hypocritical and often a result of a knee-jerk reaction to the sensationalistic investigative reporting that has dominated the news media and has led to a loss in objectivity and a polarization of views regarding the use and abuse of drugs in sports.

Contrary to what most people believe (the media's irresponsible sensationalism has resulted in the widely held mistaken view that the use by athletes of anabolic steroids and other performance-enhancing drugs is a problem on par with heroin and cocaine abuse), the use of drugs, such as anabolic steroids, by athletes is a problem, not because of the addictive and dangerous side-effects of these compounds, but because these drugs offer an unfair competitive advantage to the athletes who use them.

Drug use by athletes should not be confused with the addict's use of illicit drugs. The athlete's reasons for the use of drugs (and the kinds of drugs used) are different from those who abuse illicit or prescription drugs. Athletes don't use drugs to escape reality — they use them to enforce the reality that surrounds them. Athletes use drugs because they, along with everyone else in this society, want to win. Winning means money, prestige, and the good life. In our society coming in second means losing, whether in sports or in everyday life.

Athletes are not totally blameless. They could ignore the tendencies and temptations; they could be less materialistic. But it is because of their achievement-oriented personalities that they respond to the societal siren call of success at any cost. They are, perhaps, the embodiment of our society's ethical and moral values.

There are, of course, other factors that play a part in the use of drugs by athletes. Athletes and nonathletes alike derive psychological as well as physical benefits from exercise. Exercise has been shown to enhance an individual's overall self-image, and a positive self-image is important for good mental health and personal happiness.

For many athletes, feelings of self-worth are dependent upon their physical status, hence the push to use performance-enhancing drugs. This is perhaps why some athletes continue to use anabolic steroids after retirement from competition, and also why noncompetitive athletes use them. With this background of need and desire, it is not surprising that the possibility of a few side effects fails to deter the average athlete from using drugs.

Use of Anabolic Steroids in Wasting Diseases

Anabolic steroids are presently being used as replacement therapy in cases of obvious deficiency, some forms of anemia, hereditary angioedema, and some vascular disorders. Anabolic steroids, because of their anabolic, anticatabolic, immunologic, and other effects, may be useful in the following ways:

- Improving postoperative recovery;
- Improving the nutritional status of patients who are on parenteral nutrition or in negative protein balance;
- Aiding convalescence in cachectic or debilitated hospitalized and nonhospitalized chronically ill patients by improving recovery and appetite, and helping to prevent associated musculoskeletal and dermal problems;
- In wasting diseases including polymyositis, muscular dystrophy, cancer, and AIDS;
- Combating the catabolic effects of long-term use of corticosteroids;
- Bone disorders, including osteo and rheumatoid arthritis, osteoporosis, and delayed fracture healing;
- For asthmatics; and
- For chronic inflammatory and autoimmune diseases.

Anabolic steroids can be useful even in conditions where they might theoretically be contraindicated. For example, a combination of nutritional supplementation and oxandrolone has been found to be useful in the treatment of alcoholic hepatitis, a condition in which the use of 17-alkylated compounds (e.g., oxandrolone) would not ordinarily be considered because of their hepatotoxicity.[1]

As well, although serious consideration must be given to their significant hormonal adverse effects on prepubertal children, anabolic steroids have proven to be of some use in the management of protein-depleted children.[2]

Thus, because anabolic steroids promote muscle and weight gain, and decrease muscle breakdown, and because they have in the past been found useful for augmenting alternative methods of nutritional support, they are potentially useful compounds for treating the wasting that often accompanies diseases such as polymyositis, cancer, and AIDS. Studies have shown that the prognosis of patients with AIDS depends to some extent on their nutritional status[3] and maintaining their body weight.[4]

To date most studies show that anabolic steroids have a positive effect on nitrogen excretion and that the use of anabolic steroids on patients on intravenous nutrition results in increased nitrogen balance and protein conservation.[5] However, more studies are needed using different preparations (both long and short-acting anabolic steroids), varying doses (from doses that represent replacement levels to those approaching the amounts used by some athletes), for various time periods (from a few weeks to several months).

The immunologic effects of anabolic steroids would make them even more useful in certain autoimmune and immune deficiency diseases.[6] As well, the immune system is now being implicated in many diseases for which anabolic steroids have been found to be useful, including aplastic anemia. It is possible that it is the immunologic effects of anabolic steroids rather than their erythropoietic or anabolic effects, as previously believed, that may be responsible for their beneficial effects in these diseases.

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Capsule Comment

Physicians and coaches, rather than being seen as part of the solution to the problem of drug use in sports, are being castigated and reprimanded if they take any part in, or even recognize, drug use.

This iniquity is in part a backlash from our society's misplaced morality, fueled by the media and individuals who derive a sense of importance and power in propagating myths and tales about drug use in sports and drug testing.

Sporting establishments are marked by bureaucratic bungling and general government ineptness (as shown by the Dubin Inquiry in Canada). In most cases, rather than share the blame, these organizations are using coaches and physicians as their scapegoats, even though some of these people are the first ones to speak openly and honestly about the pervasive use of drugs by amateur athletes. Banning coaches such as Charlie Francis is another sign that sporting agencies and governments are not yet willing to deal with the issues of drug use in sports in a realistic and objective manner.

Athletes such as Ben Johnson, and men like Charlie Francis (Ben Johnson's coach) and Dr. Jamie Astaphan (his sports physician), who advised and who monitored the use of performance-enhancing drugs by athletes, are not, as the government sporting agencies would have you believe, an aberration in the world of amateur sports; they are the norm. Penalizing them for doing what is routinely done elsewhere in the athletic world is a whitewash of reality.

Because of the deficiencies of drug testing methods, and the emphasis society puts on winning, it is impossible to eliminate or even to reduce significantly the use of performance enhancing drugs by athletes. An athlete who tests negative in a drug test may well be using drugs that cannot be detected, or using masking or other techniques to escape detection. Also since athletes obtain most of these drugs, especially growth hormone and anabolic steroids, from the black market, stemming the legal flow of these drugs has little effect on their use.

Although bureaucrats at every level of medicine, sports, and government are willing to chastise Charlie Francis and Dr. Astaphan, few are able to see the valuable services these men provided to the athletes under their care. While it is true that both Dr. Astaphan and Charlie Francis advised Ben Johnson (and other athletes) about the use of anabolic steroids, they were not responsible for the athlete's use of these and other performance-enhancing drugs. In my experience, athletes who are not advised and monitored regarding anabolic steroid use will self-administer them, usually in higher doses and for longer periods of time. The recently revealed East German steroid program shows quite dramatically that, with proper counseling and monitoring, low doses of anabolic steroids at specific intervals effectively enhance performance.

By properly monitoring the use of performance-enhancing drugs, Francis and Dr. Astaphan may have minimized the use of these compounds and helped the athletes avoid any potential adverse reactions. As well, many athletes who came under their care and who previously self-administered anabolic steroids, invariably had their doses and time intervals on the drugs reduced dramatically.

Rather than banning these people, Athletics Canada should have made a sincere effort to reach some sort of compromise with them. As shown in his new book *Speed Trap* (see the book review on p. 15), Francis is informed and aware about the issues surrounding the use of performance-enhancing drugs by athletes. His expertise and knowledge might have been useful to the Canadian federal and provincial sporting organizations in arriving at a realistic solution to the problem of drug use by athletes.

Unfortunately, the officials involved in running the various gov-

ernment agencies show a naiveté common to those in decision making positions within the sporting hierarchy. Their strategy so far has been a failure. Rather than decreasing the use of drugs in sports and protecting the health of athletes, legislation against drug use and extensive drug testing have increased drug use and subsequently led to the use of more dangerous drugs.

The validity of any course of action is measured by the effects produced. By any reasonable standard the war on performance-enhancing drugs (like the war on illicit drugs) has been a failure. The prohibitionist stance, consisting of authoritative rules, and enforced through government and legal agencies, has had its chance.

Rather than being preoccupied with what is perceived as being politically right, but in fact is politically expedient, it is time to use an enlightened approach to solve the existing problems

Use and Side Effects of Growth Hormone

Growth hormone (GH) use by athletes has escalated dramatically in the past 5 years. In the early 1980s the use of natural GH was not a widespread phenomenon. Testing for anabolic steroids was lax, and no testing was done for testosterone. Athletes were not inclined to use untested or difficult-to-get drugs when they could use compounds that were easily accessible and that they knew worked. Secondly, there was a scarcity of GH, and what there was was usually reserved for the treatment of pituitary dwarfism.

Today athletes are more inclined to use any promising compound that cannot be detected. Along with this increased use of GH is an increase in the use of drugs and nutritional substances that may raise endogenous GH levels. Athletes often use combinations of GH stimulators in the hope of increasing GH secretion even further. There is in fact some basis for this belief — the synergistic effect of clonidine, propranolol, L-dopa, and others has been documented.[1]

As well, it would appear that all the tests for human GH release and the conditions under which GH is released act via different mechanisms. For example, in obesity, the basis for the derangements in GH secretion (an impairment of GH secretion elicited by all stimuli known to date) is likely associated with a state of chronic somatostatin hypersecretion.[2] As well, the mechanisms by which insulin-induced hypoglycemia, L-dopa, and arginine stimulate GH secretion are all different,[3] involving various mechanisms including neural and humoral influences that can stimulate GH directly, and other factors that effect the release or withdrawal of somatostatin and growth hormone-releasing hormone (GHRH).

Some forms of exercise increase GH secretion. To date, no study has fully defined how and when this occurs, and what mechanisms are responsible for this increase. Although no one has been able to maximize endogenous GH levels without the use of drugs, work is progressing in this area.

At present there is considerable research aimed at determining how, when, and under what conditions GH is released.[4,5] Recent studies have shown that the pattern of GH release is more complex than first realized. The human pituitary gland secretes GH in volleys consisting of multiple secretory bursts, without measurable intervening tonic secretion.[6] This pattern is due to high-frequency GH-releasing hormone secretory events superimposed on low-frequency episodes of somatostatin withdrawal.

Adverse Effects

Extended use of excessive amounts of exogenous human GH may produce some changes that are normally seen in cases of endogenous GH excess, including acral bony changes, changes in facial features and facial bones, voice changes, glucose intolerance (possibly resulting in relative insulin deficiency and diabetes), hypogonadism, peripheral nerve compression, cardiac enlargement, hypertension, and increased serum cholesterol and triglycerides.[7] As yet, I have not witnessed any significant adverse effects in athletes who have used GH. Although there is little information on the side effects of GH in healthy individuals, one recent study has shown that GH administration to children with short stature who are otherwise normal is devoid of detectable diabetogenic effects.[8]

We are not witnessing the changes normally seen in acromegalics because GH is used by athletes for short periods of time, with long breaks between use, and because the amount of GH used does not approach the levels seen in most acromegalic patients. Perhaps if athletes used larger amounts of GH continuously for a number of years, some of the adverse effects would appear.

Exogenous GH may lead to the formation of two kinds of antibodies. The first kind, produced by one third of patients receiving synthetic GH, is non-neutralizing and does not reduce the effect of GH. The second kind, produced by approximately 3% of people, is capable of neutralizing

GH. It seems to neutralize only exogenous GH, but there is a possibility that endogenous GH may also be neutralized, leaving the individual permanently GH deficient. In a recent study antibody formation occurred more commonly with the methionyl product (e.g., Protropin), compared with both the pituitary-derived GH and the natural-sequence GH (e.g., Humatrope).[9]

Creutzfeldt-Jakob Disease

Before 1986, GH was freeze-extracted from human pituitaries harvested during postmortems. It was commercially available as Crescormon and Asellacrin. However, the natural form of GH (extracted from human pituitaries) contains a viral contaminant (a slow virus) implicated in several cases of a fatal neurologic disease, Creutzfeldt-Jakob disease (CJD). Since there is no way to screen GH batches to assure their safety, distribution of all products derived from human pituitary glands has been stopped in North America and in many other countries.[10]

Today biosynthetic GH, produced through recombinant DNA technology using the gene for human GH, is used almost exclusively. It is equal in potency to pituitary human GH.[11] Trade names for the synthetic GH include Bio-Tropin (Bio-Technology); Genotropin (Sumitomo); Humatrope (Lilly); met-HGH; Norditropin (Nordisk); Protropin (Genentech); Saizen (Serono); and Somatonorm (Kabi-Vitrum). The amount of GH per vial depends on the brand. Generally the vials are 5 mg (10 IU) of lyophilized, sterile somatrem per vial.

Athletic use of GH began in the mid 1970s. I recall remarking on the use of GH by athletes at a medical committee meeting held in conjunction with the 1978 World Championships in Powerlifting. Perhaps thousands of athletes used GH from the late 1970s to 1986, all of it derived from cadaveric pituitary glands. In early 1986, in the third update of my book *Drug Use and Detection in Amateur Sports*, I stated that as yet no one could predict just what the repercussions would be for those athletes who used cadaveric GH. Since there seems to be a 15-year average incubation interval from midpoint of GH treatment to onset of symptoms, the great majority of potentially exposed athletes have not yet attained the requisite incubation period for expression of CJD, although several cases have been reported in other patients treated with GH.[12] It would appear that over the next 10 years we will have our answer since we presently are seeing cases of CJD in hypopituitary patients who started GH before 1970.[13]

I believe that few athletes will develop CJD since the duration of pituitary GH therapy is a major risk factor for CJD, and many athletes used GH for relatively short periods of time in those crucial years. As well, it appears that there may be a genetic predisposition to CJD limiting the number of exposed individuals who will eventually develop the disease.[14]

Several reports cited an increase in certain cancers in patients who had received GH. However, in a recent study it was found that GH treatment probably did not contribute to new tumor development – any deaths in patients receiving GH were due mainly to recurrence or progression of intracranial tumors and potentially avoidable metabolic consequences of hypopituitarism.[15]

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Blood Doping and Erythropoietin

The work capacity of muscles depends on their oxygen supply and, therefore, to some extent on hemoglobin concentration. Thus using infusion of red blood cells (or reinfusion of autologous stored cells) or erythropoietin (EPO) could theoretically increase both hemoglobin concentration and performance (aerobic capacity, endurance, and stamina) in athletes. Several studies[1,2] have shown this to be true, while others have reported on the use of blood as an ergogenic aid.[3]

Blood Doping

Blood doping involves removing some of the athlete's own blood several weeks before a competition, and then reinfusing the blood into the athlete close to the competition. By reinfusing his own blood after he has already made up for the loss, the athlete increases his effective oxygen transport mech-anism. The extra supply of blood enables him to carry more available oxygen to the muscle tissue. This extra oxygen supply allows an increased production of ATP by aerobic oxidation of glucose and ketones. This in turn allows increased intensity and duration of muscular contraction and decreased lactate production.

Blood doping was banned by the International Olympic Committee (IOC) in 1986, and selective testing has begun. As in any other physiologic reaction, the introduction of a natural substance into the body causes homeostatic changes to occur. In the case of blood doping, those hormones and compounds that ordinarily stimulate the formation of blood (e.g., erythropoietin) are dramatically reduced when blood is given.[4] Tests for blood doping involve the changes that take place.

The evidence so far suggests that blood doping is an effective ergogenic aid for endurance athletes, such as marathon runners, skiers, and cyclists, whose work capacity depends on a ready supply of transported oxygen. Although the desired effect of blood doping is to increase oxygen delivery, something that is not a factor in the strength sports where anaerobic contraction is common, blood doping is also being used by some strength athletes. No studies, however, have been done to show what effects, if any, blood doping might have on performance that does not depend on maximal oxygen intake.

Erythropoietin

Erythropoietin (EPO) is a circulating glycoprotein that stimulates red blood cell formation in higher organisms. It is currently being bioengineered by a number of firms. Measurable amounts are found in urine and plasma; thousand-fold concentrations can be found in animals that are severely anemic or hypoxic.

Before the ready availability of EPO, androgenic or anabolic steroids were used in treating various anemias. Studies suggest that, within the normal range of hemoglobin in men, androgens are a determinant of the red cell mass.[5] Once EPO became available, anabolic steroids were put on the back shelf. Recently, however, it has been shown that anabolic steroids increase the erythropoietic response in part by increasing the sensitivity of the erythroid progenitors to erythropoietin. Thus androgen therapy significantly augments the action of exogenous EPO such that lower doses of EPO are sufficient for an adequate hematopoietic response.[6]

Because of its potential to boost an athlete's performance significantly by increasing the red blood cell count and hence the oxygen-storing capacity of the blood, EPO is now being used by a growing number of athletes as an alternative to blood doping. EPO has the same effect on the body as blood doping. However, it is far simpler to administer, impossible at present to detect, and has fewer side effects. By using EPO to increase the number of red blood cells, athletes could theoretically enhance performance in endurance events.

Although more frequently used by endurance athletes, EPO is also being used by a small number of strength athletes. In two strength athletes that I know who used EPO, the effects were negligible. One strength athlete who self-administered both anabolic steroids and EPO had a Hb of 15.2 before using anabolic steroids, 16.2 while on anabolic steroids but before the use of EPO, and 17.8 after using both anabolic steroids and EPO for a 2-month period.

Because endogenous and exogenous EPO are identical, the use of this compound cannot be detected. Nevertheless it has been banned by the IOC under the category of peptide hormones and analogues.

Adverse Effects of Blood Doping and EPO

Side effects complicate approximately 3% of all transfusions and range from mild immune effects (and rarely anaphylactic reaction)[7] to post-transfusion hepatitis[8] and acquired immunodeficiency syndrome (AIDS).[9]

To limit the hazards of disease transmission and sensitization, an athlete's own cells are often used. As well the transfusion should be performed in a hospital-like setting, where all precautions are made. However, even autologous blood is unsafe if it is not collected, stored, and transfused under careful medical supervision.

Although EPO does not have the adverse effects associated with blood transfusions, it can lead to life-threatening side effects if the hemoglobin and hematocrit increase excessively. Unmonitored use of EPO, leading to markedly increased blood volume and viscosity, can result in cardiovascular and neurologic complications such as congestive heart failure, hypertension, coronary insufficiency, and stroke.

Since androgens potentiate the effects of EPO (see above), the concomitant use of anabolic steroids and EPO may increase the incidence of life-threatening effects secondary to hemoconcentration.

There have been several suspicious deaths in athletes who have used EPO. Although no conclusive proof was found that the deaths were caused by EPO, the deaths are suspect because of the unusually high number that occurred among a population of athletes who would benefit from the use of EPO.

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Clenbuterol: A New Anabolic Drug

Clenbuterol, a drug used for the treatment of asthma, is being used increasingly by athletes because of its anabolic properties. This compound, like other third-generation β_2-selective adrenergic agonists, has increased β_2 selectivity and thus is a more specific bronchodilator, with fewer cardiovascular and neuromuscular side effects.[1]

Of the newer β agonists, the most currently used are carbuterol, clenbuterol, fenoterol, mabuterol, procaterol, reproterol, rimiterol, salbutamol, terbutaline, and tolbuterol. These agents are taken orally, injected, or inhaled (with the exception of clenbuterol, which is only effective orally).

Studies in animals have shown that β-adrenergic agonists have potent growth-promoting effects, resulting in measurable increases in lean muscle mass and loss of body fat. Not all β agonists, however, have anabolic properties, and it appears that various compounds have different anabolic and antilipogenic actions.[2] Of those tested, clenbuterol, cimaterol, and to a lesser extent, fenoterol

influence muscle growth via ß-adrenoceptor stimulation resulting in increases in muscle mass, body weight, and muscle protein synthesis rate.

Clenbuterol prevents muscle atrophy,[3,4] and decreases myofibrillar protein breakdown.[5] It also causes a significant increase in protein synthesis and skeletal and cardiac muscle growth (mainly type II muscle fiber types), a decrease in subcutaneous and total body fat, and an increase in energy expenditure.[6-10] In one study the chronic administration of clenbuterol caused hypertrophy of histochemically identified fast- but not slow-twitch fibers within the soleus, suggesting that the role of $ß_2$ receptors is in regulating muscle fiber type composition as well as growth.[11] Other studies have shown that clenbuterol decreases subcutaneous fat by increasing lipolysis and depressing lipogenesis.[12,13]

The above studies have also shown that clenbuterol does not significantly affect plasma insulin, GH, or triiodothyronine levels, whereas cimaterol increases serum GH significantly[14] (making it more popular than clenbuterol with some athletes). One study, however, found that clenbuterol was effective as a stimulus for insulin secretion in isolated human pancreatic islets. The increase in insulin secretion induced by clenbuterol was inhibited by propranolol, indicating that the response was mediated by activation of ß receptors.[15]

Clenbuterol affects insulin paradoxically. Studies have shown that in humans clenbuterol increases serum glucose and glucose-induced insulin secretion,[15] the opposite of what you would expect from a lipolytic drug since insulin decreases fat breakdown and, in turn, reduces the lipolytic effects of clenbuterol.[16]

Since studies are contradictory,[17,18] it is not known if the anabolic effect of clenbuterol on muscle is directly mediated by ß-adrenoceptors, even though its effect on cardiac and fat mass and energy expenditure are reduced by ß antagonists. As well, it appears that the anabolic effect may be independent of other anabolic hormones including the sex hormones.[19]

The anabolic effects of clenbuterol (as well as cimaterol and fenoterol) may persist with chronic use,[20] although some studies have found that intermittent use (most notably a 2 day on and off regimen) is needed to prevent the attenuation of the growth response in rats.[21] The vascular effects of the compounds (increases in muscle blood flow) that modify the nutrient flow into the muscle are short-lived and may not account for the prolonged anabolic effects of these compounds.[22]

Side effects with clenbuterol appear minimal, although there is some evidence that clenbuterol treatment induces pressor effects in normotensive animals under stress.[23] In humans the most common adverse effects, headaches, nervousness, and inability to sleep (usually seen at the higher doses), are common to most other sympathomimetic amines such as the amphetamines, ephedrine, and propanolamine.

The usual dose of clenbuterol for asthma is 20 to 40 µg twice a day. The substance is resorbed almost completely enterally and has a half-life of 34 hours.

Although several studies of animals have documented clenbuterol's anabolic effects, no human studies have as yet been done to determine its effects on athletic performance. As is often the case, effects seen *in vitro* or in animals under controlled conditions do not translate fully when the same compound is used in humans.

Lately, clenbuterol has been used increasingly by athletes, usually in combination with one or more compounds. Some athletes use it with GHB (see premier issue) or GABA (gamma amino butyric acid), claiming they feel better and more motivated on these combinations. Clenbuterol is often used with GH and anabolic steroids.

Many athletes compare clenbuterol with GH since both seem to have similar effects. However, most feel that clenbuterol is not as effective as GH. Clenbuterol, while useful as a lipolytic agent, is not as useful for increasing muscle mass. This view is supported by a study that compared the responses of dwarf mice to dietary administration of clenbuterol, daily injections of GH, or both treatments combined.[24] The study showed that in dwarf mice:

1. GH, with or without clenbuterol, induced an increase in body weight growth and tail length growth;
2. Clenbuterol alone did not affect body weight or tail length;
3. Both GH and clenbuterol reduced the percentage of whole-body fat and increased the protein : fat ratio;
4. Both also increased protein synthesis rates of whole body and muscle, although the magnitude of the increase was greater in response to GH than to clenbuterol.

In rats clenbuterol is effective in maintaining lean body mass under conditions of food deprivation but not under fasting conditions.[25] Clenbuterol may be useful for athletes wishing to maximize lean body weight (e.g., body-builders and athletes in sports with weight classes).

To further cloud the issue, it appears from the literature that the many putative effects of clenbuterol rapidly diminish with time. One study found that the density of $ß_2$-adrenergic receptors in the cerebral cortices and cerebella of rats receiving the same repeated-treatment regimen was reduced with a time course similar to the loss of behavioral responsiveness.[26] In another study the inhibitory effect that one dose of clenbuterol had on the sexual activity of normally sexually active male rats disappeared when the clenbuterol was given daily for a 1-week period.[27]

Many athletes are using clenbuterol in combination with GH and while some are finding that there is

an increased lipolytic effect over using GH alone, others are not. One study found that clenbuterol may actually inhibit the GH stimulation that occurs secondary to other substances or drugs.[28]

A recent study supports the possible additive effect of clenbuterol and GH.[29] This study also concluded that:

- Clenbuterol likely does not mediate its effects via the GH axis.
- Muscles from animals treated with GH alone exhibited an increase in DNA concentration not seen in muscles from the other treatment groups.
- Increases in glycogen utilization (perhaps along with the increases in insulin and glucose serum levels found in other studies) may be responsible for the anabolic properties exhibited by β_2 agonists such as clenbuterol.
- Clenbuterol increased the cross-sectional area of both fast-twitch glycolytic (FG), and fast-twitch oxidative glycolytic (FOG) fibers in muscles. Neither clenbuterol nor GH resulted in any change in fiber percentage frequency in either muscle.

In practice, clenbuterol is not the anabolic wonder drug that the literature makes it out to be. While the use of clenbuterol and hypertrophic stimuli may lead to a significant hypertrophic growth response in some animals,[30] this does not appear to happen when clenbuterol is used by athletes.

I have found that athletes do not add appreciable weight when on clenbuterol, but they do seem leaner (i.e., they likely have increased their lean muscle mass). Some studies have shown that these compounds inhibit protein breakdown more than they inhibit protein synthesis.[31] The fact that these compounds inhibit protein synthesis may explain why their use does not result in significantly increased overall muscle mass.

Some athletes feel that clenbuterol is useful for maintaining muscle mass and strength in the time interval between going off anabolic steroids (so as to avoid detection) and the drug-tested event. The athlete seems to lose much less muscle mass and strength in the few weeks before a drug-tested meet when he goes off oral anabolic steroids but stays on clenbuterol, and often one or more other compounds such as GH, GH stimulators (e.g., certain amino acids), GHB, and GABA. Most athletes find that any effects from clenbuterol rapidly diminish with continued use, even though most are using clenbuterol 2 days on and 2 days off (sometimes rotated with ephedrine) in an attempt to stave off the tolerance to this drug.

Whatever its effects, the use of clenbuterol among competitive athletes is becoming epidemic. Athletes view it as a relatively innocuous drug that has been well tested in asthmatics. Also, although banned by the IOC (testing for this compound and other ß agonists, by gas chromatography-mass spectrometry,[32,33] has become routine), clenbuterol cannot be detected a few days after its use.

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Literature Review

The following is a selection of relevant citations from journals, accompanied by abstracts and commentaries.

1. Bahrke MS, Yesalis CE III, Wright JE. **Psychological and behavioral effects of endogenous testosterone levels and anabolic-androgenic steroids among males. A review.** *Sports Med* 1990; 10(5): 303–337.

Abstract

This study, carried out by three of the members of this newsletter's editorial board, examines in detail the psychological and behavioral effects of endogenous testosterone levels and anabolic-androgenic steroids. The authors looked at the relationship between moods, behavior, and endogenous plasma testosterone levels, as well as the effects of anabolic steroids and corticosteroid administration. They found that while a relationship between endogenous testosterone levels and aggressive behavior has been observed in various animal species, it is less consistent in humans. The authors conclude that, although the use of exogenous anabolic-androgenic steroids may have psychological and behavioral effects in some patients and athletes, the

effects are variable, transient upon discontinuation of the drugs, and appear to be related to type (17 α-alkalated rather than 17 ß-esterified), but not dose, of anabolic-androgenic steroids administered. The roles of genetic factors, medical history, environmental and peer influences, and individual expectations are likewise unclear. The evidence at present is limited and much additional research will be necessary for a complete understanding of this relationship.

Comment

This exhaustive review of the available literature (278 references are cited) on the psychological and behavioral effects of anabolic steroids points out the difficulty of coming to any definitive conclusions about the effects and side effects of anabolic steroids. Other recent reviews, while noting that there is an association between androgens and aggression in animal studies, also concluded that the evidence for a possible effect of androgens on aggression is inconclusive.[1] However, even in animal studies there is some evidence that hormone-dependent aggression is activated by learned responses or experience, although the level of aggression, once activated, depends on the serum testosterone concentration.[2]

Because of lack of clear-cut associations between androgens and aggression, it is difficult to support much of what is being said about the sensationalized "roid rage" — an uncontrollable anger and hostility that supposedly results from the use of anabolic steroids. It is even more difficult to support the prohibitionist government reactions to this unfounded sensationalism.

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2. Guzman M, Saborido A, Castro J, Molano F, Megias A. **Treatment with anabolic steroids increases the activity of the mitochondrial outer carnitine palmitoyltransferase in rat liver and fast-twitch muscle.** *Biochem Pharmacol* 1991; 41(5):833–835.

Abstract

The authors of this study found that treatment of male rats with the anabolic steroids fluoxymesterone or methylandrostanolone increased the activity of the outer carnitine palmitoyltransferase in liver and fast-twitch muscle mitochondria. This effect was not potentiated by physical exercise and was not observed in heart and slow-twitch muscle mitochondria. Anabolic steroids did not affect the sensitivity of the liver enzyme to inhibition by malonyl-CoA. On the basis of their data, the authors concluded that androgens may have an important physiological role in the regulation of fatty-acid oxidation in liver and fast-twitch muscle mitochondria. In addition, their results are at odds with the notion that the metabolic effects of anabolic steroids on muscle are only evident in conjunction with physical training.

Comment

This study shows that some of the metabolic effects of anabolic steroids are independent of physical training. It has always been my contention that the androgenic/anabolic hormones are powerful metabolic modulators that might prove useful in a wide variety of conditions and diseases (see Use of Anabolic Steroids in Wasting Diseases, p.3), with or without accompanying physical exercise. On the other hand, while some of the metabolic effects of anabolic steroids may be independent of physical training, others may be enhanced by the synergistic anabolic effects of nonexhaustive exercise. Further research on the metabolic effects of anabolic steroids, and on finding new compounds with selective metabolic effects, is needed.

3. Lundberg U, Wallin L, Lindstedt G, Frankenhaeuser M. **Steroid sex hormones and cardiovascular function in healthy males and females: a correlational study.** *Pharmacol Biochem Behav* 1990; 37(2):325–327.

The relationship of serum estradiol and testosterone levels to systolic (SBP) and diastolic blood pressure (DBP) and heart rate (HR) was examined in healthy nonsmoking males and females, 30–50 years of age. Postmenopausal women and women taking oral contraceptives were excluded from the study. Testosterone levels in women were positively correlated with SBP, DBP, and HR, after removing the effects of age and body mass. Positive correlations were also found between estradiol and SBP and HR in women. No systematic relationships were found between steroid sex hormones and cardiovascular measurements in men. The findings suggest a role of steroid sex hormones in cardiovascular function of women, whereas the relationship in men is less clear.

Comment

It is interesting that, in light of the usual medical warnings about the effects of androgenic/anabolic steroids on blood pressure, in men no distinct correlation was found between high blood pressure and the sex hormones, especially the higher levels of testosterone.

In my experience, the cardiovascular effects of anabolic steroids, other than those effects that can be attributable to raised levels of serum cholesterol, seem to be minimal in athletes not predisposed to hypertension or heart disease. Most athletes taking anabolic steroids experience a slight increase of systolic blood pressure and heart rate. These increases may be secondary to increased fluid

and sodium retention, and to the effects of anabolic steroids on the adrenal cortex and the circulating catecholamines. The slight increases seen in blood pressure may have adverse effects on potentially or overt hypertensive individuals. Decreasing salt intake, and perhaps medication, may be necessary in some athletes.

4. Dabbs JM. **Age and seasonal variation in serum testosterone concentration among men.** *J Chronobiol Int* 1990; 7(3):245–249.

Abstract

This study looked at the seasonal effect on serum testosterone. Testosterone concentrations were assayed from a single serum sample from 4,462 military veterans, ages 32–44. The results show that mean testosterone levels declined with age and varied with month of testing, with a seasonal peak in November (for men in their early 30s) to December. The age effect was greater than the seasonal effect. The author notes that both effects may bear upon behavior and should be treated as possible sources of error in studies of testosterone.

Comment

Athletes who don't use drugs might be able to make some use of their late fall peaks of serum testosterone — perhaps by scheduling their training and competitions around this time period. It would have been interesting, for purposes of drug testing, to have measured urine testosterone and epitestosterone and determine age and seasonal effects.

5. Goldberg L, Bents R, Bosworth E, Trevisan L, Elliot DL. **Anabolic steroid education and adolescents: do scare tactics work?** *Pediatrics* 1991; 87(3):283–286.

Abstract

This study looked at the opinions (level of agreement) of high school varsity football players with regard to reported effects of anabolic steroids both before and after two different education interventions. Lectures and handouts of a balanced education program (potential risks and benefits) were compared with a risks-only (negative or "scare tactics") presentation, in a controlled manner. Those receiving the balanced review significantly increased their agreement with 5 of 10 targeted adverse effects, while no change occurred for any risks among those taught by the negative intervention. The authors conclude that a teaching model that only emphasizes the untoward consequences of anabolic steroids is ineffective, even in the short term. A balanced education approach can improve understanding of the potential adverse effects of these drugs. Additional strategies may be required to change young athletes' attitudes toward anabolic-androgenic steroid use.

Comment

My stance for the past two decades has been that scare tactics do not work. In fact these scare tactics have alienated the athlete from the medical profession and their sports bodies. In a move that was reminiscent of McCarthyism, my 1984 book, *Drug Use and Detection in Amateur Sports*, was banned by Sports Canada on the basis that it was supplying athletes with the wrong kind (i.e., unbiased and objective) of information. This prohibitionist attitude on the part of the various sports bodies and government agencies, supported by their counterparts in the scientific and medical community, has no place in sports, or anywhere else.

6. Walters MJ, Ayers RJ, Brown DJ. **Analysis of illegally distributed anabolic steroid products by liquid chromatography with identity confirmation by mass spectrometry or infrared spectrophotometry.** *J Assoc Off Anal Chem* 1990; 73 (6): 904–926.

Abstract

This study looked at black market anabolic steroid products — primarily oil-based injectables or tablets that often do not contain the ingredients declared on the label. An analytical scheme based on a reverse-phase liquid chromatographic (LC) system for screening, tentative identification, and quantitation is presented.

Comment

Over 200 samples of black market anabolic steroids had been analyzed at the time that this paper was written in late 1989. On looking over the results it appeared that at that time over 75% of the compounds tested had some anabolic steroid present (although in many cases not the ones named in the label). This situation has since changed. Today more than 85% of the black market anabolic steroids, whether in pill form or injectable, contain not a trace of active hormone. The less connected the athlete, the greater the likelihood of getting bogus anabolic steroids. The only athletes in North America who are assured of real anabolic steroids are those who have the necessary medical, pharmacologic or veterinary contacts, or who are able to obtain their anabolic steroids directly from other countries (e.g., parts of Europe and many of the Third World countries, including Mexico, the Middle East, Africa, and Central and South America).

7. Lebl J, Zemkova D, Kopecky A, Zikan J, Marcek P. **[The effect of increased production of androgens on the development of body build morphology. Case report of an androgen-active tumor in a monozygotic twin].** *Cesk Pediatr* 1990; 45(7): 408–410.

Abstract

The authors present an account of monozygotic twins; one of the twins had an androgen-active adenoma of the adrenal cortex dur-

ing early puberty that led to a difference in body type compared to her normal twin. Four years after resection of the tumor, endocrine and anthropometric characteristics of the two sisters were evaluated: the hormonal status of both is normal, the somatic differences are manifested by a different final height, biacromial width, and chest circumference. The results may prove useful as a precedent for evaluation of risks associated with administration of anabolic steroids in children.

Comment

From this study we see that hormonal changes during the formative childhood years result in some changes that are permanent, even when the hormonal profile returns to normal later on. While this is not as evident in mature adults with abnormal levels of the sex hormones (e.g., in men the use of anabolic steroids leads to morphological changes that are completely reversed on discontinuation of the exogenous hormones), irreversible changes can take place when excessive amounts of other hormones are present. Examples are the acral and facial changes seen in acromegalics that persist even when GH levels are returned to normal.

8. Volta C, Ghizzoni L, Muto G, Spaggiari R, Virdis R, Bernasconi S. **Effectiveness of growth-promoting therapies. Comparison among GH, clonidine, and levodopa.** *Am J Dis Child* 1991; 145(2):168–171.

Abstract

In this study the authors compared the ability of GH, clonidine, and levodopa to stimulate growth in short and slowly growing children. They found that the use of GH resulted in the greatest increments in height velocity, while clonidine came a distant second, with levodopa having even less of an effect.

Comment

The consensus among athletes is that the use of exogenous GH is much more effective as an ergogenic aid than GH stimulants such as the amino acids (arginine, ornithine, lysine, and levodopa). Some athletes find that clonidine is useful, but side effects include feeling groggy and tired. These adverse effects counter any ergogenic effects from the putative increased GH secretion.

9. Wheeler GD, Singh M, Pierce WD, Epling WF, Cumming DC. **Endurance training decreases serum testosterone levels in men without change in luteinizing hormone pulsatile release.** *J Clin Endocrinol Metab* 1991; 72(2):422–425.

Abstract

Several studies have suggested that total and bioavailable testosterone levels are reduced in some male athletes. Such changes may be related to loss of body weight, increased serum cortisol, or alterations in LH pulsatile release. This study was set up to determine how endurance training affects androgen levels. The authors measured serum total testosterone, sex hormone-binding globulin, free androgen index, LH, FSH, PRL, cortisol, and weight in 15 previously sedentary males. Over 6 months of training, the men increased weekly running mileage to an average of 56 km per week. Total testosterone and free androgen index levels decreased significantly. PRL and cortisol also decreased, while single sample LH and FSH remained unchanged. There was a significant reduction in weight, which did not correlate with changes in serum testosterone levels. LH pulsatile release was not altered by training in the subset of five runners. These data confirm previous findings of physiologic reduction in serum testosterone and PRL levels and suggest that the testosterone decrease is not related to changes in LH pulsatile release, weight, or increased serum cortisol levels.

Comment

There are ways to train in order to maximize the endogenous anabolic hormones such as testosterone and GH, and decrease the endogenous catabolic hormones. Since overtraining can lead to a catabolic hormonal profile, it should be avoided by most athletes. Ideally, finding ways to maximize an anabolic profile may be an alternative to the use of anabolic drugs in sports. By following certain exercise regimens and manipulating diet so as to maximize the effects of endogenous anabolic hormones such as testosterone, GH, and insulin, an athlete can obtain a significant ergogenic effect. At times the effect can be on par with the use of performance-enhancing drugs without the stigma and adverse effects.

10. Burgat V. **[Residues of drugs of veterinary use in food] Les résidus de médicaments a usage vétérinaire dans les aliments.** *Rev Prat* 1991; 41(11):985–990.

Abstract

This study shows that hormonal and nonhormonal residues are present in small amounts in certain foods, but that they create no public health problem as long as their toxicologic significance is evaluated scientifically. This evaluation, which is made for each veterinary drug before applying for authorization to market, leads to the definition of tolerable residual levels as a measure designed to protect the consumer.

Comment

Several studies have documented, in some cases using techniques almost identical to the ones now used by IOC labs, the presence of residues of anabolic steroids in food, including nortestosterone, methyltestosterone, and trenbolone.[1-5] My concern lies not in the health implications of these residues but in the possibility of false-positive tests when the foods containing these residues are eaten by athletes before drug-tested competitions. I am aware of at least one case where a positive

test for anabolic steroids may have resulted from the ingestion of residue-tainted meat.

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2. Evaluation of certain veterinary drug residues in food. Thirty-second report of the Joint FAO/WHO Expert Committee on Food Additives. *World Health Organization Technical Report Series* 1988, No.763: 40.
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11. Fiegel G. **[Drugs interacting with anabolic steroids.] Quali farmaci interagiscono con gli steroidi anabolizzanti.** *Clin Ter* 1991; 136(6):415–420.

Abstract

The author presents a list of possible interactions when anabolic steroids are used in conjunction with other substances. Altogether 53 substances that may give rise to interactions if used simultaneously with anabolic steroids are listed in alphabetical order.

Comment

A number of substances can interact with anabolic steroids, sometimes leading to adverse effects. Most athletes using anabolic steroids use other drugs, either for increased ergogenic effects, or to counteract the adverse effects of the anabolic steroids. It is plausible that without effective medical supervision and monitoring, these athletes are exposing themselves to potentially harmful drug interactions.

12. Goudreault D, Masse R. **Studies on anabolic steroids—6. Identification of urinary metabolites of stenbolone acetate (17 beta-acetoxy-2-methyl-5 alpha-androst-1-en-3-one) in humans by gas chromatography/mass spectrometry.** *J Steroid Biochem Mol Biol* 1991; 38(5):639–655.

Abstract

This is the sixth of a series of studies in which the researchers at the IOC Montreal laboratory look at the metabolism of a number of anabolic steroids, in this case stenbolone acetate. Nine metabolites were detected in urine after oral administration of a single 50-mg dose. Stenbolone, the parent compound, was detected for more than 120 hours after administration. Most of the stenbolone acetate metabolites were isolated from the glucuronic acid fraction. Comparison of stenbolone acetate urinary metabolites with that of methenolone acetate shows similar biotransformation pathways, indicating that the position of the methyl group at the C1 or C2 position in these steroids has little effect on their major biotransformation routes in human.

Comment

This study and others (see the premier issue of this newsletter for studies four and five) have been carried out to delineate the metabolites and excretion patterns of commercially available anabolic steroids. The results of these studies are subsequently used to improve the detection of these compounds in urine.

Book Review

Francis C. *Speed Trap.* 1990 306 pp. Available in Canada from Key Porter Books, $24.95, and in the U.S. from St. Martins Press, $18.95.

Charlie Francis was Ben Johnson's coach. This book details the author's career, the rise and fall of Ben Johnson, and the use of drugs in sports.

In *Speed Trap*, Francis describes the use of drugs in track and field. There is no guilt, no remorse, no hiding — it's a realistic account of drug use in sports today and the associated greed and hypocrisy that surrounds amateur sports.

The book chronicles Ben Johnson's training, his victory at the Seoul Olympics, and his fall from grace. Although we are presented with various scenarios on how and why Ben Johnson tested positive in Seoul, ultimately Ben's positive steroid test will remain a mystery. Was his positive test due to use of injectable stanozolol, the last injection being too close to the meet to have cleared from his system? Or was he surreptitiously given tablets of stanozolol to take — or perhaps Ben took some oral stanozolol thinking that it wouldn't be detected at the time of the meet? I don't think we'll ever truly know.

Speed Trap is enlightened reading for anyone who believes in the purity of amateur sport. However, this book should be read by anyone interested in amateur sports, regardless of their views. The insight that the author shows is refreshing. The reality of sports today is that it is fast becoming polarized. Those who are sophisticated enough to use drugs and get away with it, or perhaps not be monitored for their use, are fast outpacing those who do not use performance-enhancing drugs or at least use less of them.

People must realize that, as in other societal groups, athletes play to win and will use whatever means they can to achieve this end.

Next Issue

The next issue will address the following:

- Problems associated with drug testing, including methods used to escape detection;
- Anticatabolic supplements;
- The anabolic, anticatabolic, and lipolytic effects of GH, as well as ways to maximize endogenous GH secretion;
- Myths and realities concerning the adverse effects of anabolic steroids;
- Use of anabolic steroids in the menopause and andropause; and
- Review of *The Anabolic Reference Guide* and the *Natural Supplement Review.*

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