

Nutritional Supplements and Doping

*Andrew Pipe, MD, and †Christiane Ayotte, PhD

*Canadian Centre for Ethics in Sport, University of Ottawa Heart Institute, and Department of Family Medicine, University of Ottawa, Ottawa, Ontario; and †Laboratoire de Contrôle de Dopage, INRS-Institut Armand-Frappier, Pointe-Claire, Québec, Canada

Context: The problems of doping in sport and the increasing use of nutritional supplements by athletes are issues that intersect to the degree that a large number of supplements may contain substances that are banned in sport. Many supplements contain substances that are associated with significant health hazards. Athletes consuming such supplement products may jeopardize their sporting status, and their health.

Objectives: To clarify and summarize the current status of dietary supplements in general, and to describe specific problems that can be associated with supplement use so that sport physicians might be better prepared to address these issues with their athlete-patients.

Data Source: An analysis of recent and relevant literature accessed through MEDLINE, and interactions with clinicians, laboratory scientists, colleagues, and athletes.

Conclusions: The dietary supplement industry is completely

unregulated in the United States; as a consequence, an abundance of supplement products of dubious value, content, and quality are now available around the world. It is known that many supplement products contain substances that are prohibited in sport—typically stimulants or anabolic steroid precursors. Many supplements contain substances (e.g., ephedrine) that have been associated with significant morbidity and mortality. Sport practitioners have particular responsibilities in addressing this issue. Athletes need to be aware of the problems that can follow supplement use, and sport authorities need to ensure that nutritional education and guidance for athletes is of the highest standard. The need for the appropriate regulation of dietary supplements is emphasized.

Key Words: Doping—Nutritional supplement—Ergogenic aid—Anabolic steroid.

Clin J Sport Med 2002;12:245–249.

INTRODUCTION

The current preoccupation with nutritional supplements demonstrated by many athletes is a reflection of certain societal trends, the presence and persistence of an aggressive, unregulated supplement industry, and the failure of many sport organizations, sport scientists, and physicians to provide appropriate education regarding the nutritional basis of athletic activity. Supplement use in the absence of a specific need, deficiency, or disease is not recommended.¹ While increased ingestion of creatine has been shown to produce small changes in performance in very specific exercise conditions, the expectations of athletes for performance enhancement have been described as “inordinate.”² Increased intake of carbohydrates prior to (carbohydrate loading), during, and after exercise has been noted to improve and sustain performance; the ingestion of caffeine has also been shown to delay fatigue and improve physical performance.^{3,4} Forty percent of the U.S. population is judged to use vitamins and minerals regularly, 14% of that population was estimated to have consumed at least one herbal/supplement product in the week preceding a re-

cent survey.⁵ More than a decade ago, the retail sales of dietary supplements in the United States generated \$3.3 billion.⁶ In 1999, it was estimated that the annual sales of supplement products in the U.S. totaled \$12 billion.⁷ The use of dietary supplements has been increasing significantly in the population at large, and it is perhaps not surprising that athletes should reflect this trend.^{8,9} But it is ironic that for many in sport, nutrition seems now to be a religion rather than a science; it has been the experience of both authors that many athletes, their coaches, and other advisors hold views regarding nutrition that are not scientific, sound, or sensible. No benefits have been demonstrated for many of the products avidly consumed by some athletes.¹⁰ Yet it is clear that an enormous appetite for such products has been created. Some athletes at the Sydney 2000 Olympic games were consuming as many as 18–20 different supplements daily; one competitor ingested 25 separate items each day (Corrigan B, Kazlauskas R. A survey of medications taken by athletes at the Sydney Olympics, 2000. Personal Communication, 2001).

The introduction in 1994 of the “Dietary Supplement and Health Education Act” (DSHEA) in the U.S. has unleashed an industry, a multitude of hucksters, and self-styled nutritional “advisors” whose products are widely advertised, particularly on the Internet, in ways that are often both grandiose and misleading. As a consequence

Accepted May 14, 2002.

Address correspondence to Andrew Pipe, MD, University of Ottawa Heart Institute, 40 Ruskin Street, Ottawa, ON, K1Y 4W7 Canada.
E-mail: apipe@ottawaheart.ca

of this legislation, it is now virtually impossible to ascertain the accuracy and validity of the labeling, content, source, or manufacturer of many commonly advertised products (Table 1). It is important to understand that there is no longer, as a consequence of the passage of the DSHEA, any independent, government regulation of these products. That such products are often advertised beneath a veneer of pseudoscientific information mixed with a variety of glowing "endorsements" serves to confuse athletes even more.

It is known that many nutritional supplements are inadvertently or deliberately contaminated with substances that may cause athletes to test positive when subjected to doping controls. In such instances, it is typical that the products in question contain stimulants, steroids, or steroidal precursors. Millions of men and women are noted to be "currently using potent drugs, widely sold over the counter as 'supplements,' despite their known adverse effects, unknown long-term risks, and possible potential for causing abuse or dependence."¹¹

Sport physicians and scientists, as well as sport administrators, must understand the complexities of the current situation and develop strategies and approaches that will permit athletes and others to appreciate both the lack of any necessity for the use of many supplements and the hazards that may be associated with their use. Principal among such strategies is the recognition that only appropriately qualified professionals should be providing nutritional assessments and guidance to athletes. The sport community is awash with a variety of individuals whose credibility and credentials in the area of sport and nutrition are suspect or self-ordained.

SUPPLEMENTS AND ANABOLIC STEROIDS

The detection of the use of anabolic steroids is based on the presence of the banned steroid, its metabolites, or a distortion of the ratio of testosterone to epitestosterone (the T/E ratio) in a urine sample. It is critical to this discussion to understand that certain steroid products available as "supplements" in the U.S. are metabolized to compounds that also are produced by the metabolism of banned anabolic steroids—19-norandrosterone, produced both by the metabolism of 19-nortestosterone (Nandrolone) or 19-norandrostenedione, is the best example of such a metabolite. Currently, the presence

above a certain level (2 ng/ml in males, 5 ng/ml in females) of 19-norandrosterone in a urine sample will result in a positive doping test as it is deemed to be indicative of the use of 19-nortestosterone (Nandrolone), a banned anabolic steroid. In the past 10 years, the percentage of samples reported positive by International Olympic Committee (IOC)-accredited laboratories for 19-norsteroids accounted for approximately 0.25% of all specimens tested.¹² Clearly it is important that athletes understand the implications of consuming "supplements" that contain steroid precursors. Sadly, it cannot be assumed that only steroid "supplements" or products containing or presumed to contain precursor compounds place an athlete at risk for testing positive. An array of other "nonhormonal" supplements also have been noted to contain steroids or precursor products (creatine, tribulus terrestris, carnitine, chrysin, various "vitamins," minerals, and herbal extracts) distributed in numerous countries have been found to be contaminated with 19-norsteroids in amounts sufficient to cause a positive doping test (Corrigan B, Kazlauskas R. A survey of medications taken by athletes at the Sydney Olympics, 2000. Personal Communication, 2001). The risks of consuming such products only can be reduced when the manufacture of nutritional supplements is appropriately and rigorously regulated.

It has been possible for a number of years for athletes to purchase a variety of androgens, prohormones, or precursors such as DHEA (dehydroepiandrosterone), androstenedione, androstenediol, 19-norandrostenedione, and 19-norandrostenediol either singly or in countless combinations. When marketed as dietary supplements, such products escape any form of regulation. It is revealing to note that an analysis of 16 different preparations of DHEA found that the content of this steroid varied from 0% to 150% of the dosage indicated on the product label; three of the products contained no DHEA whatsoever.¹³ More troubling for sport physicians and sport organizations is the fact that products containing androstenedione have been contaminated with amounts of 19-norandrostenedione sufficient to cause positive doping tests.¹⁴

The issue of steroid precursors came to the forefront in North America in 1998 when the use of androstenedione by a professional baseball player, Mark McGwire, became the subject of media scrutiny and public criticism.¹⁵ Marketed as a so-called "dietary supplement," this steroidal precursor is widely available from a variety of sources in North America and elsewhere. It is alleged that sales of this product increased dramatically following the revelation of its use by this well-known professional athlete.¹⁶ It is also quite clearly forbidden by the IOC and all International Sport Federations, and in the U.S.A. by the National Football League and the National Collegiate Athletic Association.

Norandrostenedione, norandrostenediol, and nortestosterone (Nandrolone) are metabolized and excreted as norandrosterone and noretiocholanolone, as has been discussed. Urine samples collected after the use of such substances will test positive as noted above and, characteristically, an athlete will immediately express surprise

TABLE 1. IOC nutritional supplement analysis

Country	Products	+ve	%age
The Netherlands	31	8	25.8%
U.K.	37	7	18.9%
U.S.A.	240	45	18.8%
Italy	35	5	14.3%
Germany	129	15	11.6%

The results of the analysis of nutritional "supplements" purchased and analyzed in various jurisdictions by the IOC. A significant proportion of the products contained or were contaminated with banned substances (+ve) not listed as ingredients by the manufacturer. [Source: *The International Olympic Committee Medical Commission, Lausanne, Switzerland, April 2002.*]

and innocence at the revelation of a positive test. A careful investigation of more than 150 nonhormonal sport supplements provided by athletes (who blamed their use for failing a doping test) revealed that steroids *not* listed on the label contaminated 18 preparations produced by 12 different manufacturers.¹⁷ Testosterone, itself a strictly regulated substance and therefore not freely available, has been identified as a contaminant and, in fact, the principal constituent of some hormonal “supplements.”¹⁸ Even those “supplement” products that clearly indicate that they contain a steroid are found to fail even the minimal standards of the DSHEA: 11 of 12 brands, containing 8 different steroids, were found to contain less than the amounts listed on the label; one brand contained testosterone.¹⁹

It is clear that those athletes who consume products that contain steroid and steroid precursor products, notwithstanding that they are marketed as “nutritional supplements,” place themselves at risk of testing positive in doping controls. This reality must be communicated to athletes and to those in their entourage. Experience suggests that this can be a very difficult task. Incredulous athletes are loath to consider that their “supplements” may produce a positive doping test, let alone that they are, in all likelihood, of insignificant or no nutritional value.¹

SUPPLEMENTS AND STIMULANTS

In 1960, the amphetamine-related death of a Danish cyclist Knut Jensen catalyzed the development of antidoping programs and drug testing in sport.²⁰ Since, and before, that time, the use of a variety of stimulants has been depressingly common in sport. Ironically, with perhaps two notable exceptions, caffeine and ephedrine, there is little evidence to support the contention that many common stimulants are capable of enhancing performance. Nevertheless athletes continue to ingest such compounds risking their health and positive doping tests in the process.

Caffeine

Caffeine is a ubiquitous substance, consumed daily by an overwhelming majority of the population in a variety of forms. Present in beverages, confectionery, pain medications, and in large numbers of dietary supplements, its use in sport is controlled by examining urine for its presence beyond a certain threshold level (12 µg/ml). There is strong evidence to support its ability to enhance performance at doses similar to those used in everyday life^{21–24} (which are highly unlikely to produce urine levels greater than the threshold noted previously). It has been conclusively demonstrated that doses of at least 9 mg/kg are required to result in the maximal allowable limit established by the IOC; doses as low as 2–3 mg/kg are effective in improving performance.^{25,26} There is marked interindividual variation in urinary caffeine concentrations following ingestion of the same caffeine dose, a fact that has important implications for an athlete and for those charged with developing the rules and regulations regarding doping control. There are sugges-

tions that caffeine is actually ergolytic at high doses, presumably because of the production of agitation, tremors, and mental distraction.²⁷

Because of its ability to impart a sense of energy and arousal, and its known capacity to accentuate endurance performance, caffeine is a favorite ingredient of dietary supplements. Such supplements are often marketed as aids to weight loss, fatigue prevention, and energy production. The presence of caffeine may not be noted on product labels or its presence may be “disguised” by the use of another identifier such as guarana or kola nut (which contain caffeine and other xanthines).

Athletes must use extreme caution when purchasing and using such products. The interindividual variations in caffeine metabolism, the unknown or concentrated quantities of caffeine in a supplement, and the ingestion of other forms of caffeine may produce elevated levels of urinary caffeine capable of producing a positive test result. This may be especially critical for younger athletes or those of small stature. It is possible that increased levels of caffeine may actually retard or impair performance. The inadequacies of the current regulation of nutritional supplements preclude the possibility of an athlete knowing, with confidence, the nature and quantity of the contents of any supplement product—hence the importance of ensuring, to the extent possible, that they understand the implications, and consider the necessity, of any supplement ingestion.

Ephedrine

Sympathomimetics such as ephedrine and related compounds have long been banned in sport. Structurally related to amphetamine, there is little evidence to support the contention that, with the exception of ephedrine, these products are capable of enhancing performance.^{28–30} Initial evaluations of the ergogenic properties of ephedrine did not demonstrate any ergogenic effects.³¹ More recently it has been shown that, particularly in association with caffeine, ephedrine can increase the duration of endurance exercise and enhance anaerobic performance.^{32–34} Ephedrine is prohibited in sport, and a positive doping test results if it is found in the urine at levels greater than 10 µg/ml.

Ephedrine is a very common constituent of nutritional supplements, and in particular is found in many products that are aggressively marketed to athletes. It is present in a broad array of products promoted to assist with weight loss or to increase athletic performance. Ephedrine is derived from ephedra-containing plant sources, and thus is often touted as a “natural” product. It is frequently identified as Ma Huang (Chinese ephedra), and in this guise (or others) may go unnoticed by consumers who may be wary of consuming ephedrine by virtue of cardiovascular or other concerns. Consumers have good reason to be cautious about the ingestion of ephedrine. Concerns about the safety of this compound continue to grow and reflect increasing evidence of the morbidity and mortality associated with its use. Cardiovascular problems predominate, particularly arrhythmias, myocardial infarctions, sudden death, seizures, and stroke (Figure

1).³⁵ The deaths of young athletic individuals following the use of ephedrine-containing “performance-enhancing supplements,” such as “Ripped Fuel” and “Ultimate Orange,” is both tragic and ironic. It is unsettling to note that such problems can emerge in the absence of any preexisting cardiovascular disease, and do not appear to be dose related.³⁶ Of equal concern is the realization that many individuals may develop an ephedrine dependency.^{37,38} Ephedrine-containing products also are suggested as being safe alternatives (“herbal ecstasy”) to drugs like methylenedioxymethamphetamine (MDMA), and may be used by athletes unwilling to participate in the use of street drugs; neuropsychiatric and cardiovascular problems may follow.³⁹ These tragedies, and the added concern that they may be under-reported, have caused both the DSHEA and the availability of ephedrine-containing products to come under attack.⁴⁰ As is the case with all dietary supplements, variation may exist between the labeling and the actual contents of the product; some products fail to list the presence of ephedrine completely.⁴¹

Athletes must exercise vigilance before purchasing, accepting, or ingesting any dietary supplement; not only may the unwitting (or calculated) consumption of ephedrine cause an athlete to test positive, there are also significant health consequences that may follow the use of such supplements.

DISCUSSION

The widespread availability and use of a multiplicity of so called “nutritional supplements” pose specific

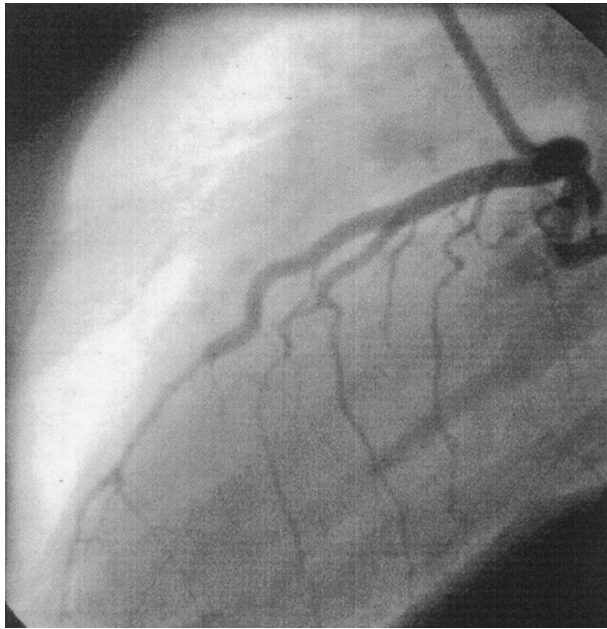


FIG. 1. Marked spasm in the left anterior descending coronary artery of a young woman following the ingestion of a “natural” dietary product containing ephedrine. Cardiac arrest and prolonged resuscitation followed. The patient survived but experiences significant cerebral deficits. [Photo courtesy of Dr. Louise Laramée, University of Ottawa Heart Institute.]

problems for athletes, coaches, and sport organizations alike. The appetite for such products, and the zealotry of those involved in encouraging their use, speaks poorly of the status of science in the preparation, training, and care of athletes. (As an aside, it is interesting to speculate about the degree to which a preoccupation with obtaining the ideal nutritional supplement—an exogenous source of performance assistance—correlates with, or evolves into, a willingness to eventually seek other forms of exogenously administered performance “enhancers.”)

Those in the nutrition, sport medicine, and sport science communities should evaluate the nature, quality, and source of the advice that is currently being provided to athletes regarding diet and performance. A firm commitment to evidence-based practice and a more rigorous scrutiny of what is presented and published in the area of sport nutrition may arrest what seems to be a descent into a world of nostrums and nutritional pseudoscience. Current practices seem all the more skewed when one considers that while athletes and others are clamoring for supplements of various micro- or pseudonutrients, we face significant problems of major nutritional deficiencies in many sport settings. It is surprising to note that, when reviewing the declarations of medication and/or supplement use that accompany drug-testing samples, products such as iron, calcium, folate, and antioxidant vitamins are infrequently encountered—amidst a tidal wave of obscure and imaginatively named supplement products.

Sport administrators need to ensure that athletes are being counseled by appropriately qualified nutrition professionals, and may wish to reconsider the wisdom of entering into sponsorship agreements with members of the nutritional supplement industry until such time as it becomes possible to verify the content, safety, quality, and labeling of its products. Sport physicians must be vigorous, and rigorous, in ensuring that the athletes entrusted to their care are in receipt of accurate information regarding their nutritional practices, and that they are not ingesting products that jeopardize their health or their status as competitors. Those involved in the development and administration of doping-control programs must continue to provide clear, unequivocal advice about the potential problems associated with supplement use while striving to be sensitive, imaginative, and credible in the delivery of those messages. Public authorities must be reminded of their responsibility to protect the public from misrepresentation and the dangers posed by hazardous products; the removal of ephedrine-containing products from the community and the regulation of dietary supplements would seem to be sensible steps.

William Osler, many years ago, suggested “One of the first duties of the physician is to educate the masses not to take medicine.” His advice, intended for a community in which “electric oil salesmen,” carnival barkers, and traveling medicine shows exploited a gullible public, may have particular relevance for sport medicine practitioners today, when terms such as “herbal,” “natural,” “alternative,” “complementary,” and “supplement” may

conceal a bizarre array of concoctions and compounds that are too often worthless and frequently harmful.

REFERENCES

1. Position of the Dietitians of Canada, the American Dietetic Association and the American College of Sports Medicine: Nutrition and Athletic Performance. *Can J Diet Pract Res* 2000;61:176–192.
2. Terjung RL, Clarkson P, Eichner ER, et al. American College of Sports Medicine roundtable. The physiological and health effects of oral creatine supplementation. *Med Sci Sports Exerc* 2000;32:706–717.
3. Applegate E. Effective nutritional ergogenic aids. *Int J Sport Nutr* 1999;9:229–239.
4. Graham TE. Caffeine and exercise: metabolism, endurance and performance. *Sports Med* 2001;31:785–807.
5. Kaufman DW, Kelly JP, et al. Recent patterns of medication use in the ambulatory population of the United States. The Slone Survey. *JAMA* 2002;287:337–344.
6. Cowart VS. Dietary supplements: alternatives to anabolic steroids? *Phys Sportsmed* 1992;20:189–198.
7. Herbal treatments: the promises and pitfalls. *Consumer Reports* 1999;64:44–48.
8. Eisenberg DM, Kessler RC, Foster C, et al. Unconventional medicine in the United States: prevalence, costs, and patterns of use. *N Engl J Med* 1993;328:246–252.
9. Eisenberg DM, Davis RB, Ettner SL, et al. Trends in alternative medicine use in the United States, 1990–1997: results of a national survey. *JAMA* 1998;280:1569–1575.
10. Armsey TD, Green GA. Nutrition supplements: science vs. hype. *Phys Sportsmed* 1997;25.
11. Kanayama G, Gruber AJ, Pope HG, et al. Over the counter drug use in gymnasiums: an underrecognized substance abuse problem? *Psychother Psychosom* 2001;70:137–140.
12. Ayotte C, Levesque F, Cleroux M, et al. Sport nutritional supplements: quality and doping controls. *Can J Appl Physiol* 2001;26(Suppl):S120–S129.
13. Parasrampur M, Schwartz K, Petesch R. Quality control of dehydroepiandrosterone dietary supplement products [Letter]. *JAMA* 1998;280:1565.
14. Catlin DH, Leder BZ, Ahrens B, et al. Trace contamination of over-the-counter androstenedione and positive urine test results for a nandrolone metabolite. *JAMA* 2000;284:2618–2621.
15. Patrick D, Antonen M. McGwire taking hits over use of power pill. *USA Today* August 24, 1998:1A.
16. Dickey C, Helmstaedt K, Nordland R, et al. The real scandal. *Newsweek* February 15, 1999:48–54.
17. Geyer H, Mareck-Engelke U, Schanzer W. Analysis of “non-hormonal” nutritional supplements for prohormones. In: *Proceedings of the 19th Koln Workshop on Dope Analysis*. Koln: Institut für Biochimie (in press).
18. Ayotte C. Nutritional supplements and doping controls. *IAAF New Studies in Athletics* 1999;14:37–42.
19. Green GA, Catlin DH, Starcevic B. Analysis of over-the-counter dietary supplements. *Clin J Sport Med* 2001;11:254–259.
20. Wallechinsky D. *The Complete Book of the Olympics*. Boston: Little, Brown & Company, 1992.
21. Nehlig A, Debry G. Caffeine and sports activity: a review. *Int J Sports Med* 1994;15:215–223.
22. Tarnopolsky MA. Caffeine and endurance performance. *Sports Med* 1994;18:109–125.
23. Bruce CR, Anderson ME, Fraser SF, et al. Enhancement of 2000m rowing performance after caffeine ingestion. *Med Sci Sports Exerc* 2000;32:1958–1963.
24. Collomp K, Ahmatdi S, Catard JC, et al. Benefits of caffeine ingestion on sprint performance in trained and untrained swimmers. *Eur J Appl Physiol* 1992;64:377–380.
25. Graham TE, Spriet LL. Metabolic, catecholamine, and exercise performance responses to various doses of caffeine. *J Appl Physiol* 1995;78:867–874.
26. Kovacs EMR, Stegen JHCH, Brouns F. Effect of caffeinated drinks on substrate metabolism, caffeine excretion, and performance. *J Appl Physiol* 1996;81:1658–1663.
27. Graham TE. Caffeine, coffee and ephedrine: Impact on exercise performance and metabolism. *Can J Appl Physiol* 2001;26(Suppl.):S103–S119.
28. Gillies H, Derman WE, Noakes TD, et al. Pseudoephedrine is without ergogenic effects during prolonged exercise. *J Appl Physiol* 1996;81:2611–2617.
29. Swain RA, Harsha DM, Baenziger J, et al. Do pseudoephedrine or phenylpropanolamine improve maximum oxygen uptake and time to exhaustion? *Clin J Sport Med* 1997;7:168–173.
30. Clemons JM, Crosby SL. Cardiopulmonary and subjective effects of a 60 mg dose of pseudoephedrine on graded treadmill exercise. *J Sports Med Phys Fitness* 1993;33:405–412.
31. Sidney KH, Lefcoe NM. The effects of ephedrine on the physiological and psychological responses to submaximal and maximal exercise in man. *Med Sci Sports* 1977;9:95–99.
32. Bell DG, Jacobs I, Zamecnik J. Effects of caffeine, ephedrine and their combination on time to exhaustion during high intensity exercise. *Eur J Appl Physiol* 1998;77:427–433.
33. Bell DG, Jacobs I. Combined caffeine and ephedrine ingestion improves run times of Canadian Forces warrior test. *Aviat Space Environ Med* 1999;70:325–329.
34. Bell DG, Jacobs I, Ellerington K. Effect of caffeine and ephedrine ingestion on anaerobic exercise performance. *Med Sci Sports Exerc* 2001;33:1399–1403.
35. Haller CA, Benowitz NL. Adverse cardiovascular and central nervous system events associated with dietary supplements containing ephedra alkaloids. *N Engl J Med* 2000;343:1833–1838.
36. Samenuk D, Link MS, Homound MK, et al. Adverse cardiovascular effects temporally associated with ma huang, an herbal source of ephedrine. *Mayo Clin Proc* 2002;77:12–16.
37. Gruber AJ, Pope HG. Ephedrine abuse among 36 female weight lifters. *Am J Addict* 1998;7:256–261.
38. Gill A. Faster, higher stronger: confessions of an ephedrine junkie. *The Globe and Mail* 2002;March 9:L3.
39. Zahn KA, Li R, Purssell RA. *J Emerg Med* 2000;18:122.
40. Fleming GA. The FDA, regulation and the risk of stroke. *N Engl J Med* 2000;343:1886–1887.
41. Gurley BJ, Gardner SF, Hubbard MA. Content versus label claims in ephedra-containing dietary supplements. *Am J Health Syst Pharm* 2000;57:963–969.