

## New Study: Clenbuterol and Heart Disease

Contributed by Dan Gwartney, MD  
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Bodybuilders and other athletes have long sought an effective pharmaceutical means of shedding body fat. Historically, three agents have been most highly regarded as fat-burning drugs; they are clenbuterol, Cytomel (T3) and dinitrophenol (DNP). Of these three, only Cytomel is clinically used in the United States, and only for rare conditions of thyroid disease, not as a weight loss agent. All three of these drugs have been shown to have dangerous side effects.

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### Potential for Harm

The most widely abused of the three drugs is clenbuterol. In part, this is due to the report that clenbuterol is anabolic in animals, as well as a potent fat-burner, though the anabolic effect seems to be minimal or absent in humans.<sup>1</sup> While clenbuterol is used by many athletes, it has found favor with female athletes and entertainers because it is not androgenic, and will therefore not cause the unwanted side effects seen with steroid abuse.<sup>2</sup>

Most experienced users of clenbuterol realize it is a drug with limited effect, and they schedule its use for brief periods, typically using a two-days-on/ two-days-off cycle. This on-and-off schedule is necessary, as clenbuterol causes a rapid down-regulation of the receptors that are responsible for its actions.<sup>3</sup> In other words, clenbuterol will quickly "burn out" the cells and stop working with prolonged use.

However, as use of clenbuterol spreads, less knowledgeable users gain access to the drug, and "inappropriate" use becomes common. The problem is magnified by the fact that clenbuterol users obtain the drug from illicit, black market sources and do not seek professional advice regarding its use, risks or side effects. The risk of harm is greatly increased when the drug is used indiscriminately, or for prolonged periods.

Most of the safety data on clenbuterol has been obtained using animal studies, due in part to its high-risk profile. There are published reports of humans suffering serious consequences with clenbuterol abuse, including overdose and heart attack, but these effects are primarily related to short-term exposure.<sup>4,5</sup>

### A Study of Horses

Recently, a study was published based on an investigation of chronic (long-term) use of clenbuterol and its effect on heart function in exercising horses.<sup>6</sup> The horse may not seem like a good comparison to humans for issues like drug abuse, but in actuality, the horse is an excellent model to use when investigating effects related to exercise.

This study was designed to evaluate any effects of clenbuterol, given five days per week, on the heart size or function of exercising horses. The horses used a treadmill at various speeds for 20 minutes a day, three days per week, and the hearts were examined by echocardiography, which allows the heart to be viewed and measured on a monitor.

The investigators discovered that after eight weeks of clenbuterol treatment, the hearts of the horses had undergone structural changes, which made them work less efficiently and also made them more prone to certain heart problems. These changes were only evident immediately following exercise, when the heart was working harder, but the authors of the study felt that the changes might have become more apparent after a longer treatment period. The data from the study also showed that the VO<sub>2</sub> max of the clenbuterol treated horses was lower, suggesting that they would become

more easily fatigued and have a lower exercise tolerance.

Sadly, the study did not collect data on changes in blood pressure in the animals, leaving some of the results open to interpretation. Previous animal studies, predominantly on mice and rats, have shown significant changes in heart size, with the heart muscle hypertrophy keeping pace with the anabolic effect on other muscles.<sup>7,8</sup> There is some contention as to whether this change in heart size affects function and if it is "negative" growth (pathologic) versus positive growth (physiologic). Several of the studies have determined through measures of RNA, protein content or enzyme levels that the change is physiologic, or a "good" growth. However, none of these studies have shown improved cardiovascular performance as a consequence of the clenbuterol induced changes.<sup>9</sup>

### The Alternative

The demonstration of the decrease in VO<sub>2</sub> max in the horse study is significant because it verifies earlier findings by other investigators that clenbuterol makes animals more easily fatigued, thus indicating that the changes may not be positive, but rather would make the person or animal more likely to suffer from the effects of exercise or stress.<sup>10,11</sup> These findings will be the focus of another report scheduled for publication by the same group.<sup>12</sup>

Considering the immediate, short-term health risks of clenbuterol, the potential long-term health risks and the legal consequences of purchasing or using the drug, one should consider other safer, legal alternatives. It might seem ridiculous to those who have experienced the immediate short-term effect of clenbuterol, but there is an alternative that works as effectively over a longer period, that is currently legal and has recently been shown to be relatively safe, when used as directed. That alternative is ephedrine and caffeine combinations, often referred to as E/C stacks.

Ephedrine and caffeine combinations have a large body of evidence proving their efficacy in promoting fat loss.<sup>13,14</sup> Currently, the only over-the-counter sources of E/C stacks are herbal preparations, typically consisting of Ma Huang and Kola Nut or Guarana, standardized for the ephedrine and caffeine content. The legal and ethical status of these products have been the source of much controversy, as a number of adverse events, including several cases of sudden death, have been attributed to the use of such products. Reviews of the cases where harm has been alleged have been mixed, and thus they remain available for retail purchase.

A recent published study looked at the safety of the herbal E/C stacks.<sup>15</sup> After six months' use, no adverse events or negative side effects could be attributed to the use of herbal E/C stacks, leading the authors to conclude, "... herbal ephedra/caffeine herbal supplements, when used as directed by healthy overweight men and women in combination with healthy diet and exercise habits, may be beneficial for weight reduction without significantly increased risk of adverse events." While the authors caution that negative consequences could be seen with unsupervised use or over-use, the results of this study, and others suggests that E/C stacks may offer a safe and legal alternative to the much riskier, illegal and possibly less effective use of clenbuterol.

### Summing Up

Clenbuterol has long been used to drop body fat by athletes and entertainers, as it has been shown in animal studies to be a potent "fat burner" with some limited anabolic effect. However, considering that the "proper" use of clenbuterol for fat loss requires certain knowledge that may be common among the more sophisticated underground users, the potential for it to be used incorrectly is great, especially as its abuse spreads to the mainstream public.

Clenbuterol has been associated with serious health consequences, including overdose and sudden death. The long-term effect of clenbuterol use on heart function was not previously studied, but it is known to cause the heart to grow, an effect that was felt to be "positive" representing a stronger heart. However, the study reviewed above shows that not only does the heart grow in ways that make it more prone to certain types of heart damage, but cardiovascular function is also compromised, making the animals more easily fatigued.

Given that clenbuterol is illegal, has both long and short-term health risks and does not promote prolonged loss of body fat, it is not a suitable choice for fat loss. Ephedrine and caffeine combinations have been shown to be safe and effective, with sustained fat loss in numerous studies. A great deal of controversy has been raised over the safety of E/C stacks, especially the less regulated herbal products. A recent landmark study has shown that use of herbal E/C stacks is reasonably safe and effective, when used as directed. These two studies should reinforce a decision to choose the safer and legal alternative of herbal E/C stacks, rather than to use the riskier, illegal drug, clenbuterol.

## References

1. Awede BL, Thissen JP, et al. Role of IGF-1 and IGF-BPs in the changes of mass and phenotype induced in rat soleus muscle by clenbuterol. *Am J Physiol Endocrinol Metab* 2002;282(1):E31-7.
2. Prather ID, Brown DE, et al. Clenbuterol: a substitute for anabolic steroids? *Med Sci Sports Exerc* 1995;27(8):1118-21.
3. Newman-Tancredi A, Verrielle L, et al. Down regulation of rat beta-adrenoceptors by clenbuterol or desipramine does not require chronic treatment: [3H] CGP-12177 binding reveals rapid (24 hour) modulation. *Brain Res Bull* 1996;41(2):93-6.
4. Chodorowski Z, Sein Anand J. Acute poisoning with clenbuterol - a case report. *Przegl Lek* 1997;54(10):763-4.
5. Goldstein DR, Dobbs T, et al. Clenbuterol and anabolic steroids: A previously unreported cause of myocardial infarction with normal coronary arteriograms. *South Med J* 1998;91(8):780-4.
6. Sleeper MM, Kearns CF, et al. Chronic clenbuterol administration negatively alters cardiac function. *Med Sci Sports Exerc* 2002;34(4):643-50.
7. Petrou M, Wynne DG, et al. Clenbuterol induces hypertrophy of the latissimus dorsi muscle and heart in the rat with molecular and phenotypic changes. *Circulation* 1995;92(9 Suppl):II483-9.
8. Lynch GS, Hinkle RT, et al. Year-long clenbuterol treatment of mice increases mass, but not specific force or normalized power, of skeletal muscles. *Clin Exp Pharmacol Physiol* 1999;26(2):117-20.
9. Wong K, Boheler KR, et al. Clenbuterol induces cardiac hypertrophy with normal functional, morphological and molecular features. *Cardiovasc Res* 1998;37(1):115-22.
10. Suzuki J, Gao M, et al. Effects of the beta-2 adrenergic agonist clenbuterol on capillary geometry in cardiac and skeletal muscles in young and middle-aged rats. *Acta Physiol Scand* 1997;161(3):317-26.
11. Dupont-Versteegden EE, Katz MS et al. Beneficial versus adverse effects of long-term use of clenbuterol in mdx mice. *Muscle Nerve* 1995;18(12):1447-59.
12. Kearns CF, McKeever KH (submitted). Clenbuterol administration disrupts central mechanisms of aerobic performance in the horse. *Med Sci Sports Exerc*.
13. Toubro S, Astrup AV, et al. Safety and efficacy of long-term treatment with ephedrine, caffeine and an ephedrine/caffeine mixture. *Int J Obes Relat Metab Disord* 1993;17(Suppl 1):S69-S72.
14. Daly PA, Krieger DR, et al. Ephedrine, caffeine and aspirin: safety and efficacy for treatment of human obesity. *Int J Obes Relat Metab Disord* 1993;17(Suppl 1):S73-S78.
15. Boozer CN, Daly PA, et al. Herbal ephedra/caffeine for weight loss: a 6-month randomized safety and efficacy trial. *Int J Obes* 2002;26:593-604.