Clenbuterol Human Effects

The effect of clenbuterol in humans is researched through examining the history and regulations of the drug. Specifically, Alberto Contador’s case is considered.

Tag Words: Clenbuterol; drugs; Beta-2 Agonist; Effects; Thermogenic; Fat; Harmful;

Authors: Jessie Yeh, Horace Lau, Danielle Lovisone with Julie M. Fagan, Ph.D.

Summary (written by Danielle Lovisone)

As a sympathomimetic and Beta-2 agonist, clenbuterol have several deleterious effects on the human body. The drug acts as a thermogenic stimulant, increasing lean muscle mass and respiratory efficiency while reducing fat. Cases on clenbuterol, including animal tests and human occurrences, support these unnatural and potentially harmful effects. With this, athletes and body builders have recently increased their use of the drug. Particularly, Alberto Contador has recently been targeted for having traces of clenbuterol in a urine drug test. Contador claims, instead of doping, this trace amount was unknowingly received from ingesting beef in Spain during the 2010 Tour de France. Although clenbuterol is banned in most areas of the world, this explanation seems plausible because the drug is poorly regulated by organizations such as the FDA. To examine Contador’s case further, our group compiled research on clenbuterol to ultimately hypothesize that Contador received this trace amount from contaminated beef. Our findings were submitted to the World Anti-Doping Agency as part of our Service Project.

Video Link

Class project 2010 fall: www.youtube.com/watch?v=ZTeJiBvbLhA
The Issue: Clenbuterol

The Effects of Clenbuterol on the Human Body By Jessie Yeh

What is Clenbuterol?
Clenbuterol is a chemical compound closely resembling the structure of an amine. Its structure consists of a benzene ring with an attached amine group very similar to that found in chemicals made by the body such as epinephrine. Epinephrine is made by the peripheral nervous system (PNS) to handle the body’s reaction towards situations that require the body’s sympathetic nervous system to take effect; more commonly known as the human body’s fight or flight response. Therefore pharmacologists classify Clenbuterol as a sympathomimetic amine (a drug resembling a chemical found in the sympathetic nervous system). Clinically given as hydrochloride salt (Clenbuterol Hydrochloride), Clenbuterol works as a decongestant and bronchodilator and is given to patients who suffer from breathing disorders such as asthma. More recently however, the use of Clenbuterol has been used both as a weight loss enhancer and a performance-enhancing drug. Its effect as a bronchodilator causes the body to increase heart rate and blood pressure, which in turn enhances the body’s BMR, or Basal Metabolic Rate, causing the body to break down and metabolize energy much quicker. Athletes have been abusing Clenbuterol as a performance enhancer to acquire energy faster and remain in the gym for long periods of time. This abuse has recently been playing a controversial role in the world of professional cycling and many sports associations have been cracking down on the use of Clenbuterol.

Effects of Clenbuterol
Because of its sympathomimetic properties and its structural similarities to epinephrine (shown in the picture below), Clenbuterol is classified as a thermogenic stimulant. Thermogenic chemicals react by increasing the body’s metabolic rate, causing organs and body systems to function quicker and longer. Although this property has deleterious consequences to a majority of cells, the increased energy from the increase of BMR causes a significant improvement in the performance for athletes, breathing for respiratory patients, and weight loss for humans. Clenbuterol increases the aerobic capacity of humans by dilating the bronchioles in the lungs. In order to compensate for the increase of Oxygen, the body’s heart rate increase along the blood pressure to accommodate and re-establish homeostasis. In turn fats are metabolized quicker and the body performs and reacts at a higher sensitive rate.

Uses of Clenbuterol in Food
Although Clenbuterol is more modernly associated with human use as a pharmacological stimulant, uses of Clenbuterol have dated back since the early 90’s as a stimulant used for show animals. Many show animals such as dogs and horses are given Clenbuterol mixed into their feed as a drug to enhance the performance, muscle rearing, and appearance of show animals. Although show
animals make up less than 1% compared to livestock slaughtered for human consumption, the FDA, Food and Drug Administration, and the FSIS, Food Safety and Inspection Service, have been banning the use of Clenbuterol and have been pushing towards stopping the use of Clenbuterol even for show animals. The fear lies in the fact that there is possibility that animals used in shows could become slaughtered for consumption, or that if Clenbuterol is allowed to be given to animals, its usage could become evasive to livestock farmers. More recently however, Clenbuterol has been used by countries in Europe and even some livestock in the US as a means of increasing leanness and protein content. The use in Europe has been more pervasive amongst the general population but is deemed illegal in the states. By increasing the leanness and protein content, farmers are able to yield a higher quality of meat.

**Effect on Consumption of Livestock Given Clenbuterol**

Often when ingested, animals breakdown Clenbuterol into non-toxic products. Scientists have determined that the effect of consuming livestock which have been given Clenbuterol to be very minimal and close to none. Even though, the FDA and FSIS have been very strict to prevent farmers from giving livestock Clenbuterol as a means of insuring high quality livestock free from additives and chemicals. Although Clenbuterol usually leads to limited side effects and the breakdown of non-toxic products, livestock that are given Clenbuterol, especially cows, do have the potential to breakdown the chemical into an even more toxic by-product called ARS found in the liver. Human consumption of animals with this toxic byproduct have shown side effects of increased heart rate, problems with blood pressure, higher risk of heart disease and heart attack, and anxiety.

Overall, the use of Clenbuterol is highly dangerous to both humans and livestock. Although Clenbuterol has the ability to create better quality livestock in the form of leaner meat and higher protein content, the risk that it imposes is far greater. Clenbuterol does have minimal effect on animals especially when the chemical is broken down into a non-toxic byproduct, but when the by-product is broken down into ARS or a more toxic form, the consequences and side effects of consumption are far greater. The FDA and FSIS have done well in banning the use of Clenbuterol in the states not only because of its possible negative tendencies, but also as a method of control hormone additives and other chemical additives in feeds to make meat less organic. By creating this less organic product, humans who consume the livestock have more potential in generating cancers or other maladies created by the chemical additives. Therefore the ban of chemicals and Clenbuterol in livestock is a definite necessity to prevent harmful effects in humans.
Brief Overview Of Clenbuterol (By Danielle Lovisone)

Clenbuterol is a Beta-2 agonist, in which it “binds to a receptor of a cell and triggers a response by the cell.”\(^{ii}\)

When used as a form of doping, clenbuterol enhances physical performance through increased skeletal muscle mass. Likewise, it can equally be utilized as a weight loss drug to reduce body fat, a common use for bodybuilders. Fittingly, according to the Olympic Movement Anti-Doping Code, clenbuterol is a Beta-2 agonist and the use of the compound is prohibited in professional sports.\(^{ii}\)

History of Clenbuterol

Clenbuterol currently serves as an important compound in a prescribed respiratory treatment in horses. The drug, NADA for Ventipulmin® Syrup (Boehringer Ingelheim Vetmedica, Inc.) was approved by the FDA in 1988 for use solely by veterinarians. Because the drug is a product of Boehringer Ingelheim Vetmedica, Inc., clenbuterol can only be found in bulk in the United States under the supervision of this company for use of NADA.\(^{iii}\)

Particularly, NADA treats airway obstruction in horses and is given in the dosage of 0.8-3.2 µg/kg twice daily.\(^{iv}\)

“The Animal Medicinal Drug Use Clarification Act of 1994 (AMDUCA) allows veterinarians to prescribe extralabel uses of certain approved animal drugs and approved human drugs for animals under certain conditions. Extralabel use refers to the use of an approved drug in a manner that is not in accordance with the approved label directions.”\(^{v}\) According to Section 530.41, clenbuterol is banned as an extralabel compound and is therefore prohibited from usage in food animals.\(^{vi}\) Of the several uses surrounding clenbuterol, the use most significant to this discussion involves utilizing the drug for repartitioning effects in food animals. The compound was used to increase mean muscle mass and decrease body fat in show and food animals, similar to the effect in humans. These animals include calves, lamb, chicken and swine.

To exemplify, in the 1990’s the HFA, the Humane Farming Industry, protested against the use of clenbuterol in veal production. The drug was used as a growth stimulant to increase the growth rate of calves.\(^{vii}\) By doing so, meat producers in the veal industry produce meat quickly and therefore increase profits, all the while compromising the health of consumers. After detrimental human side effects were discovered, the FDA banned clenbuterol in food products in 1991.\(^{viii}\)

The FDA seemingly takes several precautions in regulating clenbuterol in the United States. For example, Chromatography and immunoassay screening are used to detect traces of clenbuterol in products.\(^{ix}\) Also, the FDA works with the Justice Department to charge clenbuterol violators under the Federal law.\(^{x}\)
Cases Involving Clenbuterol
Several cases can be examined to support harmful side effects of clenbuterol. Take for instance an experiment described in The Journal of Animal Science. Three groups of male Westar rats were examined, each group having different restrictions on food supply contaminated with clenbuterol. The findings indicate that animals that lacked restriction in diet, consuming clenbuterol, underwent changes in body composition and increased in body weight. Also, studies from Vietnam on the effects of clenbuterol in food sources for swine indicate rapid growth. “Clenbuterol comes in powder form and causes rapid weight gain in pigs, producing a leaner meat. Producers administer it 21 days before slaughter, mixing 1 kilogram into 1,000 kilograms of food. Previously pigs required a year to reach to 100 kilograms, but Clenbuterol has reduced that to three months.”

Although clenbuterol is banned in the United States, several cases displaying the harmful effects of the compound have surfaced over the years. Firstly, poor regulations by the FDA allow for U.S. citizens to illegally smuggle clenbuterol from Canada. This occurred during the case of Vitek Supply Corporation, in which executives smuggled clenbuterol into the United States and added to feed for veal and lamb. Additionally, clenbuterol has been discovered in different cases involving show animals, which can potentially be slaughtered as food. Cases involve administering clenbuterol to livestock to improve physical appearance. Numerous cases have appeared across State Fairs, with as much as “30 percent or more of exhibitors hav[ing] used clenbuterol on their show animals.” The exhibitors can easily receive clenbuterol from veterinarians or through illegal importations from Canada.

International cases of clenbuterol also occur with respect to contaminated food. Contaminated food has occurred in Portugal, Italy, Spain and France. Most recently, clenbuterol cases have surfaced in China. “In February 2009, 70 people fell ill after eating pork products contaminated with clenbuterol.” Other cases specifically in China, occurring since 1998, have affected a total of 1,750 people.

Recently, several cases of clenbuterol usage have been discovered in professional athletes, violating the Olympic Movement Anti-Doping Code and World Anti-Doping Agency. Callum Priestly, a British hurdler, tested positive in March for clenbuterol and was suspended for two years. Polish canoeist Adam Seroczynski also tested positive for clenbuterol. Perhaps the most popular present case involves three-time Tour de France winner Alberto Contador. Tested on July 21, current test results reveal clenbuterol. Because the urine test indicated a “small concentration,” Contador insists that the doping incident is a result of clenbuterol contaminated beef in Spain. According to Franklyn-Miller, it was unlikely for the rider to eat meat before a race day in the mountains. However, Michael Audran, an expert closely associated with the World Anti-Doping Agency, insists that the sample was so small that it was unlikely Contador was using the drug and thus received clenbuterol from contaminated food.
Legal Issues of Clenbuterol (By Horace Lau)

According to the US Department of Justice, is:

"Control status: Clenbuterol is currently not controlled under the Controlled Substances Act (CSA). However, clenbuterol is listed by the World Anti-Doping Agency and the International Olympic Committee as a performance enhancing drug and therefore athletes are barred from its use. At present, no states have placed clenbuterol under control."

At the same time, under U.S. Food and Drug Administration’s regulation, Clenbuterol is illegal to use in animals, which linked to its ability to induce weight gain and a greater proportion of muscle to fat. The use of clenbuterol is prohibited in the US and it’s not licensed or allowed to use clenbuterol for any purposes even it is not under CSA.

The first alerts and warnings about the clenbuterol were dispatched by and to USDA and FDA in the early '90s. At the same time, FDA also warned and notified U.S. Customs to ban and stop the illegal import of clenbuterol and is strictly following up with law enforcement engagements. In 1991, FDA and FSIS were alerted that the veterinary drug clenbuterol was being illegally used to gain competitive advantage in some show animals such as calves, lambs, and swine. FDA takes regulatory action against persons involved in the use or distribution of clenbuterol, FSIS tests meat and liver for illegal residues to help keep contaminated meat out of consumer channels. FSIS and FDA coordinate findings with the Justice Department, which handles prosecution of violators of Federal law. According to USDA officials, show animals comprise less than one percent of the millions of food animals slaughtered in the United States. Nevertheless, the illegal use of clenbuterol could be a public health concern if show animals were to be slaughtered for human food with clenbuterol residues in the liver or in the muscle tissue (meat).

Since the first alert in 1991, USDA and FDA have been working with state departments of agriculture and alerted them about possible illegal use of clenbuterol. FDA also alerted U.S. Customs to block the illegal import of clenbuterol and is following up with enforcement activities. At the same year, FSIS also announced it would condemn meat that tests positive for clenbuterol residues. When an animal shows a positive clenbuterol urine screening test, the animal is identified for tracking during transport to slaughter plants. But in the US, Clenbuterol has been approved for use in animals for the treatment of asthma related symptoms. It is not however FDA approved for human use.

World Anti-Doping Code
In 2004, the World Anti-Doping Code is the document harmonizing regulations regarding anti-doping in all sports and countries. It is established by The World Anti-Doping Agency and was implemented by sports organizations prior to the Olympic Games in Athens, Greece, harmonizing the rules and regulations governing anti-doping across all sports and all countries for the first time. Clenbuterol appear on the code list and ban from athletes.

Case Studies
In 1994, traces of clenbuterol residues were found in animals at stock shows held in Ohio and Oklahoma. In Tulsa, a clenbuterol test of champion animals disqualified six animals including steers, sheep, and a hog.
In 1995, two champion steers were disqualified because residues were found at the National Western Stock Show in Denver. FDA is also undertaking investigations concerning the sale of feed with clenbuterol and its possible use in veal calves in several states. In September 2006 over 330 people in Shanghai were reported to have been poisoned by eating pork contaminated by clenbuterol that had been fed to the animals to keep their meat lean. There are also other informal reports on localized food contamination cases by clenbuterol in the U.S., which led to setting rules that limit consumption of this medicine only to horses. In February 2009, at least 70 people in one Chinese province (Guangdong) suffered food poisoning after eating pig organs believed to contain clenbuterol residue. The victims complained of stomachaches and diarrhea after eating pig organs bought in local markets. In the 2010 Tour de France, Alberto Contador tested positive for clenbuterol. He claims it was due to food contamination, citing the 50 picogram ($5 \times 10^{-11}$ g) per millilitre concentration of the drug in his sample.

**The Service Project**

(written by Jessie Yeh, Horace Lau and Danielle Lovisone; all compiled by Danielle Lovisone)

Mission: To hypothesize that Alberto Contador received a positive urine sample on July 21, 2010 for clenbuterol from eating contaminated beef in Spain. Our hypothesis was emailed to the World Anti-Doping Agency.

Submitted to the World Anti-Doping Agency regarding Alberto Contador’s case:
(Submitted via email as Student Inquiry to info@wada-ama.org)

22 November, 2010

To whom it may concern:

Controversy surrounding the Alberto Contador clenbuterol case is ever intensifying as the results of the urine test from July 21 and 22 have yet to be released. With regard to this issue, research has been compiled by colleagues and me, students at Rutgers University in New Brunswick, New Jersey. We write to you suggesting our hypothesis that Alberto Contador ingested clenbuterol from contaminated beef eaten in Spain.

Chemically, clenbuterol follows an aromatic benzyl backbone with an attached amine group giving it its amine classification and properties. A chemical very similar to clenbuterol is that of other chemical Beta-2 agonists such as epinephrine and norepinephrine which derives from a dopamine backbone structure (Hayas, 1994). Beta-2 agonists are especially important in the human *fight-or-flight* response coupled with the human body’s sympathetic nervous system. What does this mean? Well it means that Beta-2 agonists are responsible for whether or not a human should increase its reaction time, movement, metabolic rate, and other homeostatic properties that are involved in sympathetic reactionary responses. Therefore clenbuterol mimics those with dopamine backbone structures such as epinephrine and norepinephrine which regulate the human body’s sympathetic nervous system and is given the title as a sympathomimetic amine (mimicking sympathetic nervous system chemicals).
Uses of Clenbuterol have become medically popular with helping patients who suffer with chronic asthma. Clenbuterol’s ability to mimic sympathoamines helps asthma patients with bronchodilation to increase oxygen intake and relax bronchiole fibers. Although clenbuterol has good potential benefits, it is not medically favorable due to its other side effects pertaining to its ability to mimic sympatioamines (Muscling, 1992). Because clenbuterol mimics epinephrine, an increase of clenbuterol into the human body has the potential to exacerbate the epinephrine response coupled with the fight-or-flight response. Mainly clenbuterol can be potentially dangerous because it has the ability to drastically alter and increase the human basal metabolic rate, more commonly known as the metabolic rate. The chemical consequences of increasing the basal metabolic rate causes humans to burn fat from food reserves and increase energy output of the body (Muscling, 1992). This scenario has caught the attention of many organizations such as the FDA and World Anti-Doping Agency, relating to animal and professional athlete abuse.

Based on the Drug Enforcement Administration, US Department of Justice, Clenbuterol is an illegal drug for human consumption, with the ability to increase lean muscle mass and reduce body fat. Clenbuterol can produce adverse cardiovascular and neurological effects, such as heart palpitations, muscle tremors, and nervousness. The symptoms, which will include increased heart rate, headache, dizziness, nausea, vomiting, fever, and chills, typically resolve within two to six days.

Since clenbuterol’s first appearance in 1990, the chemical amine has made several international headlines in regards to human abuse (Duncan, 2000). Because clenbuterol increase the basal metabolic rate and allows abusers who sample the substance to increase energy output, it is seen as a cheat drug to help athletes continue energy metabolization in times of body fatigue coupled with long-distance muscle aggravation (Spann, 1995). The abuse of clenbuterol by professional athletes made international headlines when Spanish Cyclist Alberto Contador was tested positive for clenbuterol in 2010. In this case, Contador claims that he ingested the contaminated beef on July 20, 2010, a rest day during the Tour de France. It is understood that the three-time Tour de France winner tested positive only on July 21, 2010 for 50 pg/mL of clenbuterol and on July 22, 2010 for half of that amount. These results appropriately reflect the biphasic half-life of clenbuterol, which is 25-39 hours. Also, because an average of 70-80% of clenbuterol is absorbed, Contador initially ingested about 2.0x10^{-10} pg/mL. With regard to the amount ingested, it remains that it is an extremely small amount of clenbuterol. In order for clenbuterol to have a substantial effect on a human, an amount of 60-120 µg/day must be taken. This amount is concluded from the use of clenbuterol by bodybuilders and athletes. It is obviously clear that Contador’s contamination (5.0 x10^{-11} g/mL) is substantially less than the amount needed for an appropriate athletic response (60-120 µg/day). If Contador had intentionally doped on clenbuterol, he would have needed to take a larger dosage of the drug to obtain a desired effect. Therefore, it seems very likely that he received the clenbuterol contamination from contaminated beef.

Furthermore, Douwe de Boer is the Dutch scientist Contador hired to write a report explaining how the consumption of contaminated meat might have caused Contador’s positive test for clenbuterol. Douwe de Boer examined the history of clenbuterol, the human effects and Contador’s case. He ultimately concluded that, because the amount detected in the urine sample
was so miniscule, Contador's positive test for clenbuterol is based on the consumption of contaminated meat (Douwe de Boer, 2010).

It has been reported that the WADA has tested meat from the butcher and slaughterhouse in Irun, Spain where Contador claims he received the contamination from. Traces of clenbuterol have not been detected in the beef and slaughterhouse. Although the tests were found negative for clenbuterol contamination, the meat may have still been contaminated. The slaughter of the contaminated animals may have been postponed to ensure contamination could not be detected through testing. Additionally, about four months passed before the WADA released the results of the beef testing. This is sufficient time for clenbuterol to pass through the cattle system and for detection to be untraceable. Essentially, the miniscule amount of clenbuterol detected and unreliability of the slaughterhouse testing suggest that Alberto Contador ingested clenbuterol from contaminated meat.

Written by: Jessie Yeh, Horace Lau, Danielle Lovisone

Sincerely,
Danielle Lovisone
Rutgers, The State University of New Jersey
School of Environmental and Biological Sciences, B.A. Biological Sciences 2011
(With attachment file of Clenbuterol research on issue added)

Editorials

Jessie Yeh
Issues in Animals and Agriculture
October 13, 2010

An Insider’s Perspective ~ Organic FOR THE WIN, Clenbuterol Kills your Soul: Yes, we all know that the FDA is extremely anal concerning the use of ‘illegal’ substances (as deemed by them) on animal feed. When it comes to Clenbuterol, an almost harmless substance that shows relatively little to no after effects, the FDA has not made any exceptions. Clenbuterol, seen as animal steroids or animal HGH, doesn’t seem to be as popular when compared to professional sports; but then again, who really watches dogs on ESPN 2? Clenbuterol works very similar to other performance enhancing drugs. Its chemical constituents deal with sympathomimetic properties whose structure is very similar to the fight or flight hormone, epinephrine. Animals given clenbuterol in their feed thus gain an advantage in the form of a thermogenic stimulant, allowing for the animals to break down food faster, rapidly increase basal metabolic rate, and increase food content. Personally, I have no care in the world whether or not the National Dog Breeders Cup uses clenbuterol or not. The FDA is banning the ingestion of clenbuterol in animal feed because of its idea that the substance is foreign, not natural, and could possibly cause side effects. But should clenbuterol be banned in the world of professional animal breeding? Does it matter? I’m not too inclined into eating dogs, cats, and horses. But clenbuterol in our food, given to animals such as cows does seem to leave a cancerous taste in my mouth. I would personally not like to see some foreign ingredient given to my cows so that my beef will have less fat content and higher protein content. Sure the beef might taste better and be of better
Nothing will ever beat the taste of a pure organic animal given by God to us to eat and enjoy.
Sure there could be many positives to clenbuterol other than the higher protein content meat. If
FDA allows for such chemicals to be added, food corporations could potentially do a wide
variety of chemical add-ons to enhance flavor, make meats less dangerous to our cholesterol,
modify meats to be able to feed more people such as the hungry, and much more. But we as
people pay a price for that; our livelihoods. Take a look in our society today ~ look at all those
unhealthy soda bingers addicted to that high fructose corn syrup and even more depressing are
those who need some sort of sweet binge from soda in the highly cancerous form of aspartame.
We as people in society are no longer healthy. What happened to good old water? Or freshly
squeezed juice? In essence, clenbuterol could be great for people especially when it shows little
to no side effects. But this columnist is going to have to side with the FDA because once we let
chemicals touch our food; we lose a little bit of our humanity. We lose our touch with nature,
our connection to our organic green earth, and we push our bodies to the limit with all these new
chemical add-ons. So in the end, we must say NO to clenbuterol and say YES to organic
products. All natural is the best!

Danielle Lovisone
The Washington Post- Letter to the Editor
Email to: letters@washpost.com

Regarding the article “Mother: Contador could quit regardless of verdict”:
I find it very likely that Contador ingested clenbuterol through contaminated beef. Clenbuterol is
a growth stimulant with a half life of 25-39 hours. The cyclist claims to have ingested the
Spanish-raised tainted beef on July 20. Urine tests throughout the race revealed Contador tested
positive only on July 21, 2010 for 50 pg/mL and appropriately on July 22, 2010 for half of that
amount.
While primarily banned, clenbuterol remains poorly regulated across the world. Conceivably,
clenbuterol could have easily been illegally injected into the Spanish beef. After all, is
clenbuterol continually regulated in food animals within the United States?
Danielle Lovisone
Vineland, New Jersey

Letters to the Editor
New York Times
620 Eighth Avenue
New York, NY 10018

5, November, 2010
Juliet Macur
New York Times
New York

Dear Madam,

SUBJECT: To the case of Contador who was notified of the positive test of Chenbuterol on Aug. 24.

Refer to the Douwe de Boer who Contador hired, he claimed the consumption of Chenbuterol is from contaminated meat. But base on the Drug Enforcement Administration of US Department of Justice, the half life of Chenbuterol in human body is 25-39 hours when it is directly absorbed (70-80%) and remains in the body for awhile. It means if he claimed he did not consume any Chenbuterol, he will still need to consume quite noticeable amount of contaminated meat within 40 hours. So, it shows the positive result is unlikely caused by contaminated meat. I hope the World Anti-Doping Agency will concern this integrity matter seriously.

Thanking you

Yours sincerely,
Horace Lau.
Senior undergraduate student.
Rutgers University

The Effects of Clenbuterol Sources:

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