SP.235 / ESG.SP235 Chemistry of Sports
Spring 2009

Scandals through the sports

SP.235 Wednesday April 15, 2009

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CBC on-line article:

- 10 Drug Scandals from CBC Sports Online | Jan. 19, 2003,

From: http://www.cbc.ca/sports/indepth/drugs/stories/top10.html

They compiled a list of 10 of the most influential – and bizarre – drug cases in the past few decades

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The List

1. E. German athletes & government sponsored cheating
2. 1983 Pan Am Games: Dawn of drug testing
3. The U.S. Track & Field coverups
4. Canada's shame: Ben Johnson
5. Last to first: Irish swimmer Michelle Smith
6. Fake dynasty: Chinese swim team
7. Tour de France: Whatever it takes
8. Baseball: Home runs in bulk
9. Cross country skiing and doping: a Nordic tradition
10. Nandrolone goes for the Grand Slam

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1983 Pan Am Games: Dawn of drug testing

- The modern age of drug testing essentially started at the 1983 Pan Am Games in Caracas, Venezuela. A team of scientists, led by chemist and drug-testing chief Manfred Donike of Germany, developed a new method for steroid testing in anticipation of two large international sporting events that year, the Pan Games and world track and field championships.
- What followed paved the way for drug testing for years to come.
- Canadian weightlifter Guy Greavette was at the centre of what became the first international drug scandal in sports. Greavette, along with teammate Michel Viau, was stripped of his medals and handed a two-year suspension after testing positive for steroids.

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1983 Pan Am Games: Dawn of drug testing

- The Pan Am drug testing caught a lot of athletes by surprise. After Greavette's positive test, a dozen American athletes in various events suddenly withdrew from the competition and returned to the U.S., and at least another dozen athletes from other countries also left without explanation.
- Nineteen athletes in total failed drug tests at the 1983 Pan Ams.

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The East Germans

Photo removed due to copyright restrictions.

A East German Women swimmer

Photo removed due to copyright restrictions.

Dara Torres (41 yrs old)

From New York Times, Dec 1991:

OLYMPICS; Coaches Concede That Steroids Fueled East Germany's Success in Swimming

- The stunning domination of international swimming by East German women for nearly two decades was built upon an organized system of anabolic-steroid use, a group of 20 former East German coaches confirmed yesterday.

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The “Women” German swimmers

Photos removed due to copyright restrictions.

At the first world swimming championships, in 1973, East German women won 10 of the 14 gold medals available, setting eight world records. Three years later at the Summer Games in Montreal, the East Germans won 10 of the 12 gold medals for individual events. When a rival coach noted with some sarcasm that the voices of many of the East German women were unusually deep -- a telltale sign of the effects of steroid use in females -- an East German coach replied, "We came here to swim, not sing."

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The “Women” German swimmers

- The victims all received Oral-Turinabol - an anabolic steroid containing testosterone made by Jenapharm. The "blue bean" had astonishing powers - accelerating muscle build-up and boosting recovery times - but its subsequent side effects were catastrophic: infertility among women, embarrassing hair growth, breast cancer, heart problems and testicular cancer. An estimated 800 athletes developed serious ailments.
- Intriguingly, some of the world records set by East German athletes while using Oral-Turinabol have not been bettered.

Reference: http://www.guardian.co.uk/sport/2005/nov/01/athletics.gdnsport3

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5. Last to first: Irish swimmer Michelle Smith

- Irish eyes were smiling during the 1996 Atlanta Olympic Games. Michelle Smith was the pride of Ireland after winning three gold and one bronze medal in the pool.
- No one else was smiling. Her rise to the top of the swimming world was extremely suspicious.
- In two previous Olympic Games, Smith's best result was 17th in the 200-metre backstroke.
- In 1993, she was ranked 90th in the world in the 400 individual medley, but after training with husband Erik de Bruin – a former Dutch discus thrower who was under a four-year suspension for failing a drug test – she vaulted into 17th in the world by the next year.

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5. Last to first: Irish swimmer Michelle Smith

By Atlanta, the 26-year-old Smith had won several European titles and trimmed a whopping 17 seconds off two personal bests.

- After her Olympic success, it was discovered that FINA, swimming's international federation, had repeatedly expressed concern that Smith was unavailable for out-of-competition drug tests from 1995 onward.

Photo removed due to copyright restrictions.

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5. Last to first: Irish swimmer Michelle Smith

Finally, in 1998, two drug testers showed up at Smith and de Bruin's home.

Smith gave them a sample, but because she was wearing a bulky sweater, the tester couldn't see what she was doing. The sample was sealed and sent to a Barcelona lab for examination. The results were shocking. The sample contained a level of alcohol that would be fatal if consumed by a human.

Photo removed due to copyright restrictions.

FINA concluded that the sample had been manipulated, that whiskey had been added as a masking agent and they suspended Smith for four years.

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6. Fake dynasty: Chinese swim team

- Dihydrotestosterone, anabolic steroids, erythropoietin and human growth hormones. All banned substances. All used by various members of the Chinese national swim team in the last 15 years.
- China did not register among the world's swimming powers until the 1990s, and when they did, they did with a bang.
- The country won four swimming gold medals at the 1992 Barcelona Olympics and then took 12 of 16 women's titles at the 1994 world championships.
- The team's sudden success fuelled suspicion of drug use, and by the next big competition, those hunches proved true.

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6. Fake dynasty: Chinese swim team

- Eleven athletes tested positive for dihydrotestosterone at the 1994 Asian Games. The big bust decimated the swim squad for the 1996 Olympics (they won just one gold), but soon enough the Chinese were back on top again. Not for long, however.

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Anabolic Steroids/Androstenedione

- Used because it increases muscle mass and strength
- Either take testosterone or one of its precursors, dehydroepiandrosterone (DHEA), androstenedione or dihydrotestosterone (DHT)

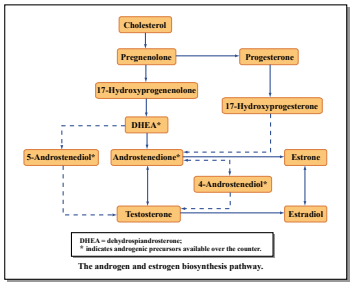

Image by MIT OpenCourseWare.

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6. Fake dynasty: Chinese swim team

- Four positive tests before the 1998 world championships along with the vials of the human growth hormone found in breastroker Yuan Yuan's luggage before the worlds signalled that doping was still thriving in China's pools.
- Though the country maintained there was no systemic doping on its swim teams, the statistics say otherwise.
- Over 40 Chinese swimmers since 1990 have failed drug tests. That's triple the amount of any other swimming country during the same period of time.

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6. Fake dynasty: Chinese swim team

- After pressure from FINA, swimming's governing body, China's swim association promised stricter drug testing and higher penalties for cheats.
- Just before the 2000 Sydney Olympics, China removed four swimmers from its team because of "suspicious" drug test results.
- Chinese swimmers were rarely on the podium in major competitions until the 2003 world aquatic championships in Barcelona. There, the women's team collected seven swimming medals, including three gold.

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7. Tour de France: Whatever it takes

- Enthusiasts say the Tour de France is the biggest, hardest, most gruelling race there is, a prize so precious that cyclists will do anything to win. And they have.
- In the past, riders have scattered broken glass and fans have tossed nails on the road to confound rivals. And that's just for starters.
- In the 1960s, riders attempted to gain a competitive edge with amphetamines and alcohol. In doing so, Britain's Tim Simpson lost his life during the 1967 Tour.

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Why amphetamines and alcohol?

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Why amphetamines and alcohol?

- Amphetamines:nervous system stimulant drugs that increase alertness, self-confidence and concentration, and decrease appetite while creating a feeling of increased energy. The chemical structure is similar to the naturally occurring adrenaline and noradrenaline that is produced by the body. The effects of amphetamines are similar to cocaine, but last longer.

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Why alcohol?

- alcohol is a central nervous system depressant.
- It would probably be used to bring the cyclists down from the speed high.

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7. Tour de France: Whatever it takes

- Some say cycling faced a near death following the 1998 doping scandal in which French officials caught an employee of the Festina cycling team with a carload of performance-enhancing drugs, including erythropoietin (EPO) – a hormone that helps the blood carry more oxygen, letting you go faster and longer on your two wheels.

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EPO/Blood doping

- EPO (Erythropoetin) is naturally produced in the kidneys to regulate red blood cell production.
- The FDA has approved it for medical use in chronic renal failure and certain types of anaemia

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EPO/Blood doping

- From the website: http://www.aranesp.com/
- CLINICAL PHARMACOLOGY: Mechanism of Action
- Aranesp® stimulates erythropoiesis by the same mechanism as endogenous erythropoietin. A primary growth factor for erythroid development, erythropoietin is produced in the kidney and released into the bloodstream in response to hypoxia. In responding to hypoxia, erythropoietin interacts with progenitor stem cells to increase red blood cell (RBC) production. Production of endogenous erythropoietin is impaired in patients with chronic renal failure (CRF), and erythropoietin deficiency is the primary cause of their anemia. Increased hemoglobin levels are not generally observed until 2 to 6 weeks after initiating treatment with Aranesp®

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Why would you want to boost your red blood cells?

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Blood doping

- From the Tour de France 2006: (Washington post)
- The drug scandal revolves around a sports doctor, Eufemiano Fuentes, the head of hematology at a Madrid hospital who had worked with several cycling teams. Fuentes allegedly helped riders and athletes from other unidentified sports engage in different kinds of drug use and blood doping to enhance their performance.
- The blood doping reportedly involved drawing oxygen-rich blood at high altitudes to obtain a concentrate of red blood cells, then injecting them back into riders before a race to boost endurance.

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Blood doping

- The best way to get around the tests is to take your own blood out of your body, purify the red blood cells (by centrifugation) and transfuse it back into you
- So basically you are giving yourself a blood transfusion using your own blood

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From the Paper: popular supplements

"EPO is an unquestionably dangerous substance for athletes to use. Potential adverse effects center on thromboembolic events due to the increased packed red blood cell count and viscosity after administration. The most common adverse effects seen with medical use of EPO are hypertension, seizures and thromboembolic events. There is little doubt in the minds of many in the medical community that several untimely deaths of elite cyclists and other athletes were related to blood doping or the use of exogenous EPO."

From Juhn, M. S. "Popular sports supplements and ergogenic aids." *Sports Medicine* 33, no. 12 (2003): 921-939.

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From the Paper: popular supplements

Text removed due to copyright restrictions.
See Juhn, M. S. "Popular sports supplements and ergogenic aids." *Sports Medicine* 33, no. 12 (2003): 921-939.

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How can you naturally boost your red blood cell count?

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How can you naturally boost your red blood cell count?

- Work out at low O_2 levels (I.e. in the mountains) and then race at high O_2 levels (I.e. sea level)
- Sleep in a altitude chamber (low O_2levels)

2009 Colorado Altitude Training 150 Tent CAT 9 Generator (Item: CAL800 from the competitive cyclist): cost: 4449.00

From their website: Lance Armstrong was fond of saying that he won the Tour in training. Besides the long miles, the mountain-based training camps, the carefully-weighed food, the guy was sleeping at altitude.

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Altitude Tent:

2009 Colorado Altitude Training 150 Tent CAT 9 Generator (Item: CAL800 from the competitive cyclist): cost: 4449.00

From their website: Lance Armstrong was fond of saying that he won the Tour in training. Besides the long miles, the mountain-based training camps, the carefully-weighed food, the guy was sleeping at altitude.

Courtesy of Colorado Altitude Training. Used with permission.

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EPO Test

- The adopted by WADA (World Anti-Doping Adgency) urine test for EPO is based on a combination of isoelectric focusing on a gel (a semi-analytical separation of proteins according to the molecules' net electric charge), the transfer of proteins from gel to a special paper and protein detection by a double immunoblotting, not well established complicated and operator-dependent procedure to immunologically detect proteins of interest with an antibody color reaction.
- Link on the web

38

EPO test

Beullens, M., J. R. Delanghe, and M. Bollen. "False-positive detection of recombinant human erythropoietin in urine following strenuous physical exercise." *Blood* 107, no. 12 (June 2006): 4711-4713.

39

EPO test

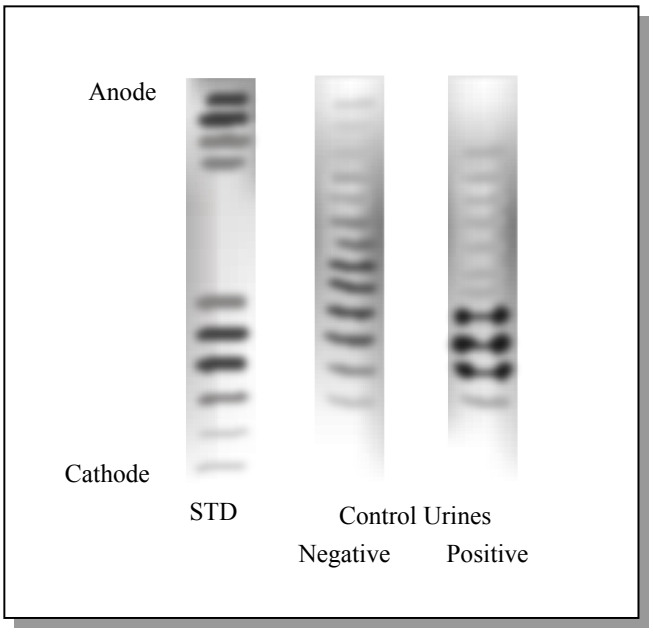

Image by MIT OpenCourseWare. Adapted from Figure 1 in Catlin, D,. et al. "False-Positive EPO Test Concerns Unfounded." *Blood* 108, no. 5 (September 2006): 1778.

40

EPO tests

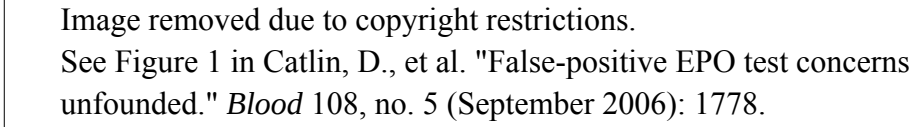
Image removed due to copyright restrictions.
See Figure 1 in Catlin, D., et al. "False-positive EPO test concerns unfounded." *Blood* 108, no. 5 (September 2006): 1778.

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A new and improved way to blood dope

- IOC announced it would retest blood samples from the Beijing Olympics for a new performance enhancing drug.
- So far three stage winners of the TDF have tested positive for Continuous Erythropoiesis Receptor Activator ("CERA") a new generation of EPO which stimulates bone marrow to produce more red blood cells and which was developed to treat anemia.

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CERA

- Roche's new anaemia drug CERA highly effective in dialysis patients with chronic anaemia
- Studies have shown that CERA has unique activity at the receptor site. It is postulated this is related to its repeated and rapid attachment and dissociation from the receptor involved in triggering erythropoiesis (red blood cell formation) together with an extended serum half life. This results in more potent stimulation of erythropoiesis, both in magnitude and duration, compared to standard epoetins.
- (reference: Roche Website at : http://www.roche.com/inv-update-2003-11-17)

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A new and improved way to blood dope

- So far, besides the cyclists who have been caught, there is evidence the drug has also made its way into track and field (Marion Jones tested positive for EPO amongst other banned substances) and officials from the World Anti-Doping Agency expect a number of positive tests among the 979 blood samples from the Beijing Olympics.
- Links;
- http://www.guardian.co.uk/sport/2008/oct/09/drugsinsport.olympics2008
- http://www.cyclingnews.com/news.php?id=news/2008/oct08/oct08news2
- http://www.bikeradar.com/news/article/olympic-riders-blood-samples-to-be-reanalysed-with-new-epo-cera-tests--18901

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More Cycling and illegal drugs

Floyd Landis won the Tour de France in 2006
"Landis allegedly tested positive for a skewed testosterone-epitestosterone ratio following his remarkable come-from-behind performance in the 17th stage of the 2006 Tour." (VeloNews.com)

Read the entire article here:
http://www.velonews.com/news/fea/12047.0.html

45

The test

Ritter, Steve. "The Dope On Testosterone Tests." *Chemical and Engineering News* 84, no. 35 (August 2006): 43-45.

Read the entire article here:
http://pubs.acs.org/cen/science/84/8435sci4.html

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The test

Ritter, Steve. "The Dope On Testosterone Tests." *Chemical and Engineering News* 84, no. 35 (August 2006): 43-45.

Read the entire article here:
http://pubs.acs.org/cen/science/84/8435sci4.html

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The Results

Floyd Landis will be stripped of his Tour de France crown and banned from the sport for two years for testing positive for synthetic testosterone after an arbitration panel on September 20, 2007 which affirmed the finding by the US Anti-Doping Agency.

Link to the Boston Globe Article

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9. Cross country skiing and doping: a Nordic tradition

- Attention cross-country skiers: If you want to cheat, you may not want to leave that blood-transfusion equipment lying around your house.
- That's what some members of the Austrian cross-country ski team did at the Salt Lake City Olympic Games. The IOC began an investigation after a cleaner found blood-transfusion materials in a residence used by the Austrians during the Games.

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9. Cross country skiing and doping: a Nordic tradition

- The team's results were reassessed, and after a three-month investigation, two athletes (non-medallists) were disqualified and two team officials were banned from the next two Winter Olympics.
- The Austrians claimed the equipment was used for ultraviolet radiation treatment of athletes' blood to treat and prevent colds and flu, not for performance-enhancing purposes.

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8. Baseball: Home runs in bulk

- Between Mark McGwire's andro usage and Ken Caminiti's revelation in Sports Illustrated about steroids in baseball, the sport is having an image crisis.
- McGwire went from the svelte American League rookie of the year in 1987 to the heavy-hitting home run king who broke Roger Maris' single-season home run record in 1998.
- McGwire said the transformation in his size was the combination of hard work and an over-the-counter testosterone-producing pill called androstenedione, or andro.

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8. Baseball: Home runs in bulk

- Andro became controversial because it is banned by the IOC, NFL, NBA and NHL, but not by Major League Baseball.
- In May of 2002, Jose Canseco announced his retirement from baseball, and as a parting shot (and perhaps a promo for his tell-all book) he said 85 per cent of all baseball players used steroids. Later, Canseco admitted to taking steroids himself.
- Later that month, Sports Illustrated published an investigative report describing professional baseball as "a pharmacological trade show." In the article, former National League MVP Ken Caminiti told the magazine "at least half the guys are using steroids."

54

8. Baseball: Home runs in bulk

See SI.com, "Bonds exposed: Shadows details superstar slugger's steroid use." March 7, 2006.

http://sportsillustrated.cnn.com/2006/baseball/mlb/03/06/news.excerpt/index.html

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From the SI website

See SI.com, "Bonds exposed: Shadows details superstar slugger's steroid use." March 7, 2006.

http://sportsillustrated.cnn.com/2006/baseball/mlb/03/06/news.excerpt/index.html

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http://sportsillustrated.cnn.com/2006/baseball/mlb/03/06/news.excerpt/index.html

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Alex Rodriguez

See Roberts, S., and D. Epstein. "Sources tell SI Alex Rodriguez tested positive for steroids in 2003." SI.com, February 7, 2009.

http://sportsillustrated.cnn.com/2009/baseball/mlb/02/07/alex-rodriguez-steroids/

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http://sportsillustrated.cnn.com/2009/baseball/mlb/02/07/alex-rodriguez-steroids/

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Marion Jones

Athlete profile

Jones pleads guilty, admits lying about steroids

Marion Jones has had her gold medals stripped from her. (link to story)

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Human Growth Hormone

- From the blood sampling paper

Text removed due to copyright restrictions.

See Section 3.1 in Birkeland, K. I., and P. Hemmersbach. "The Future of Doping Control in Athletes: Issues Related to Blood Sampling." *Sports Medicine* 28, no. 1 (1999): 25-33.

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Human Growth Hormone

- From the blood sampling paper

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See Section 3.1 in Birkeland, K. I., and P. Hemmersbach. "The Future of Doping Control in Athletes: Issues Related to Blood Sampling." *Sports Medicine* 28, no. 1 (1999): 25-33.

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More Baseball Scandals

- Roger Clemens's former trainer Brian McNamee said that he injected both Roger Clemens and his wife with HGH
- Clemens testified in front of Congress (see link) and threw his wife under the bus

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SI photoshoot

- Debbie Clemens took HGH before this SI swimsuit photoshoot

Photo removed due to copyright restrictions.
http://nyystadiuminsider.com/uploaded_images/clemdeb-700541.jpg

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10. Nandrolone goes for the Grand Slam

- Over the past decade, the sporting world has seen a rash of positive tests for the banned steroid nandrolone, giving it the unofficial title as the most common drug used – intentionally or inadvertently – by athletes today.
- Nandrolone has been implicated in hundreds of recent doping cases involving athletes in just about every sport, especially track and field, cycling, soccer and tennis.
- And almost immediately after these failed drug tests, the denials and excuses follow. The most common reason for a positive test? Contaminated nutritional supplements, vitamins and energy drinks.

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Text removed due to copyright restrictions.

"Hammer Nutrition Sued: Rebekah Keat, Mike Vine File over Supplement Contamination." *Inside Triathlon* (April 2008): 12.

68

Back to Supplement contamination

- Because of the unusual number of positive tests, scientists believe the steroid may be contained in improperly labeled nutritional supplements popular with high-performance athletes. However, the IOC and IAAF, track and field's governing body, stipulate that athletes are responsible for what they put in their bodies.

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The next level of cheating - epigenetics!

- There currently is no test for seeing if you have excessive methylation of your DNA
- If you employ the concepts of epigenetics to your own system, is that cheating?

70

Cheating or just good genes?

Lee, S-J, and A. C. McPherron. "Regulation of myostatin activity and muscle growth." *PNAS* 98, no 16 (2001): 9306-9311.

Myostatin is a transforming growth factor-β (TGF-β) family member that plays an essential role in regulating skeletal muscle growth (1). Myostatin is expressed initially in the myotome compartment of developing somites and continues to be expressed in the myogenic lineage throughout development and in adult animals. Mice carrying a targeted deletion of the myostatin gene have a dramatic and widespread increase in skeletal muscle mass. Individual muscles of myostatin null mice weigh approximately twice as much as those of wild-type mice as a result of a combination of muscle fiber hyperplasia and hypertrophy. The myostatin sequence has been highly conserved through evolution (2). Remarkably, the human, rat, murine, porcine, turkey, and chicken myostatin sequences are identical in the biologically active C-terminal portion of the molecule following the proteolytic processing site. The function of myostatin also appears to be conserved across species, as mutations in the myostatin gene have been shown to result in the double muscling phenotype in cattle (2–5).

These findings have raised the possibility that pharmacological agents capable of blocking myostatin activity may have applications for promoting muscle growth in human disease settings as well as in livestock animals. To identify novel strategies for blocking myostatin activity, we investigated the regulation of myostatin signaling. Here, we present evidence that myostatin, like TGF-β, may normally exist *in vivo* in a latent complex with the propeptide (the portion of the precursor protein upstream of the proteolytic processing site) and that on activation, myostatin may signal by binding to activin type II receptors.

Source: Lee, S-J, and A. C. McPherron. "Regulation of Myostatin Activity and Muscle Growth." *PNAS* 98, no. 16 (2001): 9306-9311.

Effect of inhibiting myostatin

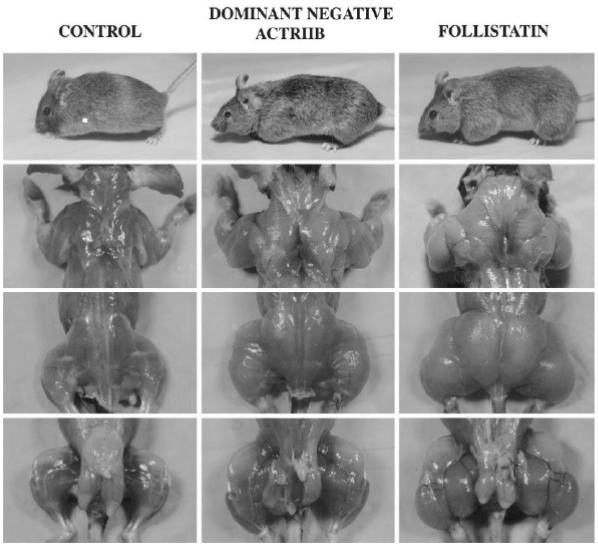
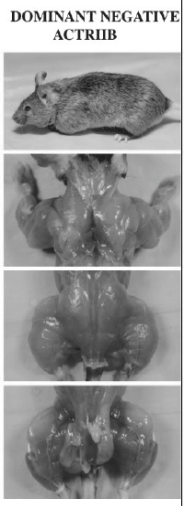


Fig. 2. Increased muscling in mice overexpressing a dominant-negative form of ActRIIB or full length follistatin. A control male nontransgenic mouse, a male transgenic mouse from the C11 line (dominant-negative ActRIIB), and the F3 male founder mouse (follistatin) are shown. Pictures of live mice are shown in the top row, and pictures of animals that had been killed and skinned are shown in the bottom three rows.

Source: Lee, S-J, and A. C. McPherron. "Regulation of Myostatin Activity and Muscle Growth." *PNAS* 98, no. 16 (2001): 9306-9311.

Dominant-Negative mutation definition: from *GeneTests: Medical Genetics Information Resource* (database online). Educational Materials: Glossary. Copyright, University of Washington, Seattle. 1993-2009. Available at http://www.genetests.org. Accessed July 10, 2009.

Dominant negative form of ActRIIB



•Dominant-Negative mutation is a mutation whose gene product adversely affects the normal, wild-type gene product within the same cell, usually by dimerizing (combining) with it. In cases of polymeric molecules, such as collagen, dominant negative mutations are often more deleterious than mutations causing the production of no gene product (null mutations or null alleles).

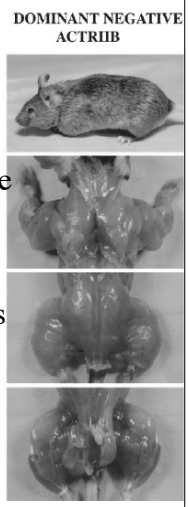
From the paper:

To determine whether activin type II receptors may be involved in myostatin signaling *in vivo*, we investigated the effect of expressing a dominant-negative form of Act RIIB in mice. For this purpose, we generated a construct in which a truncated form of Act RIIB lacking the kinase domain was placed downstream of a skeletal muscle-specific myosin light chain promoter/enhancer. From pronuclear injections of this construct, we obtained a total of seven founder animals positive for the transgene. All seven showed significant increases in skeletal muscle mass with individual muscles weighing up to 125% more than those of control nontransgenic animals derived from similar injections (Table 1).

73

Source: Lee, S-J, and A. C. McPherron. "Regulation of Myostatin Activity and Muscle Growth." *PNAS* 98, no. 16 (2001): 9306-9311.

Dominant negative form of ActRIIB



From the paper:

"These data showed that expression of a dominant-negative form of Act RIIB can cause increases in muscle mass similar to those seen in myostatin knockout mice."

(myostatin knockout mice, the increase in muscle mass has been shown to result from increases in both fiber number and fiber size since myostatin is the inhibitor which prevents muscle cells from dividing)

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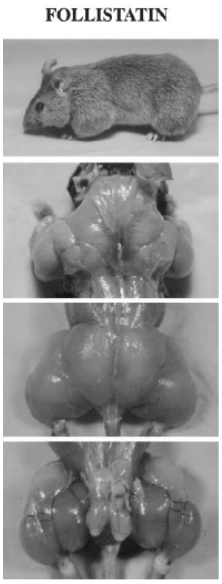
Source: Lee, S-J, and A. C. McPherron. "Regulation of Myostatin Activity and Muscle Growth." *PNAS* 98, no. 16 (2001): 9306-9311.

Follistatin

- Inhibits myostatin

The most dramatic effects on skeletal muscle were obtained by using the follistatin construct. We obtained two founder animals (F3 and F66) that showed increased muscling (Table 1, Figs. 2 and 3*b*). In one of these animals (F3), muscle weights were increased by 194–327% relative to control animals, resulting from a combination of hyperplasia (66% increase in fiber number to 13,051 in the gastrocnemius/plantaris) and hypertrophy (28% increase in fiber diameter to 55 μm). Although we have not analyzed muscle weights of myostatin knockout mice in a hybrid SJL/C57BL/6 background, the increases in muscle mass observed in the F3 founder animal were significantly greater than the increases we have seen in myostatin null animals in other genetic backgrounds (unpublished Similarly, our data do not show definitively that follistatin is blocking myostatin activity *in vivo* to promote muscle growth. In this regard, the extraordinary degree of muscling seen in one of the follistatin-expressing founder animals suggests that other follistatin-sensitive ligands may be involved in regulating muscle growth. One obvious candidate is GDF-11, which is highly related to myostatin (1, 18–20) and also expressed in skeletal muscle (unpublished results). Moreover, it is known that GDF-11 activity in *Xenopus* can be blocked by follistatin (18). Other candidate ligands would also include the activins, which have been shown to be capable of inhibiting muscle cell differentiation *in vitro* (33).



75

Source: Lee, S-J, and A. C. McPherron. "Regulation of Myostatin Activity and Muscle Growth." *PNAS* 98, no. 16 (2001): 9306-9311.
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The next level

Wagner, K. R. "Muscle Regeneration Through Myostatin Inhibition." *Curr Opin Rheumatol* 17, no. 6 (2005): 720-4.

Abstract:□□
"Myostatin is an endogenous, negative regulator of muscle growth. Selective inhibition of myostatin may have broad clinical utility by improving regeneration in diverse and burdensome muscle disorders. An understanding of this potential is relevant because inhibitors of myostatin have recently entered clinical trials. RECENT FINDINGS: This article reviews the structure and function of myostatin, the effect of inhibiting myostatin in models of disease, and potential therapeutic approaches to blocking myostatin pharmacologically. The possibility that a myostatin inhibitor will promote muscle regeneration in human disease, as seen in animal models, is suggested by the observation that loss of myostatin results in muscle hypertrophy in a human subject.
SUMMARY: Multiple approaches to inhibiting myostatin are suggested by the recent elucidation of its signaling pathway. An inhibitor of myostatin may be the first drug specifically designed to enhance muscle growth and regeneration.

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We have altered the genetics of mice, why not humans?

Potential targets

- Insulin like growth factor (IGF-1): A decrease in the production of anabolic hormones such as testosterone, growth hormone and insulin-like growth factor-1 impairs the capacity of skeletal muscle to incorporate amino acids and synthesize proteins.
- overproduction of hemoglobin for endurance
- growth hormone for recovery and strength;
- synthetic genes that metabolize fats and carbs with super human speed and efficiency for speed and endurance

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How do we do this?

- Gene therapy of course!

Haisma, H. J., and O. de Hon. "Gene Doping." *Int J Sports Med* 27, no. 4 (2006): 257-66.

Abstract:

"Together with the rapidly increasing knowledge on genetic therapies as a promising new branch of regular medicine, the issue has arisen whether these techniques might be abused in the field of sports. Previous experiences have shown that drugs that are still in the experimental phases of research may find their way into the athletic world. Both the World Anti-Doping Agency (WADA) and the International Olympic Committee (IOC) have expressed concerns about this possibility. As a result, the method of gene doping has been included in the list of prohibited classes of substances and prohibited methods. This review addresses the possible ways in which knowledge gained in the field of genetic therapies may be misused in elite sports. Many genes are readily available which may potentially have an effect on athletic performance. The sporting world will eventually be faced with the phenomena of gene doping to improve athletic performance. A combination of developing detection methods based on gene arrays or proteomics and a clear education program on the associated risks seems to be the most promising preventive method to counteract the possible application of gene doping.

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How do we do this?

- Gene therapy of course!

Unal, M., and D. Ozer Unal. "Gene Doping in Sports." *Sports Medicine* 34, no. 6 (2004): 357-62.

Abstract:
"Gene or cell doping is defined by the World Anti-Doping Agency (WADA) as "the non-therapeutic use of genes, genetic elements and /or cells that have the capacity to enhance athletic performance". New research in genetics and genomics will be used not only to diagnose and treat disease, but also to attempt to enhance human performance. In recent years, gene therapy has shown progress and positive results that have highlighted the potential misuse of this technology and the debate of 'gene doping'. Gene therapies developed for the treatment of diseases such as anaemia (the gene for erythropoietin), muscular dystrophy (the gene for insulin-like growth factor-1) and peripheral vascular diseases (the gene for vascular endothelial growth factor) are potential doping methods. With progress in gene technology, many other genes with this potential will be discovered. For this reason, it is important to develop timely legal regulations and to research the field of gene doping in order to develop methods of detection. To protect the health of athletes and to ensure equal competitive conditions, the International Olympic Committee, WADA and International Sports Federations have accepted performance-enhancing substances and methods as being doping, and have forbidden them. Nevertheless, the desire to win causes athletes to misuse these drugs and methods. This paper reviews the current status of gene doping and candidate performance enhancement genes, and also the use of gene therapy in sports medicine and ethics of genetic enhancement."

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Recreational Athletes

- Should we be tested?
- How often are varsity athletes tested?
- Comments?

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