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Matthew H. Nanci
mattnanci@gmail.com

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The Imaginary Performance Enhancer: Human Growth Hormone

Matthew Nanci

University of Connecticut

Wall-to-wall, the mall store lines every shelf with vitamins, powders and supplements. But, this is no pharmacy.

This is a place focusing on self-betterment. Pushing oneself to obtain an edge over others. Attempting to obtain an edge over one's body.

It is one of the thousands of stores across the country that specialize in selling dietary supplements, a \$32 billion industry, according to Forbes.com.

With products that challenge consumers by making claims such as, "If you're serious about performance and results, you need the ALL-NEW MuscleTech Performance Series" or "Maximize your workout gains with the entire Beyond RAW line," the focus is on attaining a higher level of fitness that is not possible without these products.

At the counter a buff man with biceps the size of a football, who appears to have skipped "legs day" a few too many times, tromps toward the counter with an armful of canisters and rolls them toward the cashier.

Training and exercise can only go so far. At least that's the message echoed among many of the products in the store.

By shopping at this store, the man is abiding by the law in purchasing legal supplements to enhance his workouts and results.

That's where human growth hormone comes into play -- as well as all the non-prescription nutritional supplements that promise to offer similar results.

For those willing to skirt the law, there are many products available on the internet that claim to boost growth hormone production, as well as websites that claim to actually sell growth hormone. While these products are available, their legitimacy and effectiveness are questionable.

“From what we know of the studies of growth hormone, it’s kind of plus or minus whether it helps on high high levels [of administration],” said Dr. Matthew Hall, an assistant professor in the department of orthopedics at the University of Connecticut. “These athletes are taking straight-up growth hormone. A lot of it. Maybe it’s helping them, maybe it’s not. So it’s hard to imagine that somebody could take a supplement that would increase their growth hormone level enough to give them performance [enhancement].”

Dr. Jeffrey Anderson, the independent program administrator for the MLB’s drug testing program, as well as the director of sports medicine and head team physician at the University of Connecticut also does not think these substances are effective.

“The likelihood that you go on the internet and buy something that actually really helps you is pretty slim,” he said.

As a means of gaining that competitive advantage, that extra edge on opponents, some athletes turn to growth hormone to better their performance on the field. Professional athletes have more resources and money, which makes it easier to illegally obtain growth hormone.

In the pros that decision could cost players millions of dollars.

Players run the risk of being suspended if caught using growth hormone, particularly in the National Football League and Major League Baseball where growth hormone is on both leagues’ banned substance list (MLB Players Association, 2011; NFL Players Association, 2012).

According to the NFL’s 2010 “Policy on Anabolic Steroids and Related Substances”, if a player in the NFL tests positive for growth hormone, discipline ranges from a four-game suspension for the first offense to a 12-month suspension from all football activities for the third

offense. After 12 months the player then has to apply for reinstatement to the NFL commissioner before they are allowed to return to their team.

Major League Baseball has similar punishments in place for substance violations. According to Major League Baseball's "Joint Drug Prevention and Treatment Program," if a player tests positive for growth hormone they will receive a 50-game suspension for a first offense, 100-game suspension for a second violation, and a permanent suspension from baseball for a third offense. Three strikes and they're out. A player may seek reinstatement after a year. If the request is approved, the player may return to baseball two years after the original suspension. As recently as March 2014, effective for the upcoming season, the MLB and the MLB Players Association have agreed to increase the first offense penalty to 100 games and the second offense penalty to 162-game suspension, a full season (ESPN.com news services, 2014).

With such stiff penalties and a lot of money at stake for the players, it would make sense if the benefits of taking growth hormone at least equaled the risks of getting caught. But the rate of return on taking growth hormone may not be what athletes expect.

As it turns out, research studies show that administering growth hormone may have no effect on athletic performance at all.

To understand the issue, it's important to first understand what growth hormone is. It is a naturally occurring hormone in the human body that is produced from the anterior pituitary, part of the endocrine system. Production is at its highest during puberty, then decreases with age.

What growth hormone does is promote lipolysis, which is the breakdown of fats and other lipids through hydrolysis to release fatty acids. It also enhances calcium retention, bone growth and bone mineralization. As a result, its biggest impact is on bone tissue, cartilage, skeletal muscle, adipose tissue (body fat), liver, kidneys and the immune system.

Growth hormone is prescribed primarily for the treatment of documented growth hormone deficiency, which is very uncommon. Still, athletes are able to get their hands on the substance. “There’s almost nobody taking it legitimately,” said Anderson. “The conditions for which it’s indicated are pretty rare. And they’re really rare in athletes because there are conditions that cause you not to grow properly and things like that.”

Dr. William Kraemer, a professor of kinesiology, physiology, neurobiology and medicine at the University of Connecticut who has studied growth hormone for nearly 30 years, says there is still a lot unknown about growth hormone and its effects. A lot of research has focused on the most common form of growth hormone, 22 kD, when he calls growth hormone a “super family” with over 100 different forms in human blood that present many different potential biological interactions.

“I don’t think there is a current consensus [on the effects of growth hormone] because I don’t think enough sports scientists really understand growth hormone very well,” he said. “We wrote the review paper in 2010, and the bottom line is I think that most people understand growth hormone based on the 22 kD monomer and its assessment in the different studies that have been done over the last 40 years, so that’s the way we look at it, especially the past 20 years.”

There is not much support for the theory that taking growth hormone enhances athletic performance. Anderson points out that, “if you’re using just growth hormone in your doping strategy with things, you’re missing the boat.”

If growth hormone is available by prescription only, and not for athletic enhancement, then how is it possible for athletes to obtain the substance?

“Human growth hormone is not super easy to get your hands on because it’s really expensive, so for people without a ton of money it’s hard to get,” Anderson said. “People with lots of money, like the people I deal with [professional baseball players], will get it through various connections.”

Another avenue where athletes can get growth hormone is from anti-aging clinics, such as Biogenesis of America, the clinic that was found to be providing performance enhancing drugs to professional baseball players.

As a whole, anti-aging medicine is not a very reputable field for doctors to be involved in. “I don’t consider it [anti-aging medicine] to be particularly ethical,” Anderson said. “It’s not scientifically based and the practitioners of it work at the fringes of ethics in our profession.”

Hall has a similar skepticism about the practice of anti-aging medicine. “Growth hormone decreases as you get older,” he said. “So the idea is that anti-aging, if you give people growth hormone supplements, then you’re trying to stave off some of the aging process. This is not scientific at all. This is only my opinion, but any time I see something that says ‘anti-aging clinic’ I’m somewhat a little bit apprehensive about it or even question that a little bit. What are the motives behind that? It’s not something that’s accepted within the medical community as a whole per se. You’re talking about probably situations where there’s either doctors or people that are thinking or doing things maybe out of the box that may not necessarily be within their scope or things that are kind of medically accepted or evidence-based treatments.”

Part of the appeal of taking growth hormone is that the side effects are not as severe as taking steroids, which are also used to enhance athletic performance. According to WebMD.com, side effects include: nerve, muscle or joint pain, swelling due to fluid in the body’s tissues

(edema), carpal tunnel syndrome, numbness and tingling of the skin, high cholesterol levels and it can also increase the risk of diabetes and growth of cancerous tumors.

In comparison, the Partnership for a Drug Free America lists some of the more severe side effects of taking steroids: tendon rupture, heart attacks, enlarged heart, risk of liver disease and liver cancer. In addition, there are many other side effects that impact the body's appearance and other bodily functions.

However, Kraemer points out that side effects of steroids can be mitigated with proper supervision of doses and that everyone is affected differently.

"I think you always have to be cautious when you take any drug," he said. "I think there's a degree of that's the thought, but in fact we don't know that to be the fact. And in fact steroids, if you look at it, done in appropriate doses have found to have very low numbers of side effects. Usually it's just in the very super maximal doses that people take that don't know what they're doing. And the other thing you've got to realize, it's very individual. This is a thing I keep harping on. Everybody's genetics responds and the epigenetics responds very differently to drugs. So, we don't know why some people would have a side effect on a drug."

Also, the long-term effects of taking growth hormone are not known because it is not something that can be studied due to ethical reasons. "The true question is whether growth hormone itself is an ergogenic," said Hall. "Ergogenic meaning something that ends up as a performance enhancer... Ergogenics are things that kind of enhance performance. The question is whether it really does that and I think that remains to be seen from the stuff that I've read. And we don't know what the long term [effects are]. How much do you take? If you take this x amount, how high is your risk for having these problems down the line? We don't really know."

Another aspect of growth hormone that is alluring to athletes is that there is no reliable test for detecting growth hormone. In a meta-analysis by Katarzyna Krych and Anna Gozdzicka-Jozefiak entitled “Doping in Sport: New Developments,” they write that because growth hormone is an internal substance from the body, that makes it difficult to differentiate from how it looks outside of the body. In addition, they write that many variables would need to be controlled for an accurate test. The amount of growth hormone present depends on age, sex, physical conditioning, diet, stress and the kind of exercise the person is participating in.

“A study of 96 athletes representing different sports revealed post-exercise elevated GH in middle-distance runners, rowers, swimmers and cyclists (Krych & Gozdzicka-Jozefiak, 2008, p. 70).” That is because the blood concentration of growth hormone can increase up to 50 times after intense exercise and maintain that level for about an hour post workout.

In addition, elevated levels of growth hormone is hard to detect because of how swiftly it moves through the body. “Because it is a hormone that you have, and also it’s very short lived. And even when you take it outside, it doesn’t last very long, so detection is a little bit more difficult,” said Hall. “That’s why it’s taken a little bit longer for the anti-doping agencies and major league baseball and stuff to come up with policies to try and test for it. And it requires a blood test.”

According to Kraemer, the World Anti-Doping Agency, an independent agency against doping in sports and that oversees testing in the Olympics, developed a test for growth hormone. Despite WADA’s test for athletes, Kraemer says the veracity of the test is still in question because it has never been challenged.

“As far as the efficacy and its false positives and things like that, that’s never really been very carefully looked at except in a couple studies,” he said. “We have yet, to my knowledge,

tested the assay in a court of law, so there has really not been a legal test of the efficacy of the assay.”

In the MLB, Anderson said it is “less hard now” to test for growth hormone due to the expansion of the drug testing program.

“There has been a huge climate shift in baseball in probably the past five years,” he said. “Mike Weiner, who passed away was the head of the players association, [and] was extremely good at bridge building. Really wonderful guy. And there was a shift in kind of the feeling of the players away from protecting people who were cheating to protecting people who weren’t. Baseball has this year, we’ve increased now the number of both urine tests that we’re doing and blood tests that we’re doing. We’re staggering our tests differently, we’re doing more post-game testing. All this sort of stuff and that’s all at the request of the players. It’s a really harmonious drug testing situation in baseball right now.”

The third aspect of taking growth hormone that appeals to athletes is that the drug could help improve recovery time from injuries.

In Kraemer’s review, “Growth Hormone, Exercise, and Athletic Performance: A Continued Evolution of Complexity” (2010), he cited multiple animal studies that found evidence to suggest growth hormone could promote healing. For example, it was found that rats could increase their recovery time from anterior cruciate ligament injuries.

While discovering such a result in rats is cause for further examination of growth hormone and healing, Kraemer advises to not get carried away and apply the same thinking to humans.

“It’s just a jump as far as how this actually works,” he said. “Because if it was really good at tendon and ligament recovery, orthopedic surgeons would be subscribing to it. And

realistically we don't see that in the orthopedic prescriptions that we see. If this was really that beneficial, it would be part of a drug regimen and we don't see that, which is kind of interesting in itself."

In addition, rats may not be the best comparison to humans. "There's a species difference and rats are quite different than humans, but what's interesting is that nobody has gone there relative human clinical care and if it was so prolific and so effective, you would think that it would be part of a rehab drug regime and you just don't see that commonly given," Kraemer said. "And it might be due to the fact that we really don't know what it does. I'm not sure we really know what 22 kD does in reality when given exogenously. I think it's been very weakly studied in humans except in the aging and then in low doses, so it's very difficult to really make guesses about what's going on."

Anderson agrees that there could be a healing element to the administration of growth hormone, but there is not enough evidence to be sure. "You can make that leap because IGF-1 [insulin-like growth factor one] plays a role in healing of tissues and there are different types of IGF-1: mechano-growth factor, which you'll find in tendons, things like that," he said. "It may improve healing. We don't have a lot of good data that supports that, but there is at least a biological explanation on how it might."

M.J. Rennie (2003) conducted a meta-analysis regarding the anabolic effect of growth hormone and did not find any support for growth hormone positively impacting performance. According to Rennie, "so far, no robust, credible study has been able to show clear effects of either medium or long term rhGH administration, alone or in combination with a variety of training protocols or anabolic steroids, on muscle protein synthesis, mass, or strength" (p. 102).

He goes on to include how there are multiple means of measuring for an increase in muscle mass and how difficult it is to notice change in time periods shorter than three months. One method is to physically measure the amount of muscle and its change in size throughout the experiment. Another way is to keep track of protein synthesis by looking at the amount of amino acids that have stable isotopes.

“When this has been done in young healthy adults, no effect on muscle protein synthesis (or indeed on muscle mass measured by other means) has been detected [50]. Furthermore, no effect has been detected in body builders and weightlifters [51, 52]. Thus, at the very least, it appears that the evidence for a sustained anabolic effect of rhGH on muscle mass in normal healthy young men, trained or untrained, is extremely slim” (p. 102).

Rudman et al. (1990) [53, 54] found that growth hormone can be beneficial for elderly men in decreasing body fat and increasing lean body muscle mass, but Rennie writes that replicating Rudman’s results have been tough.

Replication may be a challenge because Rudman’s 1990 study “did not have a placebo, was not blinded and did not perform an intention-to-treat analysis (Hau Liu et al., 2007, p. 107).

Therefore, Rennie concludes that unless growth hormone administration was paired with resistance training, there appears to be no increase in muscle mass or strength in healthy middle aged to elderly men [55, 56].

Overall, Rennie summarizes his meta-analysis with this, “The balance of evidence suggests that, in healthy adults, growth hormone does not build muscle and provides no athletic advantage. Growth hormone abuse, however, does cause disease. This message needs to be taken on board by coaches, team doctors, and potential abusers” (p. 104).

“We must tell athletes the truth: growth hormone does not ‘work’ or at least not as they think it does and that it is associated with all kinds of immediate and long term hazards—everything from decreased performance to cancer” (p. 104).

In fact, taking growth hormone might do the opposite of work. It may actually hurt athletic performance.

In a study by Kai Lange of the Danish Institute of Sports Medicine, trained endurance athletes who were given growth hormone could not complete cycling tasks (Rennie, 2003).

“There is good evidence that hGH administration exacerbates the pronounced increase in lipolysis that occurs during exercise and, in addition, increases the production of lactate and protons by working muscles. The inevitable metabolic acidaemia and consequent reduction in the rate of glycogenolysis in muscle and liver could explain the acutely decreased performance. Furthermore, because of the effect of rhGH in decreasing glycogen storage in muscle and liver, it will make recovery from exercise more difficult” (p.104).

Overall, taking growth hormone remains a big question mark as to what effects it has on athletic performance. Kraemer says researchers have really only scratched the surface when it comes to understanding growth hormone and its role.

“I think where a lot of assumptions have been made, relative to GH’s efficacy and its basically use as an anabolic drug, it hasn’t necessarily been carefully looked at across the board by a number of investigative laboratories,” he said. “The number of laboratories that have looked at this are relatively few. Under a dozen. Maybe under ten. Maybe under six that have really started to try to study this. So we have to kind of take it in context of the fact that we think we know a lot about the pituitary gland, but in reality, there is probably much more that we don’t know. I would guesstimate that we probably understand maybe about five percent of the territory

of how pituitary functions and most of it's related to clinical pathologies and clinical replacement therapies and things like that, but it's promoted sometimes beyond the data so to speak. Beyond the facts."

Researchers in the United States will probably not be the ones to conduct such research due to ethical concerns and institutional review boards.

"I don't ever see any opening for us to ever study this in young people. And also with the unknown aspects of it, it's questionable whether it would be ethically right to do that," Kraemer said.

In addition, even if such a study were approved where young and healthy athletes to be given growth hormone, it would probably be difficult to find participants.

"The question is what are you trying to prove and what is the purpose of the study," he added. "And if it's performance, then you have to give it to performance-related athletes and then that would violate pretty much their competitive status if they were in the study."

According to Anderson, it was previously thought about 20 years ago in sports medicine that anabolic steroids did not benefit athletes, when actually they were seeing significant performance enhancement. However, no studies could be done to definitively find out if the consensus was correct. But doctors were eventually able to ascertain the truth about anabolic steroids, "by people finally listening to people who were using them," Anderson said.

"If you look back at the older literature on anabolic steroids, what they tested people with were pharmacologic doses. So if you're going to replace somebody's normal testosterone, you use x number of milligrams with things. What the dopers were doing is they were using a thousand times pharmaceutical doses and that really works. It increases your risk of side effect, but it makes you bigger, faster, stronger and it wasn't until people started to actually listen to

what people were doing, that you had documentation of what happens with it. But it's still unethical. You can't run a human study and superdose people with steroids to do it."

In cases like that, medicine has to practically stumble onto the results because it's not something that can be researched. "In medicine we learn a lot of our stuff that way. We learn a lot from patients who do what we tell them not to do," Anderson said.

As the top-heavy man departs the store with supplements clenched in his hand, he is probably contemplating how to implement his recent purchase into his next workout and the work he has ahead of him. What he doesn't have to worry about ordering growth hormone boosting supplements that aren't legit. And he doesn't have to think about is the legal and professional repercussions of taking an illegal substance that may not have any effect.

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