Medical Science

To Cite:
Kowalski B, Kriese N, Szyszkowski J, Komorowska E, Tucka B, Woś P, Zgrzywa Z, Wądołowska P, Zawadzka I, Jaworski J. Human growth hormone abuse in elite sports: physiological efficacy, adverse health effects, and anti-doping challenges: A narrative review. *Medical Science* 2026; 30: e75ms3850
doi: https://doi.org/10.54905/disssi.v30i170.e75ms3850

Authors' Affiliation:
Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warsaw, Poland

***Corresponding author:**
Bartłomiej Kowalski,
Medical University of Warsaw, Żwirki i Wigury 61, 02- 091 Warsaw, Poland; ORCID: 0009-0003-5856-2663; Email: bartex010.2001@gmail.com

ORCID List:

Bartłomiej Kowalski	0009-0003-5856-2663,
Natalia Kriese	0009-0001-8278-1044,
Jakub Szyszkowski	0009-0000-3217-6981,
Ewelina Komorowska	0009-0001-4103-7745,
Brygida Tucka	0009-0004-1785-2186,
Paweł Woś	0009-0003-2604-6170,
Zuzanna Zgrzywa	0009-0005-1032-8063,
Paulina Wądołowska	0009-0005-5646-1775
Izabella Zawadzka	0009-0008-3149-2550,
Jakub Jaworski	0009-0004-7140-9679

Peer-Review History
Received: 03 September 2025
Reviewed & Revised: 01/October/2025 to 21/March/2026
Accepted: 03 April 2026
Published: 18 April 2026

Peer-review Method
External peer-review was done through double-blind method.

Medical Science
pISSN 2321–7359; eISSN 2321–7367

DISCOVERY SCIENTIFIC SOCIETY

Human growth hormone abuse in elite sports: physiological efficacy, adverse health effects, and anti-doping challenges: A narrative review

Bartłomiej Kowalski*, Natalia Kriese, Jakub Szyszkowski, Ewelina Komorowska, Brygida Tucka, Paweł Woś, Zuzanna Zgrzywa, Paulina Wądołowska, Izabella Zawadzka, Jakub Jaworski

ABSTRACT

Athletes abuse recombinant human growth hormone (rhGH) in an attempt to lose body fat and build muscle mass. However, extensive clinical studies have demonstrated that even doses of rhGH, which promote large increases in reported "lean body mass" do not translate into increased myofibrillar strength. Most of this increased lean mass is due to water retention and collagen synthesis. Furthermore, the long-term clinical management of both intentional and severe supratherapeutic abuse of hGH has taught us that the negative health consequences of chronic use include marked insulin resistance and acromegalic cardiomyopathy. From an anti-doping perspective, it represents one of the most formidable analytical challenges. Since exogenous hGH is biologically and immunochemically identical to the endogenous hormone, this structural parity severely complicates detection for the World Anti-Doping Agency (WADA). Ongoing scientific research has led to the development of isoform and biomarker-based tests to detect abuse of hGH by athletes. To continue to protect the health and safety of athletes and to promote integrity in competitive sports, WADA and allied anti-doping authorities must continuously advance hGH detection methodologies to combat ongoing abuse. This Volume summarizes current detection methods and aims to catalyze the development of next-generation analytical strategies.

Keywords: human growth hormone, sports doping, somatropin, performance enhancement, World Anti-Doping Agency.

1. INTRODUCTION

The use of human growth hormone in sport: The sports world has long linked the never-ending quest for excellence with the search for an unfair advantage. Over the years, athletes have used numerous substances to enhance sporting performance. Today, one of the most widely used performance-enhancing drugs is human growth

hormone (hGH). The first reports of the abuse of hGH surfaced in the 1980s; however, at that time, hGH was still being derived from cadaveric pituitary glands. Besides being expensive, these glands were a limited resource that posed a risk of Creutzfeldt-Jakob disease transmission (Macintyre, 1987). This situation changed in the late 1980s when scientists developed recombinant human growth hormone (rhGH). The almost unlimited supply of rhGH led to a massive increase in the illicit use of the hormone at all levels of sport - professional and amateur.

Athletes believe rhGH to be highly anabolic and lipolytic, thereby increasing both muscle and lean body mass while reducing subcutaneous fat stores and accelerating recovery from injury (Holt, 2009). There is, however, a large discrepancy between athletes' beliefs about the effects of rhGH and those reported in the scientific literature.

Human growth hormone (hGH), or somatropin, is a growth factor of considerable interest in sports medicine. This narrative review aimed to critically and systematically assess the scientific literature related to the use of hGH in sport. This paper aims to provide a concise summary of the current state of knowledge on the role of the hGH/IGF-1 axis in exercise physiology, as well as the potential performance-enhancing and adverse health effects of chronic exogenous hGH administration. This paper also provides a brief overview of the anti-doping tests utilized by WADA to monitor the abuse of hGH in sport.

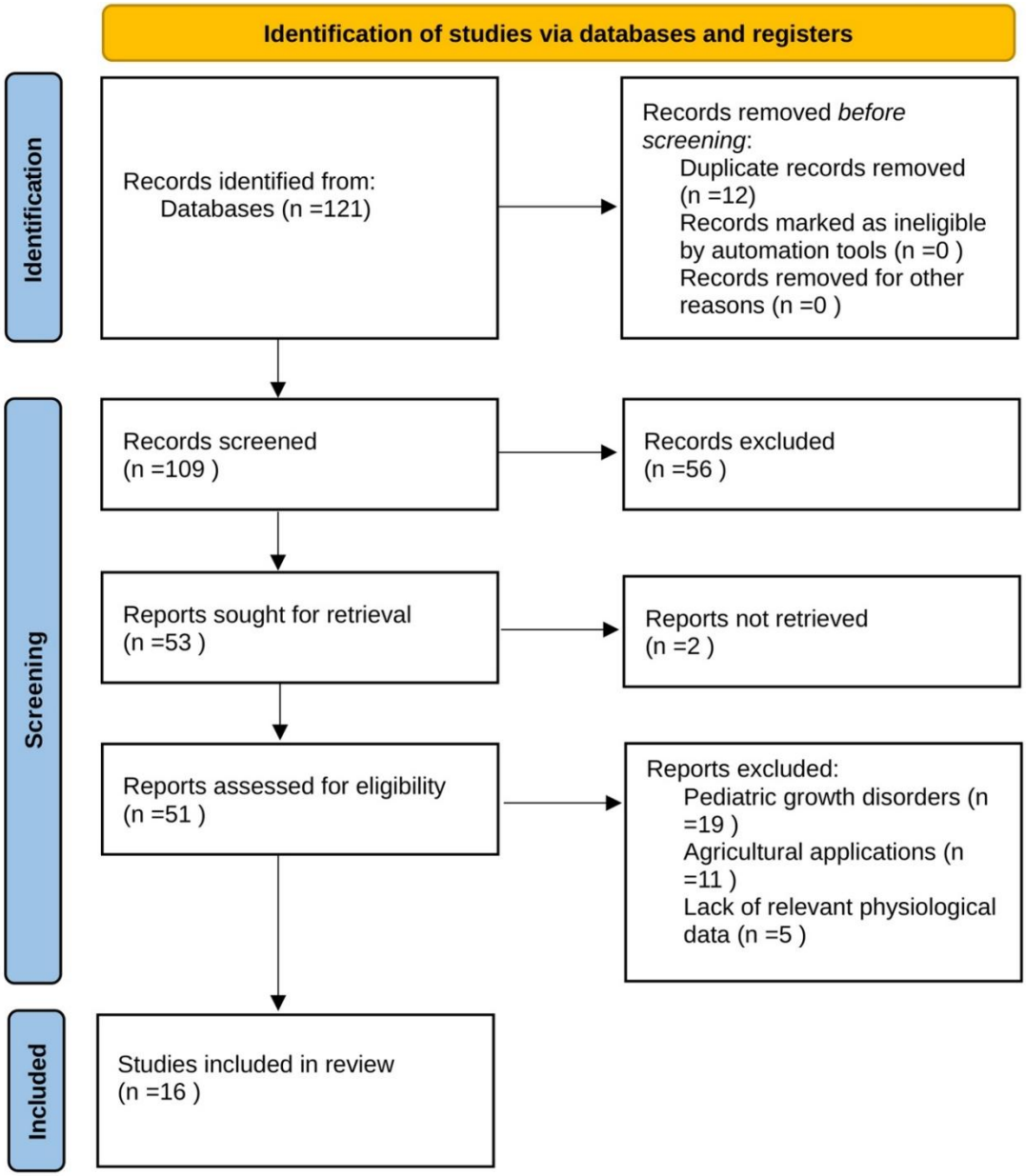

Figure 1. PRISMA 2020 flow diagram detailing the literature search, record screening, and study selection process.

2. REVIEW METHODS

We identified key studies by searching two large databases, PubMed and MEDLINE, using specific terms such as growth hormone, IGF-1, sports doping, and detection methods. Our first search found 121 studies, which we illustrated in a PRISMA flow diagram (Figure 1). Then we systematically reviewed these studies and excluded those focused on pediatric growth disorders or on the use of hormones in agricultural applications. We only kept the studies on how exercise and doping affect human physiology. After carefully reviewing all remaining studies, we selected 16 for inclusion in our review: original research and comprehensive reviews published from 1987 to 2023.

3. RESULTS & DISCUSSION

The Physiology of the GH/IGF-1 Axis in Exercise: Biochemical Pathways

The regulation of the somatotropic axis by the hypothalamus is mediated by two specific neuropeptides, growth hormone-releasing hormone (GHRH) and somatostatin, which stimulate and inhibit, respectively, the pulsatile release of growth hormone (hGH) from the anterior pituitary gland (Sönksen, 2001). To fully understand the muscle-growth potential of growth hormone and to explain why myofibrillar protein accretion does not always follow the predicted outcome in athletes, it is important to consider the cellular events that follow growth hormone receptor binding.

In addition to the 20-kDa alternative splice variant, the principal transcript of the growth hormone gene produces the 22-kDa isoform, which is primarily secreted into the blood and binds to the growth hormone receptor (GHR) at the cell surface. The Growth Hormone Receptor (GHR) is a member of the class I cytokine receptor superfamily. This superfamily of receptors is involved in a wide variety of biological functions, including lipid and glucose metabolism, growth and development, and cell survival. The binding of the 22-kDa form of growth hormone induces the dimerization of two adjacent receptors. Active JAK2 kinase subsequently phosphorylates target proteins. The STAT proteins are key components of the GH signal transduction cascade, and STAT5b is the most heavily phosphorylated STAT isoform (Holt et al., 2010). The phosphorylated STAT5b dimers subsequently translocate to the nucleus, where they bind to specific sequences in the target gene promoters. Primary among these genes is the insulin-like growth factor-1 (IGF1) gene in the growth hormone-stimulated hepatocyte.

Hepatocytes secrete the vast majority of circulating IGF-1, which immediately links with IGFBP-3 and the acid-labile subunit (ALS) to assemble a ternary complex. This structural formation functions as a biological storage pool. This complex stabilizes the hormone and prolongs its systemic half-life.

Once the hormone is bound to the IGF-1R on the surface of target cells, a cascade of cellular activities is triggered. The hormone-receptor interaction results in receptor autophosphorylation and recruitment of the adapter protein insulin receptor substrate-1 (IRS-1). The interaction of the activated receptor with IRS-1 results in the activation of the lipid kinase phosphatidylinositol 3-kinase (PI3K). Once activated, PI3K initiates a vital signaling cascade by phosphorylating Protein Kinase B (Akt). This kinase then stimulates the mammalian target of rapamycin (mTOR), acting as the master regulator of cellular protein synthesis (Holt, 2009).

Understanding that genetics largely dictate adult human muscle fiber types and prevent them from changing clarifies the rationale for increased muscle protein synthesis at supraphysiological growth hormone levels. The GH/IGF-1/mTOR pathway in mature skeletal muscle promotes the formation of connective tissue elements—mainly collagen and matrix metalloproteinases—instead of synthesizing new contractile proteins. Wallace et al., (1999) reported that acute sessions of both aerobic and resistance exercise stimulated endogenous GH release, thereby mediating lipolysis and countering the hypoglycemia that would otherwise develop during such exercise. With supraphysiological exogenous rhGH, however, normal negative feedback on the pituitary gland is strongly impaired. Exogenous growth hormone effectively dampens endogenous GH release from the pituitary. Additionally, it leads to hyperinsulinemia and resultant hyperglycemia due to increased blood levels of insulin-like growth factor-1. The growth of tissue with supraphysiological levels of growth hormone is therefore largely associated with an increase in extracellular tissue volume. Figure 2 illustrates how exogenous rhGH injection overstimulates the liver to produce IGF-1, while simultaneously triggering a strong negative feedback loop that suppresses the natural secretion of endogenous hGH from the hypothalamus and anterior pituitary gland.

Ergogenic Efficacy: Myths vs. Reality and Statistical Outcomes

The reason athletes use rhGH as an ergogenic aid to build muscle mass, increase power and endurance, and enhance performance is that growth hormone plays a direct role in increasing muscle hypertrophy, maximal power, and performance capacity. However, all

recent double-masked, placebo-controlled studies of growth hormone administration in healthy, well-trained adults have not found any significant increase in maximal voluntary strength or aerobic power (VO2 max) (Ehrnborg et al., 1999; Holt, 2009).

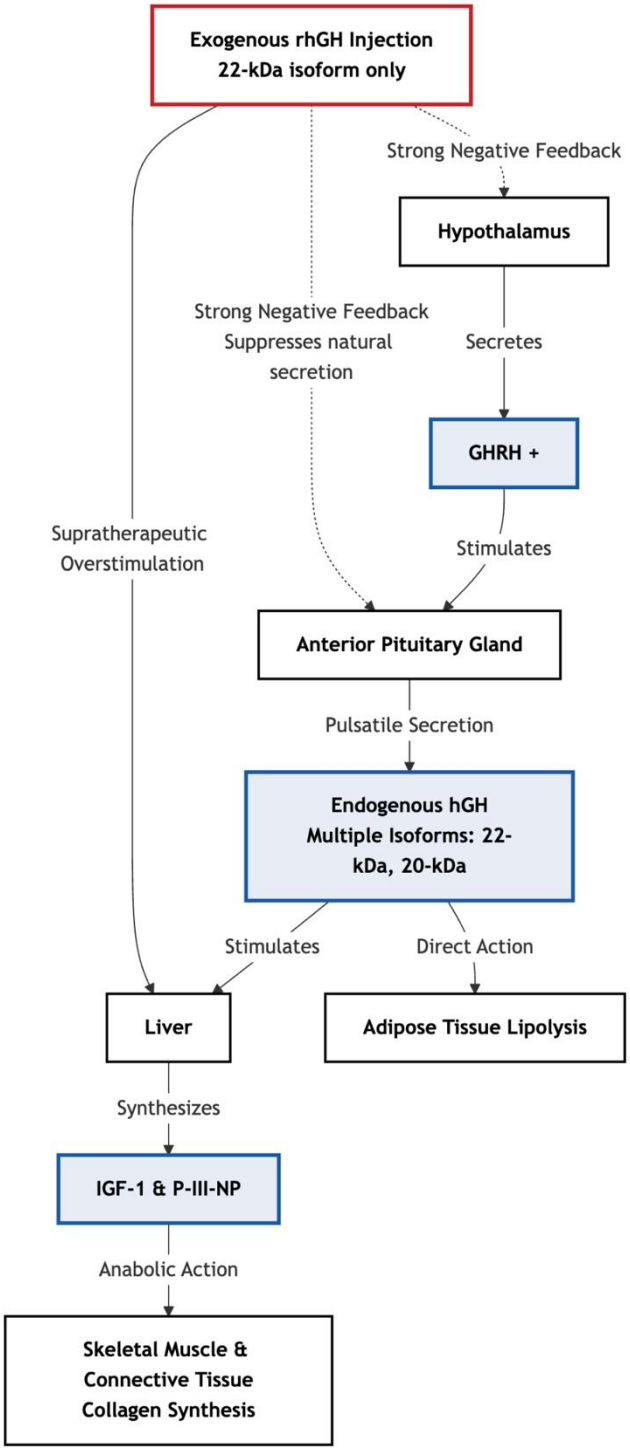

Figure 2. Physiological regulation of the GH/IGF-1 axis and the profound negative feedback loop induced by exogenous rhGH doping.

Researchers have employed several strategies to determine the ergogenic effects of rhGH on exercise performance. "Some studies have involved muscle function tests, body composition measured by DXA, and isometric dynamometry. Several studies involved administering supratherapeutic doses of rhGH to patients at 1-2.5 mg/day for 4-8 weeks, compared with a placebo group. These studies demonstrated a mean increase in LBM of 2.1 to 2.8 kg (all studies were statistically significant at $p < 0.01$). Clearly, since all were

athletes, they believed they had gained more muscle mass. However, upon further analysis of body composition changes using BIS and bromide dilution, up to 75% of the gain in LBM was attributable to fluid retention (increases in ECF). The analysis attributed the other 25% to increases in connective tissue. This structural change is also reflected in the increase in serum levels of amino-terminal propeptide of type III collagen (P-III-NP), which studies have shown to increase by 50% to 100% within weeks of rhGH administration (Powrie et al., 2007; WADA, 2018).

The purpose of doping with growth hormone (GH) was to increase the force of contraction of the actin-myosin interaction. However, the important factor is the statistical comparison of means (i.e., the effect size relative to measurement error) between the rhGH groups and the placebo group in each trial to determine whether actual athletic performance improved. In the case of the maximal strength tests of one repetition maximum (1RM) for the biceps curl, bench press, and leg press, all p-values were above 0.05 (Saugy et al., 2006). This finding means that, despite the increase in force of the myofibrillar contractile apparatus, the increase in whole-muscle action was not detectable, given the normal measurement error in such trials. There were no increases in power during the Wingate test, except in a few cases where the increase was only 3% to 4% and was explained by edema-induced increases in body mass (Holt, 2009).

There is no convincing or statistically significant body of evidence that rhGH improves athletic performance. This lack of evidence is why it is relatively little used in this context within the performance-enhancing drugs community. There are several reasons why the relatively expensive rhGH is requested. Studies have shown a major lipolytic effect in humans, with clinically and statistically significant reductions in total body fat mass over 8 weeks (usually by between 1.5 and 2.0 kg) ($p < 0.05$) (Ehrnborg et al., 1999). A leaner, more aesthetically pleasing physique is therefore a sought-after goal in sports such as bodybuilding, where physical appearance is of prime importance. Elite performers do not use drugs in isolation. Thus, drugs are frequently combined. This combination includes the use of rhGH with AAS and exogenous insulin. Studies reported no increase in strength with rhGH supplementation. However, when combined with testosterone, researchers reported 'synergistic' gains in sprint performance. The muscle fibers did not increase in size as they do with other anabolics, so it is not stimulating pure myofibrillar growth. Nonetheless, there has been a statistically significant exponential increase in collagen synthesis, which is important for healthy tendon and ligament repair following microtrauma, the first step in the development of structural injury (Holt et al., 2010). This ability to train hard and recover rapidly from injury places rhGH in a unique category of performance-enhancing drugs, which have the potential to be the game winner in certain sports. Table 1 summarizes the impact of growth hormone on physiological parameters.

Table 1. Perceived vs. Evidence-based effects of rhGH supplementation in athletes.

Physiological Parameter	Athlete Perception (Myth)	Clinical Evidence (Reality)
Muscle Strength	Significant increase in maximal power and strength	No significant increase in contractile myofibrillar force
Lean Body Mass (LBM)	Substantial myofibrillar hypertrophy	Increase in LBM is primarily due to fluid retention and collagen synthesis
Fat Mass	Rapid reduction in subcutaneous adipose tissue	Proven potent lipolytic effect, reducing total body fat mass
Injury Recovery	Accelerated healing of tendons and ligaments	Plausible; supported by proven increases in collagen synthesis markers (e.g., P-III-NP)
Aerobic Capacity	Enhances VO2 max and endurance	No clinical evidence supports improved oxygen uptake

Clinical and Systemic Adverse Health Effects of hGH Abuse

Off-label use of recombinant human growth hormone (rhGH) at supra-therapeutic doses for bodybuilding and athletic enhancement has become a significant and increasing problem in the field of performance-enhancing drugs. This review aims to provide a detailed description of the medical problems associated with supratherapeutic levels of rhGH following chronic misuse of large amounts of the drug by athletes in an attempt to gain a performance advantage. Extensive research documents that excess growth hormone occurs after administration of excessive amounts of the hormone. Consequently, athletes who chronically self-administer large multiples of the normal clinical dose of growth hormone will exhibit the signs and symptoms of acromegaly to gain a performance advantage in sports.

Growth hormone (hGH) functions as a powerful counterregulatory hormone to insulin. Chronic high-dose GH treatment leads to severe glucose intolerance because of a profound decrease in glucose uptake by skeletal muscle and fat. It is associated with pronounced insulin resistance, hyperinsulinemia, and finally, impaired glucose tolerance or overt type 2 diabetes mellitus (Sönksen, 2001).

The most serious side effects of growth hormone are cardiovascular. Chronic IGF-1 hypersecretion resulting from continuous exogenous administration of recombinant human growth hormone (rhGH) directly exerts a hypertrophic effect on cardiomyocytes. We have echocardiographically examined athletes who use growth hormone and anabolics (bodybuilders and powerlifters) and found, on average, concentric left ventricular hypertrophy (LVH) with an increased left ventricular mass index (LVMI) that is clearly above the physiological limits of the so-called "athlete's heart, " defined by Holt et al., (2009). Growth hormone and its receptor also promote interstitial myocardial fibrosis. This fibrosis disrupts cardiac conduction and increases the risk of arrhythmias and diastolic dysfunction, which can lead to acromegalic cardiomyopathy. Together with LVH and AAS-induced hypertension, endothelial dysfunction significantly increases the risk of myocardial infarction and sudden cardiac death.

Excessive connective tissue accumulation causes biomechanical impairments, such as soft-tissue swelling in the carpal arch, which can lead to carpal tunnel syndrome and can be a major cause of disability for athletes who must undertake repetitive activities. Arthralgia, myopathy, and significant peripheral edema secondary to sodium and water retention are also common complaints. There is also a theoretical oncological risk. Systemic activation of the IGF-1 receptor triggers potent mitogenic and anti-apoptotic effects. Long-term activation of this cell-surface receptor may promote the growth of pre-existing, clinically inapparent microtumors, leading to unpredictable consequences for the athlete's long-term health and survival (Ehrnborg et al., 1999).

The Anti-Doping Arms Race: Advanced Detection Methodologies

Detection of recombinant human GH (rhGH) doping has been, for many years, one of the most difficult tests for the World Anti-Doping Agency (WADA). The reasons are several: on the one hand, the hormone's highly pulsatile endogenous profile, which peaks significantly during deep sleep and exercise. On the other hand, the hormone's half-life in the systemic circulation is approximately 15-20 minutes. Finally, synthetic recombinant rHGH shares an identical amino acid sequence with the major 22 kDa pituitary isoform, making them indistinguishable by standard protein analysis (Bidlingmaier et al., 2009). In the meantime, WADA is using two alternative approaches:

1. The Isoform Differential Immunoassay: Human Growth Hormone: exogenous vs. endogenous. Endogenous human pituitary growth hormone (hGH) consists of a heterogeneous mixture of protein isoforms. While the major component is the 22-kDa form of GH, other components include smaller 20-kDa forms and acidic and basic forms. In contrast, the recombinant human growth hormone (rhGH) administered to athletes as a performance-enhancing drug consists solely of the 22-kDa monomer. Upon injection of rhGH, there is an excess of the 22-kDa GH in the pituitary gland and hypothalamus, resulting in a strong negative feedback on all other forms of GH except the 22-kDa form of the hormone. The WADA isoform test uses specific monoclonal antibodies to measure the 22-kDa-to-non-22-kDa ratio of GH in blood samples, and samples with isoform ratios higher than normal indicate exogenous rhGH administration. The half-life of GH is short (24-36 hours) (McHugh et al., 2005).

2. The Biomarkers Test (GH-2000 Method): Out-of-competition testing requires an extended detection window, making it essential to identify reliable biomarkers of human growth hormone (hGH). The effect of growth hormone (GH) as a protein lasts only a few hours due to rapid degradation, whereas the induced metabolic and structural effects persist significantly longer; thus, these effects also serve as markers for detecting GH abuse. In the GH test in question, the methodology measures two GH-dependent proteins: insulin-like growth factor-1 (IGF-1) and the amino-terminal propeptide of type III collagen (P-III-NP). P-III-NP is a sensitive marker for soft tissue and bone metabolism. The production of P-III-NP is almost exclusively regulated by the GH/IGF-1 pathway. An athlete administering supratherapeutic doses of recombinant human growth hormone (rhGH) will exhibit a surge in serum IGF-1 and P-III-NP concentrations, characterized by an exponential profile. The Isoform Test has a very short detection window of only a few hours. However, IGF-1 and P-III-NP levels remain elevated for 2-3 weeks following rhGH administration (Powrie et al., 2007). Table 2 summarizes both methods.

The decision limits (DLs) for validation must be strictly gender- and age-specific and 100% free of false alarms. The DLs for the biomarker test will be derived from multivariate discriminant analysis scores for the clean athlete, based on a comprehensive dataset (thousands of samples per marker per sport), using a large sample size to ensure robustness. An athlete's total biomarker score will be above the maximum range for the demographic cohort determined (i.e., a score that is over 99.99% specificity for the demographic

cohort, which will be set normally at +2SD of the mean for the demographic cohort, with the cut-off at +3SD at the end of the distribution for the demographic cohort). In this case, an abnormal finding triggers a formal report, reflecting the significant success achieved by coupling isoform and biomarker tests in forensic sports endocrinology.

Table 2. Analytical methodologies employed by WADA to detect rhGH doping.

Detection Strategy	Primary Target / Biomarker	Principle of the Test	Detection Window
Isoform Differential Immunoassay	Ratio of 22-kDa hGH to non-22-kDa isoforms	Exogenous rhGH (purely 22-kDa) suppresses endogenous heterogeneous pituitary secretion.	Short (typically 24 to 36 hours post-injection)
Biomarkers Test	Serum IGF-1 and P-III-NP concentrations	Measures downstream physiological markers of hGH action, which remain elevated longer than the hormone itself.	Extended (up to several weeks following cessation of administration

4. CONCLUSION

The physiological reality of rhGH abuse sharply contradicts athletic expectations. Delivering supratherapeutic doses to the body results in no increase in myofibrillar hypertrophy or absolute strength. The observed physical changes are actually just the result of collagen synthesis and fluid retention. Chronic abuse exposes athletes to severe pathological risks, causing profound insulin resistance and cardiomyopathy. One of the biggest challenges in deterring this abuse is detection: exogenous rhGH shares the same molecular structure as endogenous hGH. While current diagnostic tests effectively identify rhGH use, they only detect it for a short time after administration. To effectively crack down on doping and protect athlete health, anti-doping authorities need to implement advanced transcriptomic and metabolomic biomarkers.

Acknowledgments

The authors have no acknowledgments to disclose.

Authors' Contributions

Bartłomiej Kowalski: Conceptualization, supervising, writing – rough preparation
Natalia Kriese: Formal analysis, investigation
Jakub Szyszkowski: Writing – rough preparation
Brygida Tucka: Project administration
Paweł Woś: Conceptualization
Izabella Zawadzka: Resources, literature review
Zuzanna Zgrzywa: Methodology, literature review
Ewelina Komorowska: Conceptualization, methodology
Paulina Wądołowska: Investigation, editing
Jakub Jaworski: Editing

Informed consent

Not applicable.

Ethical approval

Not applicable. This article does not contain any studies with human participants or animals performed by any of the authors.

Funding

This research did not receive any external funding like specific grant from funding agencies in the public, commercial, or nonprofit sectors.

Conflict of interest

The authors declare that they have no conflicts of interest, competing financial interests or personal relationships that could have influenced the work reported in this paper.

Data and materials availability

All data associated with this study will be available based on the reasonable request to corresponding author.

REFERENCES

1. Bidlingmaier M, Suhr J, Ernst A, Wu Z, Keller A, Strasburger CJ, Bergmann A. High-sensitivity chemiluminescence immunoassays for detection of growth hormone doping in sports. Clin Chem 2009;55(3):445-453. doi: 10.1373/clinchem.2008.112458.
2. Ehrnborg C, Bengtsson BA, Rosén T. Growth hormone abuse. Baillieres Best Pract Res Clin Endocrinol Metab 1999;13(1):55-73. doi: 10.1053/beem.2000.0054.
3. Holt RI, Böhning W, Guha N, Cowan DA, Sönksen PH. The detection of growth hormone abuse in sport. Expert Rev Endocrinol Metab 2010;5(2):283-294. doi: 10.1586/eem.10.13.
4. Holt RI, Erotokritou-Mulligan I, Sönksen PH. The history of doping and growth hormone abuse in sport. Growth Horm IGF Res 2009;19(4):320-326. doi: 10.1016/j.ghir.2009.04.009.
5. Holt RI. Is human growth hormone an ergogenic aid? Drug Test Anal 2009;1(9-10):412-418. doi: 10.1002/dta.58.
6. Macintyre JG. Growth hormone and athletes. Sports Med 1987;4(2):129-142. doi: 10.2165/00007256-198704020-00004.
7. McHugh CM, Park RT, Sönksen PH, Holt RI. Challenges in detecting the abuse of growth hormone in sport. Clin Chem 2005;51(9):1587-1593. doi: 10.1373/clinchem.2005.047845.
8. Powrie JK, Bassett EE, Rosen T, Jørgensen JOL, Napoli R, Sacca L, Christiansen JS, Bengtsson BA, Sönksen PH. Detection of growth hormone abuse in sport. Growth Horm IGF Res 2007;17(3):220-226. doi: 10.1016/j.ghir.2007.01.011.
9. Saugy M, Robinson N, Saudan C, Baume N, Avois L, Mangin P. Human growth hormone doping in sport. Br J Sports Med 2006;40(Suppl 1):i35-i39. doi: 10.1136/bjsm.2006.027573.
10. Sönksen PH. Insulin, growth hormone and sport. J Endocrinol 2001;170(1):13-25. doi: 10.1677/joe.0.1700013.
11. Wallace JD, Cuneo RC, Baxter R, Ørskov H, Keay N, Pentecost K, Dall R, Rosén T, Jørgensen JO, Cittadini A, Longobardi S, Sacca L, Christiansen JS, Bengtsson BA, Sönksen PH. Responses of the growth hormone (GH) and insulin-like growth factor axis to exercise, GH administration, and GH withdrawal in trained adult males: a potential test for GH abuse in sport. J Clin Endocrinol Metab 1999;84(10):3591-3601. doi: 10.1210/jcem.84.10.6037.
12. World Anti-Doping Agency (WADA). Guidelines: Human Growth Hormone (hGH) Biomarkers Test. World Anti-Doping Agency, Montreal, 2018.