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## Human Growth Hormone Abuse in Male Weightlifters

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### Abstract

In a study of performance-enhancing substance use among 231 experienced young male weightlifters, we found that 27 (12%) reported illicit use of human growth hormone (HGH) or its bioactive derivative, insulin-like growth factor-1 (IGF-I). All of these 27 men also reported use of anabolic-androgenic steroids (AAS) and 22 (81%) met criteria for current or past AAS dependence. Fifteen (56%) also reported current or past dependence on opioids, cocaine, and/or ecstasy. These findings suggest that among young male weightlifters, illicit HGH use has become a common form of substance abuse, frequently associated with both AAS dependence and classical substance dependence.

### Introduction

Human growth hormone (HGH), once an expensive performance-enhancing drug used primarily by elite athletes,<sup>1,2</sup> has now become cheaply available over the Internet.<sup>3–6</sup> However, few studies have as yet assessed the prevalence or correlates of illicit HGH use. Anonymous surveys have produced disparate results; an American study claimed that 11 (5%) of 224 10th-grade boys and one (0.5%) of 208 girls had used HGH,<sup>7</sup> but a German survey of 2287 adolescent students found a prevalence of only 0.5% in boys and 0.3% in girls.<sup>8</sup> An anonymous survey of 100 anabolic-androgenic steroid (AAS) users in Wales found that 12 (12%) users reported having tried HGH,<sup>9</sup> and a similar Welsh study nine years later found that the prevalence had risen to 25 (24%) of 102 AAS users.<sup>10</sup> An interview study found only one HGH user (0.6%) among 176 self-declared AAS users (171 men, 5 women) in Wales,<sup>11</sup> and another found only one (4%) HGH user among 25 American women who had used AAS.<sup>12</sup> A subsequent interview study of experienced male weightlifters found that 3 (6%) of 48 AAS users reported lifetime HGH use, and one additional AAS user reported use of the bioactive derivative of HGH, insulin-like growth factor-1 (IGF-I).<sup>13</sup> None of the 45 comparison weightlifters in this study reported use of HGH or IGF-I.

Notably, the above studies were conducted at a time when HGH was more expensive than it is today.<sup>6</sup> By contrast, a recent interview study of 32 AAS users seeking treatment at a Swedish addiction clinic (30 male, 2 female) reported that 15 (47%) had used HGH and 5

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#### Declaration of Interest

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(16%) IGF-I.<sup>14</sup> These individuals used many classical drugs of abuse, including cannabis, opioids, and amphetamines – suggesting that AAS and HGH were often part of a larger pattern of polysubstance abuse in this population.

There is substantial evidence that long-term supraphysiologic levels of HGH may cause adverse effects – as suggested by studies of acromegaly, a naturally occurring disorder characterized by prolonged supraphysiologic levels of HGH. Acromegalic patients show standardized mortality rates about twice that of the general population,<sup>15</sup> and the magnitude and duration of HGH elevation are the primary determinants of survival.<sup>16,17</sup> Acromegaly is particularly associated with adverse cardiovascular effects, including cardiomyopathy, hypertension, valve dysfunction, and arrhythmias.<sup>18–20</sup> Supraphysiologic levels of HGH may also lead to diabetes mellitus,<sup>21</sup> impaired respiratory function,<sup>22</sup> and possibly various malignancies.<sup>23,24</sup> The risk of these outcomes in illicit HGH users remains to be determined. However, given the potential for adverse physical consequences associated with long-term HGH use, it is imperative to explore the phenomenon of illicit HGH use. Therefore, in an effort to augment the limited data on the characteristics of illicit HGH users, we present preliminary findings on HGH and IGF-I use obtained in an ongoing study of American male weightlifters.

## Methods

Since 2005, we have evaluated male weightlifters and other athletes in a study exploring risk factors for AAS use. We have recruited men aged 18–40 in Florida, Massachusetts, and California, using methods designed to obtain a representative sample of experienced weightlifters while attempting to minimize selection bias, as described in detail previously.<sup>13,25</sup> In particular, the study's focus on AAS and other performance-enhancing drugs is not disclosed during the recruitment process. Study participants receive demographic questions; the Structured Clinical Interview for DSM-IV (SCID);<sup>26</sup> a computerized battery of psychological rating scales; physiological measures including fat-free mass index (FFMI);<sup>27</sup> and detailed questions regarding history of use of both classical and performance-enhancing drugs – the latter including not only AAS, but also HGH, IGF-I, thyroid hormones, clenbuterol, and others. We have described these methods in greater detail elsewhere.<sup>25</sup>

For this paper, we compared 1) all men reporting lifetime use of HGH/IGF-I with 2) men reporting lifetime AAS use but no HGH/IGF-I use and 3) men reporting no AAS or HGH/IGF-I use. We performed these comparisons using linear and logistic regression (using ranked data in cases of skewed distributions) with adjustment for study site (Florida, Massachusetts, or California), age (modeled as quintiles of the distribution), ethnicity (white versus non-white), and years of regular weightlifting (defined as attending a commercial gymnasium  $\geq 3$  days per week). Alpha was set at 0.05, 2-tailed. Note that we did not adjust for the effect of multiple comparisons and that therefore some differences, especially those of marginal significance, might be attributable to chance.

## Results

Of 248 participants seen as of June 2009, 231 yielded evaluable data; 17 were excluded because of incomplete data ( $N = 2$ ), presence of AAS ( $N = 6$ ) or other drugs ( $N = 5$ ) in urine or hair samples despite denial by the participant, or implausibly high muscularity and low body fat despite denial of AAS use ( $N = 4$ ; see operational criteria for this exclusion previously reported (25)). Of the 231 evaluable men, 100 (43%) reported lifetime AAS use and 131 (57%) did not. Twenty-six men who reported lifetime HGH use and one additional man reported use of IGF-I, but not HGH. Since IGF-I is the bioactive derivative of HGH, we

classified this man with the other HGH users, bringing the total to 27. Strikingly, all of these 27 men were also AAS users (Figure 1); none of the 131 non-AAS-users reported use of HGH or IGF-I ( $p < 0.001$ , by Fisher's exact test). All of the HGH users first tried HGH after having already tried AAS; the mean (SD) latency from first AAS use to first HGH use was 4.5 (4.1) years (range 0.5–19 years).

The 26 men who had specifically taken HGH reported a median (interquartile range) lifetime duration of HGH use of 23 (10, 55) weeks; the 7 men reporting use of IGF-I (6 of whom had also used HGH) reported a median IGF-I use of 9 (8, 10) weeks. Users typically reported using 15–20 units of HGH per week and 50–75  $\mu\text{g/day}$  of IGF-I, but these estimates should be considered approximate, especially given the uncertain authenticity of illicitly obtained preparations. Notably, the 27 HGH/IGF-I users typically reported very long-term AAS use, with a median total lifetime AAS use of 173 (91, 390) weeks. By comparison, the 73 AAS users without HGH/IGF-I use reported a median of only 24 (10, 42) total weeks of AAS use (mean estimated difference in ranks [95% confidence interval] 31.8 [20.8, 42.7];  $p < 0.001$ ). Indeed, 22 (81%) of the HGH/IGF-I users had a history of current or past AAS dependence, as diagnosed by modified DSM-IV criteria that we have recently published.<sup>28</sup> By contrast only 9 (12%) of the 73 AAS users without HGH/IGF-I use displayed a history of AAS dependence (odds ratio [95% confidence interval]: 28.1 [6.4, 123.2];  $p < 0.001$ ).

The HGH/IGF-I users were older, had lifted weights for longer, and were strikingly more muscular (i.e., higher in FFMI) than either comparison group (Table 1). The HGH/IGF-I users were the least well educated of the three groups, with only 19% having graduated from college despite their greater mean age. All groups showed a substantial lifetime prevalence of non-alcohol substance dependence, with the HGH/IGF-I users showing the highest prevalence of all. This contrast became even more striking when we deleted cases of cannabis dependence, the most common form of non-alcohol substance dependence. More than half of the 27 HGH/IGF-I users reported a history of dependence on at least one drug other than cannabis or alcohol, including opiates ( $N = 8$ ), methylenedioxymethamphetamine ("ecstasy") (8), cocaine (7), stimulants (1), and/or polysubstances (1). The prevalence of these forms of substance dependence among the HGH/IGF-I users was slightly higher than among AAS users who had not used HGH/IGF-I, and markedly higher than among weightlifters who had used neither AAS nor HGH/IGF-I (Table 1).

## Discussion

In an ongoing study of 231 experienced male weightlifters aged 18–40, we found that illicit HGH use is common, often prolonged, and closely associated with abuse of or dependence upon both AAS and classical drugs – a finding consistent with the European data cited earlier (10, 14). In this context, it is difficult to determine whether HGH abuse arises solely as a comorbid substance abuse disorder in a population with high rates of AAS use and of classical substance dependence, or whether prolonged HGH use might develop into a true chemical dependency in its own right. Although HGH does not produce a “reward” of acute intoxication in the manner of classical dependence-inducing drugs such as alcohol or opioids, the possibility remains that its metabolic effects, or perhaps even subtle hedonic effects, might themselves be sufficiently reinforcing to induce a dependence syndrome in some individuals. Further studies of the neurobiology underlying HGH abuse will be needed to understand this distinction more fully.

Notably, the 27% prevalence of lifetime HGH/IGF-I use among AAS users in the present study was significantly greater than the 8% prevalence among 48 AAS users in our similar previous study of weightlifters in 2003<sup>13</sup> ( $p = 0.009$  by Fisher's exact test) – likely reflecting

the increasing availability and decreasing price of HGH in recent years. When interpreting these findings however, it should be recognized that young male weightlifters, while probably the largest consumers of HGH<sup>6,10,14</sup> are not the only population that uses this hormone illicitly. In particular, many non-weightlifters, often older than age 40, receive prescriptions for HGH from “anti-aging” clinics, compounding pharmacies, and other possibly illegal sources.<sup>29</sup> These individuals likely differ from the population evaluated in the present study.

Despite its apparently growing popularity, there is little evidence that supraphysiologic HGH produces anabolic effects in non-HGH-deficient individuals<sup>30–33</sup> – although it might have such effects when used in conjunction with AAS (30, 31) or shortly after stopping AAS use.<sup>34,35</sup> Conversely, as reflected in the acromegaly literature, there is substantial evidence that long-term supraphysiologic levels of HGH may adverse cardiovascular,<sup>18–20</sup> metabolic,<sup>21</sup> and respiratory effects<sup>22</sup> as well as increase the risk for certain types of malignancy.<sup>23,24</sup> Importantly, long-term AAS use also impairs cardiac function<sup>36,37</sup> – raising the ominous possibility of additive cardiotoxic effects,<sup>38</sup> given the overlap between illicit HGH and AAS use.

Our findings regarding HGH abuse have implications not only for public health in general, but for practicing clinicians as well. Most notably, given the observed overlap between HGH abuse, AAS use, and classical substance use, individuals with chemical dependencies, especially those reporting AAS use, should be routinely questioned about HGH use. Identification and awareness are essential first steps to curb the increasing numbers of HGH-using individuals. In addition, future investigation into the underlying neurobiology of HGH abuse will be necessary to better understand potential adverse effects, delineate possible reinforcing effects, and to explore potential treatment interventions.

We acknowledge several limitations to this study. First, like almost all studies of substance abusers in the field, our findings rely on retrospective self-reports by individuals using illicit substances of uncertain potency or authenticity. Thus, the possibilities of recall bias and other forms of information bias must be recognized. Second, despite our methods to minimize selection bias described above, the possibility remains that the HGH users in this study were not fully representative of the source population from which they were drawn. Although selection bias and information bias cannot be entirely eliminated in naturalistic studies of illicit substance abusers, it will be important to retest our findings in other populations of weightlifters and other individuals at risk for HGH abuse. Third, as previously noted, we did not adjust for the effect of multiple comparisons in our analysis. Although there are reasons to favor this approach,<sup>39,40</sup> the greater possibility of chance associations must be considered when evaluating the tests of significance that we have reported.

In summary, our preliminary observations suggest that illicit HGH abuse has become common among young American male weightlifters, and is often associated with polysubstance abuse, embracing both performance-enhancing and classical drugs. With the declining price and greater availability of HGH, future years may see even larger numbers of users, ingesting HGH for even longer periods at higher doses. Escalating abuse of HGH may eventually pose significant health problems,<sup>18–24</sup> given evidence that long-term supraphysiologic levels of HGH may be associated with elevated morbidity and mortality.

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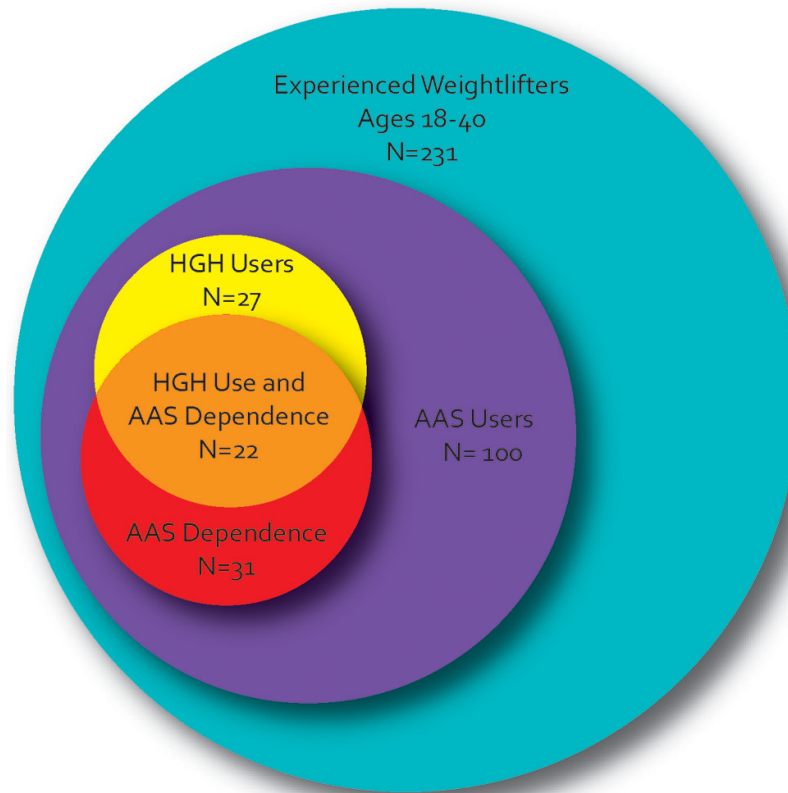
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**Figure 1.** Association between anabolic-androgenic steroid use, anabolic-androgenic steroid dependence, and human growth hormone use in 231 young male weightlifters.

**Table 1**

Demographic Features of HGH Users, Other AAS Users, and Comparison Weightlifters

	Group			Between-Group Comparisons		
	I. HGH plus AAS Use (N = 27)	II. AAS but no HGH use (N = 73)	III. No AAS or GH Use (N=131)	Group I vs. Group II	Group I vs. Group III	Group II vs. Group III
Age, Yrs.	32.5 (4.7)	29.2 (6.2)	27.8 (5.8)	0.01 <sup>a</sup>	< 0.001 <sup>a</sup>	0.09 <sup>a</sup>
Years of regular weightlifting	11.6 (4.7)	9.8 (6.1)	8.4 (5.0)	-0.5 (-2.3, 1.2)	0.4 (-1.3, 2.1)	0.9 (-0.2, 2.1)
Fat-free mass index, kg/m <sup>2</sup>	26.2 (2.8)	23.3 (2.3)	22.8 (1.9)	2.8*** (1.8, 3.8)	3.4*** (2.5, 4.3)	0.6 (0.0, 1.2)
		N (%)		Mean Difference (95% confidence interval) <sup>b</sup>		
				Odds Ratio (95% confidence interval) <sup>b</sup>		
Income > \$30,000	21 (78)	45 (62)	71 (54)	1.3 (0.4, 3.8)	1.6 (0.6, 4.3)	1.2 (0.6, 2.3)
Never married	15 (56)	56 (77)	105 (80)	0.6 (0.2, 1.8)	0.7 (0.2, 1.8)	1.1 (0.5, 2.5)
Grad 4-yr college	5 (19)	20 (27)	62 (47)	0.5 (0.2, 1.6)	0.2*** (0.1, 0.6)	0.4*** (0.2, 0.8)
Alcohol dependence <sup>c</sup>	4 (15)	17 (23)	19 (15)	0.5 (0.1, 1.7)	0.7 (0.2, 2.5)	1.5 (0.7, 3.1)
Substance dependence <sup>d</sup>	19 (70)	41 (56)	50 (38)	2.1 (0.8, 5.5)	4.2*** (1.6, 10.8)	2.0* (1.1, 3.7)
Non-cannabis substance dependence <sup>e</sup>	15 (56)	31 (42)	22 (17)	1.6 (0.6, 4.1)	5.6*** (2.1, 15.0)	3.6*** (1.7, 7.4)

<sup>a</sup> By t test, two-tailed.

<sup>b</sup> Estimates adjusted for age, study site, and ethnicity (see full text of paper).

\* p < 0.05;

\*\* p < 0.01;

\*\*\* p < 0.001

<sup>c</sup> Lifetime history of alcohol dependence.

<sup>d</sup> Lifetime history of dependence on any classical drug of abuse other than alcohol (excludes AAS dependence).

<sup>e</sup> Lifetime history of dependence on any classical drug other than alcohol or cannabis (excludes AAS dependence).