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**ORIGINAL ARTICLE**

# Injecting human growth hormone as a performance-enhancing drug—perspectives from the United Kingdom

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**Abstract**
Injectable human growth hormone has been used as a performance-enhancing drug in the United Kingdom since at least the mid-1980s. However, because of its prohibitive cost and limited supply it was initially restricted to a relatively small number of people. More recently data suggest that there has been a large increase in the use of the hormone within some sections of the general population. Here the hormone is usually taken as part of a high-dose polydrug regimen (which includes multiple types of anabolic steroids) predominately to enhance physique and/or bodily aesthetics. However, detailed systematic studies of the cultural diffusion of this drug (including the motivations for use, prevalence, patterns of use, and supply network) are lacking. Moreover, questions about growth hormone's efficacy, effectiveness, and safety (including risks from injecting and the use of adulterated products) when used as a performance-enhancing drug remain largely unanswered. This article reviews the data that are available on the self-directed use of growth hormone in the United Kingdom and the associated risks to individual and public health.

**Keywords:** *Growth hormone, performance-enhancing drugs, drug adulteration/counterfeits, anabolic steroids, Needle and Syringe Programmes, 20th century history, United Kingdom, harm reduction, body image, acromegaly, causality, observational research.*

## Background statement

This article includes information on growth hormone products that are available unlawfully on the illicit market in the United Kingdom. Some of these products (Table III) use the same generic and/or proprietary names (and trademarks thereof) as legitimate products that have been licensed by drug regulatory authorities (British Medical Association & Royal Pharmaceutical Society of Great Britain, 2008, pp. 405–406). The authors make no

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claim as to the authenticity of the products being sold on the illicit market; their listing herein serves to inform healthcare professionals of some of the names of products that they may encounter when providing health care to users.

## An introduction to growth hormone

> . . . the question has been raised as to the existence of the anterior [pituitary] growth hormone . . . final proof for the growth hormone as a separate entity can only be obtained by the isolation of the hormone freed from other active components as well as from inert proteins . . . we will describe a method . . . for isolating a protein from the anterior lobe of ox pituitary, which can be shown to have the biological characteristics of the growth hormone. (Li, Evans, & Simpson, 1945)

Human growth hormone (hGH) (somatotropin) is an endogenous peptide hormone involved in the regulation of a diverse number of physiological processes including linear growth; protein, carbohydrate, and lipid metabolism (which includes effects on body composition such as anabolic and lipolytic actions); cardiovascular health; physical performance; and well-being (Gibney, Healy, & Sönksen, 2007; Simpson et al., 2002; Velloso, 2008). The hormone is secreted in a pulsatile manner from the somatotrope cells of the anterior pituitary gland predominately during deep (slow wave) sleep (Holl et al., 1991; Takahashi, Kipnis, & Daughaday, 1968). However, a range of physiological stimuli including exercise, food intake, and stress also modulate secretion (Gibney et al., 2007; Giustina & Veldhuis, 1998; Sutton & Lazarus, 1976). Feedback from peripheral and central signals modulates secretion through the hormones ghrelin and growth hormone-releasing hormone which promote release, and somatostatin, which inhibits release (Veldhuis, 2003). Changes in the amount (and rate of secretion) of growth hormone also occur throughout life, with the highest being during puberty[1] with a decline thereafter (usually beginning around ages 18–25) (Giustina & Veldhuis, 1998).

Growth hormone mediates both direct and indirect effects that are initiated through binding to the growth hormone receptor that is expressed in virtually every tissue in the body (Kaplan & Cohen, 2007). It is the latter, indirect, effects that have been studied in most detail, being mediated by insulin-like growth factor-1 (IGF-1) (Daughaday et al., 1972), which is produced by the liver and other tissues in response to stimulation by the hormone (Kaplan & Cohen, 2007; Le Roith, Bondy, Yakar, Liu, & Butler, 2001).[2]

In 1921, two researchers at the University of California, Herbert Evans and Joseph Long, briefly described the growth-promoting properties of a crude extract derived from bovine anterior pituitary when it was injected intraperitoneally into rats (Evans & Long, 1921).[3] Using a similar technique, Smith and Smith subsequently demonstrated that

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[1]High levels are also seen in the neonatal period (Giustina & Veldhuis, 1998).

[2]This indirect signaling pathway is part of the reason why exogenous IGF-1 is used as a performance-enhancing drug by some individuals (Llewellyn, 2009, pp. 544–545; Velloso, 2008).

[3]Prior to this equivocal data had been presented. Schäfer (1908), Robertson (1916), and Goetsch (1916) all reported accelerated growth of rodents fed on anterior pituitary lobes, while Cushing found that "repeated subcutaneous injections of sterile extracts or emulsions of the *whole gland*, or of the *posterior lobe alone* . . . we apt to lead to emaciation" and "Sandri's experiments in feeding young mice with bovine anterior lobe were quite negative. The feeding of posterior lobe arrested development—an effect attributed to the toxicity of the active principle . . . More recently Aldrich, and similarly Lewis and Miller, have reported negative results after feeding [anterior pituitary lobes] to young rats" (Goetsch, 1916, p. 32) (*our emphasis*). See Brown (1984, pp. 369–389) for a discussion of the methodological limitations of these experiments.

normal growth could resume in hypophysectomized[4] tadpoles (Smith & Smith, 1922). Later, Evans, with his colleagues Choh Li and Miriam Simpson, went on to extract a pure form of this "growth hormone" protein from bovine anterior pituitaries, which they reported caused a resumption of growth in hypophysectomized rats (Li & Evans, 1944; Li et al., 1945). Subsequently, Wilhelmi, Fishman, and Russell (1948) developed an extraction method that allowed a crystalline form of growth hormone to be produced, which along with reducing "the tedium of the many repeated steps of the [existing] process" (Wilhelmi et al., 1948) increased the yield of the hormone, allowing researchers greater freedom to study the effects of this peptide (Li, Evans, & Simpson, 1948; Tattersall, 1996; Wilhelmi et al., 1948). By 1956, both monkey and human forms had been prepared (the latter being derived from the pituitary glands of cadavers) (Li & Papkoff, 1956), and while the first treatments in human patients using bovine growth hormone were equivocal[5] (Lewis, Klein, & Wilkins, 1950; Shorr, Carter, Kennedy, & Smith, 1953), metabolic changes (including anabolic effects) were reported in short-term studies when individuals were treated with monkey or hGH (albeit this was initially restricted to the treatment of a small number of individuals) (Beck, McGarry, Dyrenfurth, & Venning, 1957; Ikkos, Luft, & Gemzell, 1958; Korner et al., 1959; Luft, Ikkos, Gemzell, & Olivecrona, 1958; Raben, 1958). Thereafter because of the limited amount of cadaveric pituitaries that were available, the supply of the hormone was predominately restricted for the treatment of childhood growth hormone deficiency (GHD) (Korner et al., 1959; Milner et al., 1979).

In 1985, treatment with growth hormone derived from cadavers was stopped after it was associated with the development of the fatal neurodegenerative disease Creutzfeldt–Jakob disease (CJD) in some individuals (Belay & Schonberger, 2005; CDC, 1985; Food and Drug Administration, 1985a; Gibbs et al., 1985; Koch, Berg, De Armond, & Gravina, 1985; Powell-Jackson et al., 1985). In the same year the first recombinant form of hGH [a biosynthetic product produced in bacteria (Flodh, 1986)], methionyl growth hormone (met-hGH, somatrem), was licensed by regulatory authorities for treating young people with GHD (Flodh, 1987; Food and Drug Administration, 1985b; Genentech, 1985; Milner, 1985). Not only could this form of growth hormone be produced in large amounts but it was also free from the causative agent of CJD. The composition of met-hGH differed slightly from the endogenous form of the hormone by the addition of a methionine residue at the N-terminal (Flodh, 1986). Shortly thereafter another form of recombinant growth hormone (rhGH, somatropin) (Fryklund, 1987) whose sequence was identical to the endogenous form was licensed for the same clinical indication. Nowadays it is rhGH products that are used exclusively for therapeutic purposes in the United Kingdom (British Medical Association & Royal Pharmaceutical Society of Great Britain, 2008, pp. 405–406).

Importantly, the development and subsequent refinement of these recombinant technologies offered a mechanism for the large-scale, potentially limitless, production of growth hormone, which afforded both sufficient hormone for "breakthrough discoveries in basic [and applied] science" (Cronin, 1997) and to significantly expand work outside of the treatment of young people with GHD (Tattersall, 1996). This included research into the role of the hormone in adults [such as its effects on body composition (e.g., Crist, Peake, Egan, Waters, 1988; Rudman et al., 1990)] and its potential for treating a range of

[4]Where the pituitary gland was removed experimentally.

[5]This is because of the differences in the structure of the hormone between the two species (Lui & Papkoff, 1956; Peterson & Brooks, 2000).

conditions, including those with adult GHD. Moreover, some were already cautioning "that plentiful supplies may also encourage abuse – that practitioners of "cosmetic endocrinology" will use the hormone to increase athletic prowess or to increase the height of children in the belief it will improve their social and economic prospects" (Blakeslee, 1987).

## The therapeutic use of growth hormone

In the UK growth hormone is licensed for a small number of therapeutic indications. In children these include those with (i) proven GHD, (ii) Turner syndrome, (iii) Prader–Willi syndrome, or (iv) pre-pubertal chronic renal insufficiency [recommended by the National Institute of Health and Clinical Excellence (NICE) (National Institute for Clinical Excellence, 2002)]. More recently growth hormone has also been licensed for use in "short children considered small for gestational age at birth . . . whose growth has not caught up by 4 years or later"[6] (British Medical Association & Royal Pharmaceutical Society of Great Britain, 2008, pp. 404–406). In adults, growth hormone is licensed for patients with pronounced GHD. NICE recommends treatment only in those with GHD that meet all the following criteria: (i) severe GHD (established by a validated method); (ii) perceived impairment of quality of life (established by a disease-specific questionnaire), and (iii) already receiving treatment for another pituitary hormone deficiency (British Medical Association & Royal Pharmaceutical Society of Great Britain, 2008, pp. 404–406, National Institute for Clinical Excellence, 2003).

## How many people use growth hormone?

> GROWTH HORMONE . . . Wow, is this great stuff! It is the best drug for permanent muscle gains . . . it will make anybody grow . . . GH use is the biggest gamble that an athlete can take, as the side effects are irreversable [sic]. Even with all that, we LOVE the stuff. (Dan Duchaine author of the original Underground Steroid Handbook, cited in Goldman, Bush, & Klatz, 1984, p. 260).

> Since HGH [human growth hormone] has been reported in the lay press to quickly build muscle on athletes, and since its cost is likely to drop dramatically, there is no doubt that HGH will soon become the "in" drug of the near future (Goldman et al., 1984, p. 110).

> I can't honestly tell you if my rave review [in the original Underground Steroid Handbook] had anything to do with increasing the drug's popularity, but today, eight years later, Human Growth Hormone is the most sought after drug in athletics (Duchaine, 1989, p. 74).

There is a lack of robust data on the incidence and prevalence of growth hormone use in the United Kingdom—an issue that extends to all estimates of performance-enhancing drug use, including anabolic steroids (Evans-Brown & McVeigh, 2009). Anecdotal reports

[6]At the time the NICE guidance was issued growth hormone was not licensed to treat children for this indication, and so the guidance does not cover this indication (National Institute for Clinical Excellence, 2002).

suggest that the hormone has been available in gyms for more than 20 years (Ellis, 1988; Garner & Miles, 1985; McKillop, 1987). However, it was not until Korkia and Stimsons' landmark study in 1992 (1993)—*Anabolic steroid use in Great Britain: an exploratory investigation*—that a more formal indication of the level of use became available. This study examined use of the hormone in a group of 110 anabolic steroids users (which included both recreational and competitive sportspersons/bodybuilders) drawn from nine geographical locations in England, Scotland, and Wales. They found that three individuals (2.72%, 3/110) had used the hormone in the previous 6 months (Korkia & Stimson, 1993), which the authors understood to be essentially "confined to those few who can afford it (ie. [sic]. dealers and high standard bodybuilders)" (Korkia & Stimson, 1993, p. 122; and supported by the findings of McKillop, 1987). Since this report we are aware of a further five published studies from the United Kingdom that have examined the use of the hormone outside of elite sport (Table I). The most recent study recruited participants from "hardcore" (see Lenehan, McVeigh, & Bellis, 1996, for a definition) gyms in South Wales (Graham et al., 2006) and found that out of 96 current anabolic steroid users, 24% were also currently using growth hormone.[7]

However, care must be taken when extrapolating these data to the wider gym population. This is because all the studies listed in Table I either recruited individuals already known to be using anabolic steroids or sampled populations from "hardcore" gyms where, typically, a high prevalence of performance-enhancing drug use is found (Lenehan et al., 1996). While it is not feasible to use probability sampling for research sites, and those participating in interviews (Korkia & Stimson, 1993, pp. 40–41), we must be cognizant that the recruitment practices and sampling frames described above could bias the data. For example, drug regimens practiced in one gym (or even multiple gyms in specific geographical areas) may not be an accurate reflection of the regimens, and so on, used in other settings (Korkia & Stimson, 1993, pp. 40–41); equally, the use of peer researchers, while providing invaluable knowledge of the population and access to this group, could also bias the data through the selection of specific individuals and groups that might not be representative of the entire group, limiting our ability to apply the findings to the wider population (i.e., limiting its generalizability).

Another data source that can provide an indication of the level of growth hormone use is from the routine monitoring and client assessments of individuals reporting performance-enhancing drug use (typically anabolic steroids) who present to needle and syringe programs (NSPs). In the counties of Cheshire and Merseyside in the north west of England, UK, one such system has systematically quantified injecting equipment transactions since 1991. Each client is identified by use of an individualized attributor code comprised of their initials, date of birth, and sex (McVeigh, Beynon, & Bellis, 2003). In recent years this system has been supplemented with a standardized assessment pro forma that provides a detailed account of client drug use and associated issues (such as adverse effects that users attribute to the drugs or their injecting practices). These data from Merseyside, along with a piece of work that examined the knowledge, attitude, and practices toward performance-enhancing drug use in current anabolic steroid users from the same area (unpublished data), provide some indication of the level of growth hormone use by those injecting anabolic steroids (Table II). Furthermore, in the case of those presenting to NSPs, it

[7]Parenthetically, the use of growth hormone for performance-enhancing reasons have been reported in a number of other countries including the United States (e.g., Cohen, Collins, Darkes, & Gwartney, 2007) and Australia (e.g., Larance, Degenhard, Copeland, & Dillon, 2008).

Table I. Studies from the United Kingdom that provide an indication of the level of growth hormone use as a performance-enhancing drug

| Author & year published[†] | Aim of study | Geographic area | Method | Population | Sample | Growth hormone use |
|---|---|---|---|---|---|---|
| Korkia & Stimson (1993) | ". . . to explore the extent of [anabolic steroid] use in Great Britain and to find out how [anabolic steroids] are used, by whom and with what consequences . . . to identify further potential users groups." | Glasgow, Kent, London, Luton, Manchester, Merseyside, Sheffield, South Wales, West Yorkshire. | Researcher-completed structured interview (face-to-face). Interviewers (n = 10) were already known by the interviewees: either "training at the same gym, were patients, or were clients at one of four different syringe-exchanges". Self-reported drug use. Participants received a £5 gift voucher (some participants received a further £5 voucher if they agreed to participate in a "quality" check of their original interview). Participants assured anonymity. | Individuals who were known by the interviewers to be current users of anabolic steroids. | 110 face-to-face interviews. Sample comprised 13 females (11.8%) aged 18–35 (mean age 25.3 ± 5.3 years) and 97 males (88.2%) aged 17–56 (mean age 27.3 ± 7.3 years). | 2.7% (3/110) of those currently reporting anabolic steroid use also reported use of growth hormone in the past 6 months. Users were all male. No data available on frequency of use nor regimens used. |
| Lenehan et al. (1996) | ". . . to provide detailed information on prevalence and patterns of steroid use within the North West of England. . . . 1. To assess the numbers using anabolic steroids. 2. To discover who uses [anabolic steroids] and what actual or potential health risks they take. 3. To assess the long- and short-term service implications." | North West of England. | Researcher-completed structured interview (face-to-face). Self-reported drug use. Participants assured confidentiality and anonymity. | Gym members who reported current use of anabolic steroids. | 386 face-to-face interviews. Sample comprised 7 females (1.8%) and 379 males (98.2%), aged 17–56 (mean age 28 years). | 5.7% (22/386) of those currently reporting anabolic steroid use also reported use of growth hormone in the past 6 months. No data available on sex of user. No data available on frequency of use nor regimens used. |
| Pates & Barry (1996) | ". . . to survey the problems and needs of anabolic steroid users using gymnasia in Cardiff." | Cardiff and "surrounding area". | Self-completed/peer researcher-completed questionnaire. Self-reported drug use. | Gym members in Cardiff and the surrounding area, as well as from other contacts who reported use anabolic steroids to the peer researcher. | 176 people were contacted by the peer researcher and agreed to participate. Sample comprised 5 females (2.8%) and 171 males (97.2%), aged 20–52 (13.6% aged under 25). | 0.6% (1/176) of those reporting anabolic steroid use also reported use of growth hormone. No data available on sex of user. No data available on frequency of use nor regimens used. |

| | | | | | | |
|---|---|---|---|---|---|---|
| Evans (1997) | "To identify unsupervised anabolic steroid regimens used by athletes." | Mid Glamorgan, South Glamorgan, Gwent. | Self-completed questionnaire. Completed questionnaires were placed in a collection box in the gym reception. Self-reported drug use. Participants assured confidentiality and anonymity. | Gym members — questionnaire aimed "to obtain specific information from users of anabolic steroids", recruited from 4 "privately owned" gyms. | The first 100 completed questionnaires were entered in the study (all anabolic steroid users). Respondents were all male and aged between 16–40+ (37% aged under 25). | 12% of those reporting anabolic steroid use also reported 'ever' using growth hormone. Users were all male. No data available on frequency of use nor regimens used. |
| Grace et al. (2001) | ". . . to examine the extent of anabolic androgenic steroid (AAS) use in a sample of recreational gym users in the Mid-Glamorgan area in South Wales, UK. Further aims were to investigate: the types of substances being used; [and,] consequences of use." | Mid Glamorgan. | Self-completed questionnaire. Researchers collected completed questionnaires on-site. Self-reported drug use. Participants assured anonymity. | Gym members recruited from 3 "non-commercial gyms" (believed to be "hardcore‡" gyms, see Grace et al., 2001, p. 191. | 170 questionnaires were distributed, and 106 were completed and returned. Response rate was 63%. Of these, 53% (56/106) reported anabolic steroid use "within the past year", all were male and aged 15–58 (mean 32.4 ± 7.5 years). | Out of the 56 individuals who reported use of anabolic steroids "within the past year", 48% reported using other performance-enhancing drugs. Of these 48%, 6% reported use of growth hormone. Users were all male. No data available on frequency of use nor regimens used. |
| Baker et al. (2006) | ". . . to identify the prevalence of abuse of certain prescription only medicines (POM) amongst health club attendees." | South Wales. | Self-completed questionnaire. Completed questionnaires were returned by pre-paid post to the researchers. Self-reported drug use. Participants assured anonymity. | Gym members recruited from "hardcore‡" gyms (number of gyms not reported). | 210 individuals were offered questionnaires, 146 were completed and returned. Response rate was 69.5%. Respondents comprised 10 females (7%) and 136 males (93%). 65.8% (96/146) of the respondents reported current use of anabolic steroids (no data available on sex of users). | 24% of the 96 individuals who reported current anabolic steroid use also reported current use of growth hormone. No data available on sex of users. No data available on frequency of use nor regimens used. |

†Of note is that all six studies examined the use of growth hormone as a subset of anabolic steroid users rather than as a discrete population, which serves to demonstrate the context in which growth hormone is often used. However, we are not aware of any data providing a sub-analysis between those anabolic steroid users who use growth hormone and those that do not (such as demographics, knowledge, attitudes and practices). ‡"Characterised by having predominantly heavy weight training equipment, competitive bodybuilders and relatively few female members" (Lenehan et al., 1996).

Table II. Data from Merseyside that provides an indication of the level of growth hormone use as a performance-enhancing drug

| Year study completed | Geographic area | Method | Population | Sample | Growth hormone use |
|---|---|---|---|---|---|
| 2007 | Merseyside. | NSP client pro forma completed by drug worker. Self-reported drug use. Participants assured confidentiality. | Assessment of *existing* anabolic steroid users attending Merseyside agency-based NSPs between September 2005 and February 2006. | Convenience sample of 85 individuals abstracted from database. Sample was all male and aged 18–50. | 21.2% (18/85) reported use of growth hormone in the last 12 months. |
| 2008 | Liverpool. | Self-completed questionnaire. Self-reported drug use. Participants assured confidentiality. | Anabolic steroid users recruited from NSPs and reference sampling (snowball) thereof. | 27 (12 participants derived from NSP; 10 from reference sampling thereof; 5 from pilot study that used same questionnaire and run during the same time as data collection from the other 22 participants). Sample was all male and aged between ~20–42 (month of birth not reported). | 29.6% (8/27) reported use of growth hormone. Of these 11.1% (3/27) reported current use and 18.5% (5/27) reported lifetime "ever" use. |
| 2009 | Merseyside. | NSP client pro forma completed by drug worker. Self-reported drug use. Participants assured confidentiality. | *Initial* assessments of anabolic steroid users reported to be presenting for the first time to agency-based NSPs between May 2006–August 2008. | 523 individuals. Sample comprised 6 females (1.1%) and 517 males (98.9%), aged between 17–60 (mean age 28.4 ± 7.4 (SD)). | 4.0% (21/523) reported use of growth hormone in the last 12 months. 9.2% (48/523) reported intention to use growth hormone for the first time in the future. |

appears that these individuals tend to add growth hormone to their drug regimens after anabolic steroid use has commenced (Table II). While data from other settings and geographic locations are required to confirm this finding, it does appear to present an opportunity for discussions with some clients before they start to use growth hormone on whether their goals can be achieved without using the drug, and, in those ultimately choosing to use the drug, provision of appropriate harm reduction advice (see "Harm reduction," below).

Parenthetically, the use of growth hormone as an "anti-aging therapy" or "well-being" drug (self-directed and, in some cases, prescribed by a clinician) appears to be gaining popularity in the United States (Drazen, 2003; Newsweek, 1996; Olshansky & Perls, 2008; Perls, 2004, 2006; Vance, 2003). However, at this time we are not aware of any studies from the United Kingdom that have examined these reasons for use.

## Is growth hormone a "performance-enhancing drug"?

> Probably the biggest blooper I made in the original Underground Steroid Handbook [USH] was proclaiming how wonderfully and effectively Human Growth Hormone (HGH) worked at promoting rapid gains in size and strength. It was the only drug I had not personally used before writing the original USH, and I simply believed all the rumors and anecdotes flying about. (Duchaine, 1989, p. 74)

> Alan [who reported using growth hormone], after acknowledging some users are very disappointed with the drug, said: "I was overjoyed with the results I got off it." . . . Alan claimed HGH effectiveness is dependent upon the application of "correct" knowledge: "I think it's depending on getting correct information and then following up the correct information really. You have to put yourself out to be able to be successful." (Monaghan, 2001, p. 146)

> Although there is little evidence that [growth hormone] improves performance in young healthy adults, randomized controlled studies carried out so far are inadequately designed to demonstrate this, not least because [growth hormone] is often abused in combination with anabolic steroids and insulin. (Holt & Sönksen, 2008)

> Somatropin [rhGH] is considered to be a controversial anabolic and performance-enhancing drug in the realm of bodybuilding and athletics. The main issue of debate is the exact level of potential benefit this substance carries . . . Most experienced individuals now tend to agree that it is the fat-loss promoting properties of somatropin that are most obvious. The drug can support muscle growth, strength gains, and increased athletic performance, but its effects are generally milder than those of the anabolic/androgenic steroids. (Llewellyn, 2009, p. 542)

In 2007, Liu et al. published a paper entitled "Systematic review: the effects of growth hormone on athletic performance." These authors analyzed data that were pooled from research studies where exogenous growth hormone in regimens of various doses and duration were given to "community-dwelling healthy participants between 13 and 45 years of age." They found, inter alia, a significant increase in "lean body mass," which the authors attribute to fluid retention rather than muscle hypertrophy, whereas nonsignificant changes were reported for both fat mass (a decrease that "approached statistical significance") and body weight ("weight increased, although the difference was

not statistically significant"). They further noted that "strength and exercise capacity did not seem to improve" and "in addition, [growth hormone use] . . . may worsen exercise capacity" (Liu et al., 2007). The authors concluded that "[c]laims that growth hormone enhances physical performance are not supported by the scientific literature" (Liu et al., 2007). However, extrapolating these findings to those using growth hormone as part of a high-dose polydrug regimen that include multiple types of anabolic drugs which users believe have synergistic (and additional) effects is problematic.[8] Indeed, as Holt and Sönksen sagely note, in such an environment "it is impossible to control for all these variables within a single trial" (2008). Moreover, perhaps the term "performance enhancing" is used too literally: the largest group of users of these types of drugs exist outside of elite sport (Bolding, Sherr, & Elford, 2002; Dawson, 2001; Korkia & Stimson, 1993; Lenehan et al., 1996). These individuals are not looking to shave time off World and Olympic records,[9] they are typically looking to enhance physique and bodily aesthetics. Here a "performance-enhancing drug" may simply be used as a "fat stripper" (i.e., for its lipolytic effects).[10]

Does any of this discourse actually matter? As researchers committed to reducing the harm associated with performance-enhancing drugs we are concerned that we could be headed for more rancorous debates over the efficacy and adverse effects on health of growth hormone when used in this way—similar to those that concerned the use of anabolic steroids for many years (Taylor, 1991, pp. 24–38; Yesalis, Wright, & Bahrke, 1989), which, because of the manner in which this dispute was played out, is thought to have been partly responsible for the credibility gap between health professionals and those using these drugs. Ultimately this adversarial approach appears to have limited the ability of health professionals to engage with these individuals to reduce harm and promote health.

## How is growth hormone used?

Growth hormone is commonly taken as part of a high-dose polydrug regimen that usually includes multiple types of anabolic steroids ("stacks"). These regimens are based on a function of availability, cost, personal goal, and meme[11] (Evans-Brown & McVeigh, 2009; Monaghan, 2001, pp. 95–155). While there are insufficient detailed studies that examine these growth hormone regimens in users from the United Kingdom (the published studies usually focus on the regimens of anabolic steroids employed), it appears from the limited data available that the hormone is typically injected subcutaneously (with some preferring the intramuscular route) in doses that are broadly in line (Andreas Kimergård, personal communication to ME-B, 2009) with those noted by Llewellyn in the genre publication *Anabolics* of "1 to 6 IU per day [0.33–2 mg] (2–4 IU being most common)" (Llewellyn, 2009, p. 543) [although some individuals use higher doses in different phases of a "on cycle" (Young & Anwar, 2007) and some use a higher

[8]Furthermore, no data are available on the 'meaning response' to growth hormone (Moerman, 2002)—that is, the expectancy and placebo effects that are mediated from the use of the hormone in this way.

[9]But if they were, could we objectively measure the "performance-enhancing" effect of a drug(s) as the difference in time between first, second, and third place on the podium? (or indeed the difference between being on the podium or not?).

[10]There are diverse structural and personal factors that serve to drive the use of performance-enhancing drugs (see Evans-Brown & McVeigh, 2009; Grogan, 2008; Mishkind, Rodin, Silberstein, & Striegel-Moore, 1986 for a discussion).

[11]We use the term meme to describe the cultural diffusion of growth hormone practices and trends (and more broadly those of performance-enhancing drugs in general) within the user community (Dawkins, 2006, pp. 189–201; See also Rogers, 2003, pp. 17–18).

dose generally (personal communication to JM, 2008)]. Clearly these regimens will result in a different pattern of exposure to the hormone compared to the pulsatile endogenous secretion. Comparatively, in a recent Internet-based study of 500 anabolic steroid users (countries of residence not reported), 25.6% (128/500) reported growth hormone use in doses that ranged from 2 to 32 IU (0.67–10.67 mg) (mean dose not reported) per day (Parkinson & Evans, 2006). This compares to therapeutic dosages for adult GHD from 0.45 to 0.9 IU (0.15–0.30 mg) per day, up to a maximum of 3 IU (1 mg) (British Medical Association & Royal Pharmaceutical Society of Great Britain, 2008, pp. 404–406). While the hormone is often taken during the "on cycle" of anabolic steroid use (Evans-Brown & McVeigh, 2009), there is significant heterogeneity in the length of these cycles between users, with some individuals apparently using growth hormone on an almost continuous basis (personal communication to JM, 2008). Little is currently known about the regimens employed when used as an "anti-aging therapy" or as "well-being" drug.

## The cost of growth hormone

The cost of growth hormone in the early years apparently prohibited its use outside of "dealers and high standard bodybuilders" (Korkia & Stimson, 1993, p. 122; and supported by the findings of McKillop, 1987)—a viewpoint supported by prices supplied by "a bodybuilder of high standard" (Korkia & Stimson, 1993, p. 157): "GH Grom is supposedly the only real GH and is widely used by rich bodybuilders, prices range from £1,200 for 6 week course of 4 iv [sic] [1.32 mg] per day up to £2,000 [which would equate to £7.14–£11.90 per International Unit (IU) (1 IU = 0.33 mg)] . . . I know very little about this one too expensive to contemplate!" (Korkia & Stimson, 1993, p. 158). From the limited data available, growth hormone purchased on the illicit market in the 1990s cost ~£6.58–20 per IU[12] (Evans, 1997, p. 56; Korkia & Stimson, 1993, p. 158; Lenehan & McVeigh, 1997, p. 74). It is reasonable to assume that the supply on the illicit market at this time was limited as compared to now, especially given the purported rise in the number of Chinese manufacturers offering cheaper products of growth hormone that are apparently predominately met-hGH [see discussion by Tober (2007) in the genre publication *Body of Science*].

Recent data drawn from a small convenience sample of products available on the illicit market in south east England in 2008 (Table III) found a number of different products on offer that varied between £1 and 8.33 per IU. It is difficult from this limited sample to infer the current market situation in the United Kingdom as a whole[13]; however, the variation in price between some of the products is striking, supporting the premise that some products available on the illicit market are likely to be adulterated[14] (something that is likely to increase as a problem as the drug gains popularity (World Health Organization, 2003, n.d.(c), and see "Adulterated growth hormone: substandard and counterfeit products on the illicit market," below).

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[12]Cost of ~£6.58 was calculated based on the report by Evans (1997) that stated that a "competitive bodybuilder reported using subcutaneous injections of 2 IU (0.66 mg) daily, which costs around £400 per month." We defined "month" as 30.42 days (365 days/12 months).
[13]Particularly as there are many different Internet sites offering growth hormone products for sale and the size/importance of this supply route has not been systematically examined.
[14]This includes substandard (World Health Organization, n.d.(a)) and/or counterfeit (World Health Organization, n.d.(b)) products.

Table III. Names and prices of growth hormone products (with cost per I.U.) that are available on the illicit market in South East England, UK. Licensed, legitimate, products listed in the British National Formulary are shown for comparison (n.b. not all delivery systems for each BNF-listed product are shown). Some of the products on the illicit market use the same generic and proprietary names and/or trademarks as legitimate products that have been licensed by drug regulatory authorities (British Medical Association & Royal Pharmaceutical Society of Great Britain, 2008:405–406). The authors make no claim as to the authenticity of the products being sold on the illicit market; their listing herein serves to inform healthcare professionals of some of the names of products that they may encounter when providing healthcare to users

| Growth hormone (brand name) | Amount supplied (I.U.) | Cost | Cost per I.U.* |
|---|---|---|---|
| Illicit market (dealer supplied)† | | | |
| Jintropin | 100 IU | £100 | £1.00 |
| Hydrotropin | 200 IU | £350 | £1.75 |
| Ancemone | 40 IU | £100 | £2.50 |
| Norditropin | 30 IU | £140 | £4.67 |
| Genotropin | 36 IU | £225 | £6.25 |
| Humatrope | 36 IU | £300 | £8.33 |
| British National Formulary§ | | | |
| Omnitrope® | 15 IU | £91.33 | £6.09 |
| Zomacton® | 12 IU | £81.32 | £6.78 |
| Saizen® | 10 IU | £73.20 | £7.32 |
| Humatrope® | 36 IU | £274.50 | £7.63 |
| NutropinAQ® | 30 IU | £230 | £7.67 |
| Genotropin® | 36 IU | £278.20 | £7.72 |
| Norditropin® | 30 IU | £231.80 | £7.73 |

†Personal communication to JM (2008). §British Medical Association & Royal Pharmaceutical Society of Great Britain (2008:405–406). *Compare to ~£6.58–£20 per I.U. in the 1990s (Korkia & Stimson, 1993:158; Evans, 1997:56; Lenehan & McVeigh, 1997:74).

## The legal status of growth hormone

In February 1993, the Advisory Council on the Misuse of Drugs [an independent statutory body established under the Misuse of Drugs Act 1971 (MDA) to advise government "on the control of dangerous or otherwise harmful drugs" (HM Government, 1971)] concluded that the use of anabolic steroids (and related drugs) for performance-enhancing reasons was now "having or appeared capable of having harmful effects sufficient to constitute a social problem" (Hansard, 1996)—a key criterion that needs to be satisfied under the MDA before a substance can be brought under its control. Subsequently, legislation was enacted in 1996 by the then Conservative Government to control the anabolic steroids along with the ancillary drugs: clenbuterol, growth hormone [named explicitly as "Somatotropin" (growth hormone of human origin (hGH)), "Somatrem" (met-hGH), "Somatropin" (rhGH)], and chorionic gonadotrophin under the MDA as Class C drugs (The Misuse of Drugs Act 1971 (Modification) Order 1996, 1996; The Misuse of Drugs (Amendment) Regulations 1996, 1996 [now revoked, and, replaced by, The Misuse of Drugs Regulations 2001, 2001 (and the drugs listed above being placed under Schedule 4 Part II)]). This made the supply (including giving or sharing), intent to supply, and production of these substances illegal without a license from the Home Office and is now punishable with up to 14 years imprisonment and/or an unlimited fine (Criminal Justice Act 2003 (c. 44), 2003). However, possession of these drugs for personal use (including import and export) remains legal if they are in the form of a "medicinal product" (as defined under Section 130 of the Medicines Act 1968) (The Misuse of Drugs Regulations 2001, 2001).

## The health effects from using growth hormone

> What about the horror stories: the bone distortions, organ problems, and premature deaths that CBS's 60 Minutes would like to attribute to Growth Hormone use? That has happened only to people having pituitary disorders; I've never even heard rumours of any bad side effects on athletes using HGH [human growth hormone]. (Duchaine, 1989, p. 74)

As noted, up until 1985 all hGH available for both therapeutic use[15] and through the illicit market were derived from cadavers. Individuals using these products were potentially at risk of exposure to the infectious agent of CJD (Belay& Schonberger, 2005). With the advent of recombinant human growth hormone (met-hGH and, subsequently, rhGH) this risk was removed. However, a letter published in the *Lancet* in 1993 suggested that cadaveric growth hormone was still available and used by powerlifters in a number of European countries, presumably, as the authors note, because the cost was "about half the price of recombinant growth hormone" (Deyssig, & Frisch, 1993). While it is reasonable to assume that this practice has become progressively rarer, it has been suggested that cadaveric growth hormone could still be available (Nelson & Ho, 2007, p. 198; Holt & Sönksen, 2008, p. 548; Tober, 2005). If this is correct users must be aware of the potential risks from using such products.

There are limited data on the adverse effects from the pharmacological actions of growth hormone when used outside of its therapeutic role (i.e., its self-directed use). Much of the risks have been extrapolated from (i) in vitro work, (ii) in vivo studies in animal models, (iii) in vivo short-term research studies in humans, (iv) replacement therapy for GHD, and, (v) the effect of the hormone when there is a sustained hypersecretion of the hormone (known as acromegaly). Indeed, one of the most commonly cited major risks is the potential for users to develop acromegaly—or, perhaps more importantly, some of the clinical features thereof (Table IV)—as a result of exposure to prolonged supraphysiological doses of exogenous growth hormone. This view is often countered (or rationalized?) as the fact that "the authorities [like to] present extreme cases of athletes suffering from these malfunctions in order to discourage others" (Grunding & Bachmann, 1995, p. 156, cited in Monaghan, 2001, p. 148) and that "comparatively few [athletes using growth hormone as a performance-enhancing drug] are seven feet tall Neanderthalers [sic] with a protruded lower jaw, deformed skull, claw-like hands, thick lips, and prominent bone plates who walk around in size twenty-five shoes" (Grunding & Bachmann, 1995, p. 156, cited in Monaghan, 2001, p. 148). While this position is perhaps understandable given the unsubstantiated views of the risks of anabolic steroid use that were promoted by the medical and scientific communities for many years, it is a naïve viewpoint given the paucity of epidemiological and clinical data that are available. Indeed, an equally convincing counter-argument to this position is provided by Holt & Sönksen (2008) who note "many patients [with acromegaly] if questioned carefully will give a history of increased strength in the first few years of their condition. Indeed, we know a rower who competed at an elite level during the early stages of his acromegaly. Not only was he one of the strongest crew, but he could also tolerate harder training sessions than his colleagues and recovered more quickly

[15]Excepting the small amount of met-hGH that was being tested in clinical trials prior to this (e.g., Kaplan et al., 1986).

Table IV. Some of the clinical features of acromegaly (Ayuk & Sheppard, 2006; Ayuk & Sheppard, 2008)

| Clinical features of acromegaly |
|---|
| Musculoskeletal |
| Arthropathy (including carpal tunnel syndrome). |
| Increased height (gigantism). |
| Protruding mandible (prognathism) which can cause malocclusion. |
| Separation of teeth (increased inter-dental spaces). |
| Enlargement of forehead. |
| Enlargement of the tongue (macroglossia). |
| Enlargement of hands and feet. |
| Sleep apnoea |
| Metabolic |
| Hyperglycaemia; Impaired glucose tolerance; Insulin resistance. |
| Impaired lipid metabolism. |
| Overt diabetes mellitus. |
| Cardiovascular |
| Hypertension. |
| Cardiomyopathy. |
| Skin |
| Sweating. |
| General |
| Headaches. |
| Tiredness/lethargy. |
| Cancer |
| Data from epidemiological studies is equivocal, and the risk from cancer remains controversial (see discussion by Ayuk & Sheppard (2008) for further details. |

afterwards." While neither provides empirical evidence on the risks from the self-directed use of growth hormone (nor the latter evidence of the performance-enhancing effects), they do serve to highlight the lack of data that is currently available (and the need for well-designed studies to examine these issues), as well as the difficulties faced by those who work to reduce harm and promote health when challenged by users for "hard evidence" on the adverse effects.

There are case reports associating the self-directed use of growth hormone with adverse effects on health (typically in those individuals using the hormone as a performance-enhancing drug, e.g., Magnavita, Teofili, & Leone, 1996; Sein Anand, Chodorowski, & Wiśniewski, 2005; Young & Anwar, 2007). However, it is difficult from these reports to determine whether the use of growth hormone played a permissive or inductive role in the aetiology of disease or is merely an artifactual association—something that is particularly relevant given that many users employ polydrug regimens. Furthermore, unravelling the role of these drugs in any adverse effect is made all the more difficult because of a lack of a systematic framework for the collection and subsequent presentation of clinically relevant information that is sufficient to allow their inclusion in a causality assessment. Indeed, after reviewing many case reports of adverse effects 'associated' (Adams, 2004) with performance-enhancing drugs, many lack detailed information on the drugs and the regimens used (that includes doses and duration),[16] as well as failing to verify the drug composition[17] and

[16]The case report by Young and Anwar (2007) being one of a few notable exceptions to this.
[17]Such as the active pharmaceutical ingredient(s) and excipient(s).

strength, which is essential when the drugs are obtained from the illicit market given the potential for adulteration (see "Adulterated growth hormone: substandard and counterfeit products on the illicit market," below). Furthermore, these reports often fail to examine potential confounding variables.

Parenthetically, the fact that growth hormone is released during deep sleep led some bodybuilders to advocate the use of the hypnotic GHB (gamma hydroxybutyrate) as a growth hormone secretagogue[18] (among other effects such as aiding sleep and for weight loss), as the drug has been shown in research studies to increase endogenous growth hormone secretion (Van Cauter et al., 1997, 2004). It was thought that this increased secretion could be harnessed for its anabolic and lipolytic effects. Though we are not aware of any evidence that supports this theory, the use of GHB in this way has been linked with acute poisoning and dependency (Anderson et al., 2006; CDC, 1990; Chin, Kreutzer, & Dyer, 1999; Gonzalez & Nutt, 2005).

## The risks from injecting

Given that growth hormone is injected, those using this drug are potentially at risk of a number of adverse effects that include bacterial infections (such as localized abscesses and systemic infections), damage to the injection site, and, in those who share injecting equipment (or reuse injecting equipment and, subsequently, share vials with others), blood-borne viruses[19] such as HIV, hepatitis B, and hepatitis C. Although we are not aware of any data specifically reporting the injecting practices for growth hormone, some limited data are available from anabolic steroid users of which growth hormone users are often a subset (Baker, Graham, & Davies, 2006; Evans, 1997; Grace et al., 2001; Korkia & Stimson, 1993; Lenehan et al., 1996; Pates & Barry; 1996). Here some studies have found relatively low levels of sharing (Bolding et al., 2002; Crampin et al., 1998; Korkia & Stimson, 1993; Lenehan et al., 1996), whereas others have reported rates between 16 and 20% (Burton, 1996; Grace, Baker, & Davies, 2001). However, the frequency of sharing events are not reported in these latter papers, and it is unclear what is responsible for the large variation between studies.

To our knowledge, the work of Crampin et al., (1998) is the only published study that has also examined HIV and hepatitis B exposure (through salivary antibody testing) in anabolic steroid users attending NSP in the United Kingdom. Here they found that out of 149 individuals, 2% (3/149) had evidence of previous or current hepatitis B infection, while none had antibodies to HIV. However, these data are drawn from samples taken between 1991 and 1996, and since this time there has been significant epidemiological shifts in HIV and hepatitis C infection[20] in the United Kingdom (Health Protection Agency Centre for Infections, 2006, 2008).

It is easy for us to dismiss the risk of blood-borne virus transmission in this population as low when compared to other groups, such as those injecting opiates and stimulants (Health Protection Agency, 2007). However, the practices and risks remain poorly characterized and the issue deserves a contemporary and systematic examination (along with the development of a robust surveillance system). Importantly, any such work must include those individuals who are not in contact with NSPs, as despite the extensive peer distribution

[18]The use of GHB as a growth hormone secretagogue is also documented in the anti-aging literature (Klatz & Kahn, 1998, p. 213–215).
[19]Sharing injecting equipment can also be a route for the transmission of bacterial infections.
[20]To-date hepatitis C infection has not been examined in PED/anabolic steroid users in the United Kingdom.

network that appears to exist (Gilliver, 2007; McVeigh, Chandler, Beynon, Evans-Brown, & Bellis, 2007), their injecting practices may differ significantly from their peers who do attend NSPs. This is particularly relevant for younger users, where it has been reported that they will not attend NSPs for fear of being labeled as an injecting drug user (personal communication to ME-B, 2008).

## Adulterated growth hormone: substandard and counterfeit products on the illicit market

> Being so far removed from the hands of legitimate pharmaceutical distributors, doctors, and pharmacists, [human growth hormone] products of doubtful origin and low quality frequently find their way to the (black) market. In the last few years, counterfeited, contaminated, and very poor quality somatropin have been located and analysed, both in the European Union and in the United States. (Tober, 2005)

> Somatropin products are high value targets for drug counterfeiting operations. Many counterfeits are highly deceptive in nature . . . [s]ome . . . are made by relabelling vials of hCG [human chorionic gonadotrophin], which bear a very close visual resemblance to somatropin. (Llewellyn, 2009, p. 543)

In common with other performance-enhancing drugs, such as anabolic steroids (Evans-Brown & McVeigh, 2009), there are concerns over the quality of growth hormone products available on the illicit market in the United Kingdom (which can be broadly defined as forms of adulteration). These concerns include the substitution of the active pharmacological ingredient from that stated on the packaging/labeling for another ingredient, the inclusion of other undeclared ingredients (active and/or excipients), no active pharmacological ingredient, under[21]- and over-strength ingredients,[22] and contamination of the product (including microbiological, chemical, and foreign matter). Although systematic and detailed studies are lacking in relation to growth hormone, there is little reason to doubt that these products would not be subject to these forms of adulteration, particularly given the unregulated nature of the illicit market. Indeed, support for this line of reasoning comes from (i) reports of counterfeit products from both manufacturers of licensed products, the US Food and Drug Administration (e.g., Serono, Inc., 2001; Food and Drug Administration, 2004), and, more recently, a report by Graham et al. (2009); (ii) the report by Dawson (2001) that some products contained nonsterile glucose rather than the hormone; (iii) anecdotal reports by both users and drug workers in the United Kingdom; and (iv) reports highlighting these issues in genre publications, where products have apparently been subject to either substitution of one type of growth hormone for another or substitution with another drug such as insulin or HCG (Llewellyn, 2009, p. 543; Tober, 2005, 2007).

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[21]'While at first glance under-strength active ingredients may not appear to be a problem, anecdotally this finding in illicitly-supplied anabolic steroids is believed to have led some users to compensate by using much larger doses. However, given the potential variability in the composition from different products (one may be over-strength, the next maybe under-strength – there is no way of knowing with products derived from the illicit market), the next time the user may get a product that is over-strength leading to an even higher does being inadvertently used.

[22]Which could also include undeclared ingredients.

## Harm reduction

While accepting that there is a paucity of empirical data that support the use of growth hormone for "performance-enhancing reasons" (as well as an "anti-aging therapy" or as a "well-being" drug), this does not mean that health and substance use practitioners cannot meaningfully engage with users and provide basic harm reduction advice and interventions. Alongside the provision of sterile injecting equipment, this could also include support to the user by helping them examine their drug use and the associated risks. It is important that those using or contemplating use consider why they want to use the drug, potential alternatives, and the particular regimen (including drugs, dose, and duration) they are considering and how they decided upon it. The basic guidelines for the reduction of drug-related harm are the same for anabolic steroids and other related drugs (Evans-Brown & McVeigh, 2009) and are provided below.

## Basic harm reduction messages for growth hormone users

- Always use sterile injecting equipment. Never share.
- Use the smallest dose of growth hormone (or any other drug) and do not adopt other users' regimens.
- Limit the length of time you take growth hormone.
- Be aware of counterfeit/fake drugs.
- Know how to inject safely (including rotating your injection site).
- Know the dangers of recreational drug use (particularly when taking growth hormone).
- Be aware of side effects. At the first sign of them, discontinue use and seek medical advice.
- Inform your GP (and any other health practitioner) of your use of growth hormone (and all other drugs) and take advantage of any health monitoring that is available.
- Just because you read something about growth hormone use on the Internet, from a magazine, or heard it from another user, doesn't necessarily mean it's true!

## Conclusion

> We need to explore not only new ways of engaging with this population (which starts with listening to them), and providing them with an environment where they can articulate, prioritise and reflect on their concerns and needs, but also where health professionals have the relevant skills and knowledge in place in order to work with, and, for, users. This will, inter alia, also require that we further develop the evidence base on both the positive and negative effects of growth hormone use, and performance-enhancing drugs in general. (Modified from Evans-Brown & McVeigh, 2009).

Robust estimates of the self-directed use of growth hormone in the United Kingdom are limited. Further, the level of risk to individual and public health that this behavior affords is currently unclear. The fact remains, however, that substantial numbers of (mainly) younger men are injecting growth hormone[23] for which we have some indication of the potential, but little evidence of actual, adverse effects. What limited research

[23]Which because it is sourced from the illicit market the quality and safety of these products will be unknown to the user.

and monitoring data from the United Kingdom does indicate, however, is that a significant number of anabolic steroid users have adopted hGH into their polydrug regimens. This has implications for the delivery of harm reduction programs, as elements of this population may be resistant to seek advice and help, stemming, in part, from the misinformation and "prophylactic lies" expounded by the scientific and medical communities in relation to anabolic steroid use for many years (Evans-Brown & McVeigh, 2009). However, there is clearly a need to engage with this user group to help them make "the healthy choice the easy choice" (Milio, 1981; World Health Organization, 1986); whether this be choosing not to use the drug, or, if this is not possible, choosing to adopt harm reduction practices.

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The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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