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New Developments in the Illegal Provision of Growth Hormone for “Anti-Aging” and Bodybuilding

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A CONSEQUENCE OF THE COMMITTEE ON OVERSIGHT and Government Reform’s recent hearing on the Mitchell Report on steroid and growth hormone (hGH) use was recognition that the misguided use of hGH by professional athletes and entertainers contributes to the far more frequent and increasing problem of anti-aging clinics, Web sites, compounding pharmacies, and producers selling the drug to the general public for medically inappropriate uses.¹ In the face of evidence of illegal distribution of hGH, in January 2007, the US Food and Drug Administration (FDA) published an alert specifying that anti-aging, bodybuilding, and athletic enhancement are not approved indications for hGH.²

Systematic reviews have found that hGH supplementation does not significantly increase muscle strength or aerobic exercise capacity in healthy individuals.³ Clinical evidence does support the therapeutic administration of hGH for children and adults with appropriate clinical indications.⁴ However, extrapolating from this evidence to conclude that hGH improves health or longevity in normally aging individuals⁵ is not justified. The American Association of Clinical Endocrinologists suggests that hGH misuse might make insurance companies less likely to cover the cost of hGH treatment for approved indications.⁶

Age-related diseases and syndromes should not be confused with adult growth hormone deficiency (GHD). In fact, adult GHD is rare; the most common causes are pituitary adenoma or treatment of the adenoma with surgery or radiotherapy.⁴ In our review of the most recent package inserts of the 7 brands of hGH indicated for adult GHD at the FDA’s Web site (<http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm>), since early 2007, the stated criteria for allowed provision of hGH for adult GHD are identical:

Somatropin [rDNA origin] for injection is indicated for replacement of endogenous growth hormone in adults with growth

hormone deficiency who meet either of the following two criteria:

Adult Onset: Patients who have growth hormone deficiency, either alone or associated with multiple hormone deficiencies (hypopituitarism), as a result of pituitary disease, hypothalamic disease, surgery, radiation therapy, or trauma; or

Childhood Onset: Patients who were growth hormone deficient during childhood as a result of congenital, genetic, acquired, or idiopathic causes.

In general, confirmation of the diagnosis of adult growth hormone deficiency in both groups usually requires an appropriate growth hormone stimulation test. However, confirmatory growth hormone stimulation testing may not be required in patients with congenital/genetic growth hormone deficiency or multiple pituitary hormone deficiencies due to organic disease.

Thus, confirmatory stimulation testing (hGH <5 µg/L⁶) is required for justifying hGH administration for adult GHD except in the case of congenital/genetic GHD or multiple pituitary hormone deficiencies (eg, gonadotropins, corticotropin, thyrotropin, and hGH) due to organic disease. Making the diagnosis of adult GHD on the basis of insulinlike growth factor 1 levels without documentation of hypothalamic or pituitary disease and, in most cases, stimulation testing is inaccurate.⁷ In spite of this, a guidance article for anti-aging practitioners states that “most of us agree with a consensus standard that an IGF-1 level below 100 ng/mL is a clear indication for replacement.”⁸ According to the FDA, the Endocrine Society,⁴ and the American Association of Clinical Endocrinologists,⁶ there is no justifiable reason to prescribe or administer hGH for adults who do not meet the diagnostic criteria for adult GHD or who do not have human immunodeficiency virus–associated muscle wasting or short-bowel syndrome, the only other FDA-approved indications for hGH.⁴

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Illegal Distribution of hGH

Recent high-profile government investigations have revealed a number of anti-aging clinics, compounding pharmacies, and pharmaceutical companies that violate the law with regard to hGH distribution. Specialty Services Distribution Inc was fined \$10.5 million for distributing hGH for nonmedical uses⁹; the FDA, the US Drug Enforcement Administration, and the Federal Bureau of Investigation conducted investigations (Operation Phony Pharm¹⁰ and Operation Raw Deal¹⁰) of national and international distribution of anabolic steroids and hGH. In Operation Which Doctor, government officials from several states are working together to “take down a nationwide distribution ring of anabolic steroids, human growth hormone and other controlled substances, by targeting the ring’s dirty doctors, its distributors that pose as clinics, and ultimately the ring’s supplier Signature Pharmacy.”¹¹

An example of how profitable illegal distribution of hGH has become involves a compounding pharmacy recently investigated by the New York State Bureau of Narcotic Enforcement.¹² The investigation revealed that the pharmacy reportedly would purchase 25 g of imported hGH for \$75 000, convert each gram into 3000 IUs of hGH, then sell the drug for \$6 to \$18 per IU, netting a profit of \$450 000 to \$1.35 million.¹²

An important feature of hGH distribution for anti-aging and bodybuilding is that the vast majority of users pay out of pocket for the drug. As a result of these cash-only transactions and the fact that hGH is often misbranded (eg, illegally imported or made into a “new drug” by combining hGH with another compound³), it is not possible to track the number of individuals receiving illegally distributed hGH. However, sources within the industry speculate that \$2 billion of hGH is distributed in the United States per year for anti-aging and bodybuilding.¹

Another consequence of a cash-only business is that there are no independent means to detect and monitor adverse events. Individuals who experienced adverse effects may have simply stopped taking the drug and ended their relationship with the Web site or clinic without reporting the problem, especially if the adverse effects subside after discontinuation of the drug. More severe health consequences would be difficult to track because there is little incentive for hGH users to pursue legal action against suppliers when causation may be difficult to prove or because there is an obvious disincentive for anti-aging practitioners to report adverse experiences with hGH.

Recent Medical Findings

A review of clinical studies of hGH use among healthy, normally aging individuals found the only benefit to be a slight increase in muscle mass.¹³ The documented adverse effects included soft tissue edema, arthralgias, carpal tunnel–like syndrome, gynecomastia, and insulin resistance with an elevated risk of developing diabetes mellitus. Contrary to pub-

lished claims,⁵ neither long-term safety nor benefit has been demonstrated in normally aging individuals. Studies have suggested that adult GHD or resistance to growth hormone action is associated with longer life spans, not shorter ones¹⁴—suggesting that, if anything, use of hGH for anti-aging or athletic enhancement would shorten, not prolong life.

Actions to Help Address the Inappropriate Distribution and Use of hGH

First, the public must be accurately informed by physicians and scientists with no vested interest in use of hGH about the health risks, fraudulent marketing, and illegal distribution of this drug.

Second, in the United States and elsewhere, entrepreneurs are now collectively making millions of dollars from “education” materials, seminars, and exhibitor-sponsored conventions in which they teach aspiring anti-aging practitioners how to create an anti-aging or age-management medical practice and administer to their patients or clients what are claimed to be interventions that stop or reverse aging—hGH, anabolic steroids, and other compounds among them.¹ Organizations that promote or indirectly profit from the medically inappropriate and illegal distribution of hGH that have been accredited by the Accreditation Council for Continuing Medical Education (ACCME) to offer American Medical Association Physician Recognition Award category 1 CME credits¹⁵ or other categories of CME credit should, at a minimum, have their accreditation revoked.

Third, distribution of hGH to anti-aging or age-management clinics and compounding pharmacies that supply these clinics should be monitored carefully because many prescriptions written for the drug from these sources do not follow FDA requirements. US manufacturers of hGH must be more effective in and held accountable for controlling the distribution of the drug to distributors that are obviously providing the drug for illegal uses.

Fourth, recently introduced legislation (S 877 and HR 4911) proposes to make hGH a Schedule III controlled substance. This designation would require distributors and dispensers of hGH to register with the US Drug Enforcement Administration and would result in stiffer penalties for improper distribution and make unapproved possession of the drug illegal. The medical community and general public should support this legislation as long as, in addition, the current limitations on drug distribution and prescription are preserved.

Fifth, congressional hearings and public media attention involving hGH should focus not only on athletes and other end users but, more importantly, on the distributors who are violating federal and, in some cases, state laws by making the drug widely available for nonapproved uses.

Sixth, medical and scientific societies, state medical boards and pharmacy boards, and the ACCME and its 7 member organizations should delineate and enforce policies that ad-

dress the ethical and professional misconduct of individuals, pharmacies, and organizations that promote, market, profit from, or contribute to the illegal distribution of growth hormone for medically unproven uses.

Conclusion

Until and unless efficacy and safety of hGH is demonstrated by unbiased scientifically rigorous clinical trials for purposes advocated by the anti-aging industry,³ hGH should not be distributed or prescribed for any purpose other than its narrowly defined clinical and legal indications. Legislative, regulatory, and professional actions are needed to effectively curtail the extensive promotion and illegal distribution and use of hGH for anti-aging and bodybuilding.

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