Antiaging medicine: what should we tell our patients?

Aging HEALTH

"Today, the bread and butter of the hucksters and quacks is the sale of hormones as the fountain of youth."

Thomas T Perls

Department of Medicine, Geriatrics Section, Boston University Medical Campus, 88 E. Newton St., Boston, MA 02118, USA
Tel.: +1 617 638 6688
Fax: +1 617 638 6671
thperls@bu.edu

The resurgence of hucksters & quacks

While promises of eternal youth in a bottle and all-encompassing cures for what ails you have been around forever, at least four events have recently converged resulting in doctors now being asked by their patients on a more frequent basis about something they saw on television or heard on the radio regarding a cure for aging. First, there is the post-war 'baby boom' generation, an extremely large number of people who are now in their late-forties to mid-sixties, many of whom are wondering how much life they have ahead of them and what they can do in order to age well.

Second, there are the popular television shows that promote science illiteracy by providing primetime and unchallenged pulpits to pseudoscience sermons from lay celebrities. Both Oprah Winfrey and Mehmet Oz are suing internet sites for using their names in order to sell resveratrol following a segment they aired professing the longevity-enhancing abilities of the pill [101]. Along with the television shows, there is the internet, conventions and magazine advertisements into which entrepreneurs gladly invest money in order to promote their antiaging wares, knowing that the monetary return outweighs the potential legal costs or risks. In a world in which the public hears of truly successful medical therapies and incredible advances such as whole genome sequencing, the gullible and unsuspecting fall more easily for multimillion dollar advertisement campaigns by people wearing surgeon's scrubs or white lab coats exclaiming that they can provide injections or pills that will make the recipient young.

Third, in the USA, with the 1994 passage of the Dietary Supplement and Education Act (DSHEA) and continued efforts by lobbyists, special interests and self-serving politicians, loopholes in the law enable hucksters to market a wide range of potions, creams and pills that, at best, cost a lot of money and, at worst, contain impurities or substances that can harm or even kill [1–4,102,103]. Finally, despite government hearings that recommend something be done in order to counter this blatant disregard for the public's health and interests [1–4,102,103], enforcement agencies are terribly underfunded and have other mandates, such as countering terrorism, that must come first.

Tell your patients what should make their guard go up

What do you say to your patient when they come to you asking: "Doctor, a celebrity on television says I can be like her if I take bioidentical hormones? Can I?"? You can help your patient become an educated consumer. If they ask you about an antiaging clinic or product, go over Box 1 with them, which details the signs of quackery and ask them how many appear in the advertising they have seen or heard. Any one of these red flags should be a tip-off that they should just walk away [5].

"...entrepreneurs gladly invest money in order to promote their antiaging wares, knowing that the monetary return outweighs the potential legal costs or risks."

Today, the bread and butter of the hucksters and quacks is the sale of hormones as the fountain of youth. This is really no different than the strategies used in Brown-Séquard's time, who in the late 1800s was advocating the injection of fluids from guinea pig testicles for rejuvenation. Hormones have long been equated with youthfulness by the lay public and so it is an easy sell. In particular, the 'growth hormone' is a marketer's dream come true, where the name itself contributes to the illusion that it is responsible for youth. Some doctors call these drugs 'bioidentical' hormones or all-natural hormones. What they mean by this varies from substances made from vegetables – such as soy or yams, which some claim have estrogen-like effects – to, more commonly, drugs that are exactly the same

future medicine part of fsg

Box 1. Signs and tricks of quackery.

- The claim is pitched directly to the media without evidence of unbiased peer review
- Claims that the purveyor's work or message is being suppressed by the scientific establishment
- Use of phrases such as "scientific breakthrough", "exclusive product", "secret ingredient" or "ancient remedy"
- Testimonials and anecdotes (including from the seller themselves)
- Claims that centuries-old remedies are credible because they have withstood the test of time
- Attempts to convey credibility with doctors' coats or the use of the words "MD", "academies" or "institutes"
- The absence of adverse reactions and the making of claims that sound too good to be true
- Simplistic rationales to dupe the lay public
- The use of celebrities and attempted associations with well-known legitimate scientists
- "The esteemed medical tradition of off-label use" in the case of growth hormone
- Misleading interpretations of studies or outright false claims that something works
- Use of disclaimers
- Use of money back guarantees
- Use of the phrase, "We are on your side"

Adapted with permission from [5].

as hormones made by human organs. The hucksters' spin is that these drugs are 'natural' and, therefore, do not cause any harm. While various hormones are indicated for specific endocrinologic diseases, they can in fact have toxic, if not life-threatening effects, especially when given under the direction of someone who is intent on selling them far outside the realm of prudent medical practice; that is, prescribing them for antiaging or age-management.

Responsible medical care & advice

The American Medical Association's (AMA) Council on Science and Public Health recently released its report, *'The use of hormones for "anti-aging": a review of efficacy and safety'* [104]. The report is based upon a compilation of peer-reviewed studies gathered from a Medline search for all reviews, controlled clinical trials and meta-analyses of such trials involving human growth hormone (hGH), dehydroepiandrosterone, testosterone or estrogens and the word 'aging'. The authors also reviewed the National Institute on Aging, the US FDA, the Agency for Health Care Research and Quality (AHRQ) and the Institute of Medicine (IOM) reports. Finally, guidelines and consensus statements were sought from the endocrinology and obstetrics and gynecology professional societies.

The following table summarizes the report's recommendations concerning the hormones most commonly sold and distributed by antiaging and age-management clinics, websites and some pharmacies [6,105]. Essentially, the report states that none of these substances have been demonstrated to confer an antiaging benefit. In some cases, such as dehydroepiandrosterone, there were neither benefits nor risks, while in others, such as hGH, the risks far outweigh any minimal benefits, if any exist at all (Table 1) [104].

> **"**...prescribing or distributing testosterone or other androgenic anabolic steroids for body-building, athletic use or other situations where the patient demonstrates normal testosterone levels would be considered professional misconduct and unethical practice.**"**

The AMA's review of the risks and benefits of these hormones in the setting of antiaging and athletic enhancement is very important given its inclusion of the consensus and position statements of the key professional medical societies as well as the Federal agencies that guard public health. I would add to the above list several other important side effects of testosterone. Testosterone administration in otherwise healthy people is associated with obstructive sleep apnea [7], low high-density lipoprotein cholesterol [8,9], hypertension [8] and atrial fibrillation [10], as well as impulsiveness and violent behavior, including suicide and irritability [11]. Some clinics, particularly when they are catering to body-builders, will add androgenic anabolic steroids (AAS), which are synthetic derivatives of testosterone [12], to the drug regimen. Many of these steroids have additional dangerous effects. Oral AAS such as

Table 1. Summary of the American Medical Association's Council on Science and Public Health's recently released report "*The use of hormones for "antiaging": a review of efficacy and safety*".

Hormose(s)	Benefits	Excess risk	Comments of risk:benefit ratio	Ref.
Estrogens plus progestin	In postmenopausal women, 'some' benefit for: Bone facture Colorectal cancer Vasomotor symptoms of menopause Topical for atrophic vaginitis	In postmenopausal women, an excess risk of: Stroke Thromboemblism Breast cancer Dementia Cognitive impairment Coronary heart disease when not initiated near age of menopause	Risks exceed benefits Not indicated for chronic conditions in postmenopausal women FDA Black Box Warning	[20–25,106]
Estrogens alone (women with hysterectomy)	Age 50–59 years, decreased risk of coronary artery disease and fracture Vasomotor symptoms of menopause Topical for atrophic vaginitis	In postmenopausal women, an excess risk of: Stroke and thromboemblism Dementia Cognitive impairment	Not indicated for chronic conditions in postmenopausal women FDA Black Box Warning	[21–23, 25–27,102, 107]
Testosterone for menopausal women with low sexual desire	Improved desire Improved desire and sexual function	Excess cases of breast cancer Increased hirsuitism and acne	In light of increased cancer rate, great caution warranted	[28–30]
Testosterone for middle-aged men with normal testicular function	No clear benefit demonstrated	Increased hematocrit Increased risk for new prostate cancer or hyperplasia uncertain	No benefit, but further study is warranted	[31]
Testosterone for older men with abnormally low testicular function	Increased lean body mass and decreased fat mass, but little change in strength; Dose-dependent increase in both muscle mass and strength	Increased combined rate of prostate events (cancer, PSA >4 and biopsies) Elevated hematocrit Dose-dependent increase in hematocrit, prostate events and leg edema	Inconsistent trial results for quality of life, sexual or cognitive function Dose-dependent benefits are countered by dose-dependent adverse events	[14,32,33]
Growth hormone for antiaging or hGH decline associated with aging	Minimal improvement in lean body mass or decrease in fat mass	Soft tissue edema, arthralgias, carpal tunnel syndrome and gynecomastia, diabetes mellitus and elevated fasting glucose	Risks outweigh the minimal benefit, if any benefit exists	[34–37]
DHEA	No benefit observed (e.g., body composition, strength and quality of life)	None reported, although no reliable study was performed for longer than a year	No benefit	[38–45,108]

DHEA: Dehydroepiandrosterone; hGH: Human growth hormone; PSA: Prostatic-specific antigen.
Data from [104].

oxandrolone (Anavar), oxymetholone (Anadrol) or stanozolol (Winstrol) are notorious for causing liver inflammation and failure [13].

Administration of testosterone that a reasonable physician would regard as falling within the accepted standard of medical care requires abnormally low morning testosterone levels to be demonstrated [14]. Besides male hypogonadism [14–16], AIDS wasting syndrome [14] is a potential indication for testosterone supplementation. Therefore, prescribing or distributing testosterone or other AAS for body-building, athletic use or other situations where the patient demonstrates normal testosterone levels would be considered professional misconduct and unethical practice in nearly all US states and a felony under US Federal law (the Anabolic Steroid Act).

In the case of hGH, medically reasonable indications for growth hormone administration in adults are quite limited in light of the substantial and prevalent risks associated with hGH in disease-free adults. In addition to the risks noted in Table 1, increased cancer risk has long been a concern. Recently, a University of California study indicated that men aged 50 years or older with an IGF-1 level greater than 100 ng/ml are at twice the risk for cancer compared with those who have lower IGF-1

levels [17]. Medically reasonable and legal indications for the use of hGH in adults include: AIDS wasting syndrome; short bowel syndrome; congenital growth hormone deficiency syndrome; and adult growth hormone deficiency syndrome. In all cases, a demonstration of anterior pituitary gland hypofunction with a valid stimulation test is required in order to meet the threshold of acceptable medical standards of care. These standards of care are fortunately reflected by US Federal law (333[e] of the Food Drug and Cosmetic Act) [18,19] and many states also have laws that limit the prescription and distribution of growth hormone to the above medically acceptable indications [6]. Refer to the website that I author for up-to-date coverage of medical and legal issues related to hGH and anabolic steroids [109].

Thus, with the above information, what do you tell your patient? I suggest that you seize this opportunity to find out what are your patient's concerns. Assure them that they do not need to be sold a bill of goods (often more than US$10,000 a year) and help them to construct and carry out a plan to achieve their key health goals. Thank your patient for coming to their senses in seeking your advice and work with them to produce a patient-tailored prevention and screening program that incorporates unbiased, evidence-based advice that, with your encouragement, will be geared towards enhancing their resilience and minimizing the known risks for age-related diseases.

Financial & competing interests disclosure

Thomas Perls has provided expert testimony and consultancy for the US Department of Justice, the USHouse of Representatives Committee on Government Oversight and Reform and the Washington State Department of Health. The author has no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.

Bibliography

1. US Federal Trade Commission: US Federal Trade Commission press release. FTC stops spammers selling bogus Hoodia weight-loss products and human growth hormone anti-aging products. US Federal Trade Commission, Washington, DC, USA (2007).
2. United States Federal Trade Commission: "HGH" pills and sprays: human growth hype? US Federal Trade Commission, Washington, DC, USA (2005).
3. US Senate, Special Committee on Aging, One Hundred Seventh Congress, First Session: *Swindlers, Hucksters and Snake Oil Salesman: Hype and Hope Marketing Anti-Aging Products to Seniors*. US Government Printing Office, Washington, DC, USA (2001).
4. Subcommittee on Health and Long-Term Care, US House of Representatives Select Committee on Aging, 98th Congress: *Quackery: A $10 Billion Scandal*. US Government Printing Office, Washington, DC, USA (1984).
5. Perls T: Antiaging quackery: human growth hormone and tricks of the trade, more dangerous than ever. *J. Gerontol. Biol. Sci.* 59A, 682–691 (2004).
6. Perls T: Growth hormone and anabolic steroids: athletes are the tip of the iceberg. *Drug Test. Anal.* 1, 419–425 (2009).
7. Sandblom RE, Matsumoto AM, Schoene RB *et al.*: Obstructive sleep apnea syndrome induced by testosterone administration. *N. Engl. J. Med.* 308(9), 508–10 (1983).
8. Bhasin S, Storer TW, Berman N *et al.*: The effects of supraphysiologic doses of testosterone on muscle size and strength in normal men. *N. Engl. J. Med.* 335(1), 1–7 (1996).
9. Singh AB, Hsia S, Alaupovic P *et al.*: The effects of varying doses of testosterone on insulin sensitivity, plasma lipids, apolipoproteins, and C-reactive protein in healthy young men. *J. Clin. Endocrinol. Metab.* 87, 136–43 (2002).
10. Sullivan ML, Martinez CM, Gallagher EJ: Atrial fibrillation and anabolic steroids. *J. Emerg. Med.* 17, 851–857 (1999).
11. Talih F, Fattal O, Malone D: Anabolic steroid abuse: psychiatric and physical costs. *Cleveland Clinic J. Med.* 74, 341–352 (2007).
12. Saudan C, Baume N, Robinson N, Avois L, Mangin P, Saugy M: Testosterone and doping control. *Br. J. Sports Med.* 40(Suppl. 1), I21-I24 (2006).
13. Stimac D, Milic S, Dintinjana RD, Kovac D, Ristic S: Androgenic/anabolic steroid-induced toxic hepatitis. *J. Clin. Gastroenterol.* 35, 350–352 (2002).
14. Bhasin S, Cunningham GR, Hayes FJ *et al.*: Testosterone therapy in adult men with androgen deficiency syndromes: an Endocrine Society clinical practice guideline. 91(6), 1995–2010 (2006).
15. Rhoden EL, Morgentaler A: Risks of testosterone-replacement therapy and recommendations for monitoring. *N. Engl. J. Med.* 350, 482–492 (2004).
16. Bassil N, Alkaade S, Morley JE: The benefits and risks of testosterone replacement therapy: a review. *Ther. Clin. Risk Manag.* 5, 427–48 (2009).
17. Major JM, Laughlin GA, Kritz-Silverstein D, Wingard DL, Barrett-Connor E: Insulin-like growth factor-I (IGF-I) and cancer mortality in older men. *J. Clin. Endocrinol. Metab.* 95(3), 1054–1059 (2010).
18. Olshansky SJ, Perls TT: New developments in the illegal provision of growth hormone for "anti-aging" and bodybuilding. *JAMA* 299(23), 2792–2794 (2008).
19. Perls T, Reisman N, Olshansky J: Growth hormone for "anti-aging": clinical and legal issues. *JAMA* 294, 2086–2090 (2005).
20. Writing Group for the Women's Health Initiative Investigators: Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the Women's Health Initiative randomized controlled trial. *JAMA* 288, 321–333 (2002).

21. American College of Obstetricians and Gynecologists Committee on Gynecologic Practice: ACOG Committee Opinion No. 420, November 2008: hormone therapy and heart disease. *Obstet. Gynecol.* 112, 1189–1192 (2008).
22. Schumaker SA, Legault C, Kuller L *et al.*: Conjugated equine estrogens and incidence of probable dementia and mild cognitive impairment in postmenopausal women: Women's Health Initiative memory study. *JAMA* 291, 2947–2958 (2004).
23. Espeland MA, Rapp SR, Shumaker SA *et al.*; Women's Health Initiative Memory Study: Conjugated equine estrogens and global cognitive function in postmenopausal women: Women's Health Initiative Memory Study. *JAMA* 291, 2959–2968 (2004).
24. Rossouw JE, Prentice RL, Manson JE *et al.*: Postmenopausal hormone therapy and risk of cardiovascular disease by age and years since menopause. *JAMA* 297, 1465–1477 (2007).
25. U.S. Preventive Services Task Force: Hormone therapy for the prevention of chronic conditions in postmenopausal women: recommendations from the US Preventive Services Task Force. *Ann. Intern. Med.* 142, 855–860 (2005).
26. Manson JE, Allison MA, Rossouw JE *et al.*: Estrogen therapy and coronary-artery calcification. *N. Engl. J. Med.* 356, 2591–2602 (2007).
27. Women's Health Initiative Steering Committee: Effects of conjugated equine estrogens in postmenopausal women with hysterectomy: the Women's Health Initiative randomized controlled trial. *JAMA* 291, 1701–1712 (2004).
28. Davis SR, Moreau M, Kroll R *et al.*: Testosterone for low libido in postmenopausal women not taking estrogen. *N. Engl. J. Med.* 359, 2005–2017 (2008).
29. The North American Menopause Society: The role of testosterone therapy in postmenopausal women: position statement of The North American Menopause Society. *Menopause* 12, 497–511 (2005).
30. Heiman JR: Treating low sexual desire – new findings for testosterone in women. *N. Engl. J. Med.* 359, 2047–2049 (2008).
31. Committee on Assessing the Need for Clinical Trials of Testosterone Replacement Therapy, Institute of Medicine: *Testosterone and Aging: Clinical Research Directions*. National Academies Press, Washington, DC, USA (2003).
32. Emmelot-Vonk MH, Verhaar HJJ, Pour HRN *et al.*: Effect of testosterone supplementation on functional mobility, cognition, and other parameters in older men: a randomized controlled trial. *JAMA* 299, 39–52 (2008).
33. Bhasin S, Woodhouse L, Casaburi R *et al.*: Older men are as responsive as young men to the anabolic effects of graded doses of testosterone on the skeletal muscle. *J. Clin. Endocrinol. Metab.* 90, 678–688 (2005).
34. Giannoulis MG, Sonksen PH, Umpleby M *et al.*: The effects of growth hormone and/ortestosterone in healthy elderly men: a randomized controlled trial. *J. Clin. Endocrinol. Metab.* 91, 477–84 (2006).
35. Liu H, Bravata DM, Olkin I *et al.*: Systematic review: the effects of growth hormone on athletic performance. *Ann. Intern. Med.* 148, 747–758 (2008).
36. American Association of Clinical Endocrinologists Growth Hormone Task Force: American Association of Clinical Endocrinologists medical guidelines for clinical practice for growth hormone use in adults and children – 2003 update. *Endocr. Pract.* 9, 64–76 (2003).
37. Molitch ME, Clemmons DR, Malozowski S *et al.*; The Endocrine Society's Clinical Guidelines Subcommittee of the Clinical Affairs Committee: Evaluation and treatment of adult growth hormone deficiency: an Endocrine Society Clinical Practice Guideline. *J. Clin. Endocrinol. Metab.* 91, 1621–1634 (2006).
38. von Muhlen D, Laughlin GA, Kritz-Silverstein D *et al.*: Effect of dehydroepiandrosterone supplementation on bone mineral density, bone markers, and body composition in older adults: the DAWN trial. *Osteoporos. Int.* 19, 699–707 (2008).
39. Nair KS, Rizza RA, O'Brien P *et al.*: DHEA in elderly women and DHEA or testosterone in elderly men. *N. Engl. J. Med.* 355, 1647–1659 (2006).
40. Jankowski CM, Gozansky WS, Schwartz RS *et al.*: Effects of dehydroepiandrosterone replacement therapy on bone mineral density in older adults: a randomized, controlled trial. *J. Clin. Endocrinol. Metab.* 91, 2986–2993 (2006).
41. Muller M, van den Beld AW, van der Schouw YT *et al.*: Effects of dehydroepiandrosterone and atamestane supplementation on frailty in elderly men. *J. Clin. Endocrinol. Metab.* 91, 3988–3991 (2006).
42. Villareal DT, Holloszy JO: Effect of DHEA on abdominal fat and insulin action in elderly women and men: a randomized controlled trial. *JAMA* 292, 2243–2248 (2004).
43. Percheron G, Hogrel J, Denot-Ledunois S *et al.*: Effect of 1-year oral administration of dehydroepiandrosterone to 60- to 80-year-old individuals on muscle function and crosssectional area: a double-blind placebo-controlled trial. *Arch. Intern. Med.* 163, 720–727 (2003).
44. Flynn MA, Weaver-Osterholtz D, Sharpe-Timms KL *et al.*: Dehydroepiandrosterone replacement in aging humans. *J. Clin. Endocrinol. Metab.* 84, 1527–1533 (1999).
45. Stewart PM: Aging and fountain-of-youth hormones. *N. Engl. J. Med.* 355, 1724–1726 (2006).

Websites

101. Smillie D: Oprah vs. the supplement sellers. *Forbes* 20 August 2009. www.forbes.com/2009/08/20/oprah-winfrey-resveratrol-business-healthcare-oz.html (Accessed 29 January 2010).
102. United States General Accounting Office: Report to Chairman, Special Committee, on Aging, US Senate: health products for seniors. "Anti-aging" products pose potential for physical and economic harm (September 2001). www.gao.gov/new.items/d011129.pdf (Accessed 31 January 2010).
103. Heinrich J: Health products for seniors: "anti-aging" products pose potential for physical and economic harm. www.gao.gov/new.items/d011139t.pdf (Accessed 31 January 2010).
104. Robinowitz CB, Guerrero MG, Reference Committee E: The use of hormones for "antiaging": a review of efficacy and safety. Report 5 of the American Medical Association Council on Science and Public Health (A09). www.ama-assn.org/ama1/pub/upload/mm/475/refcome.pdf (Accessed 4 March 2010)
105. Committee on Oversight and Government Reform: Committee holds hearing on myths and facts about human growth hormone, B12, and other substances. (12 February 2008). oversight.house.gov/story.asp?ID=1740 (Accessed 4 February 2010).
106. FDA-approved prescribing information for PREMPRO (conjugated estrogens/medroxyprogesterone acetate tablets). www.wyeth.com/content/showlabeling.asp?id=133 (Accessed 3 February 2010).

107. FDA-approved prescription information for PREMARIN (conjugated estrogens tablets, USP).
www.wyeth.com/content/showlabeling.asp?id=131
(Accessed 3 February 2010).

108. National Institute on Aging: Tips from the National Institute on Aging: can we prevent aging?
www.nia.nih.gov/HealthInformation/Publications/preventaging.htm
(Accessed 4 February 2010).

109. Website authored by Thomas Perls containing up-to-date coverage of medical and legal issues related to human growth hormone and anabolic steroids.
www.hghwatch.com
(Accessed 4 March 2010).

Affiliation

• Thomas T Perls, MD, MPH
Department of Medicine, Geriatrics Section,
Boston University Medical Campus,
MA, USA
Tel.: +1 617 638 6688
Fax: +1 617 638 6671
thperls@bu.edu