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Human Growth Hormone for Improved Strength and Increased Muscle Mass in Athletes

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ON JULY 20, 2006, ONE OF SPORT'S SUPERSTARS, BARRY BONDS OF the San Francisco Giants, breathed a sigh of relief.¹ A federal grand jury failed to indict the star slugger. His trainer was then released from jail where he had been held in contempt of court for failing to testify against Bonds. Allegations of using performance-enhancing drugs have plagued Bonds' rise toward the career home run record, having surpassed Babe Ruth's mark in May 2006 and now lying second behind Hank Aaron. Various sources have claimed that Bonds has used human growth hormone (HGH) and steroids to boost his performance. Bonds has always denied the allegations.

Use of HGH by athletes has come to popular attention in recent years, especially with a number of high-profile arrests and banning of cyclists in the Tour de France.² Besides anabolic steroids, the most commonly used performance-enhancing hormones are erythropoietin (EPO), insulin, and HGH.² HGH is banned by the International Olympic Committee, the National Collegiate Athletic Association (NCAA), and all major sporting leagues. Tests for illicit use have serious limitations due to natural variability in HGH levels, normal daily fluctuation, and the need to test within 24 hours of injection. A new detection test was used at the 2004 Olympics in Athens and the 2006 Winter Olympics in Torino with no positive samples detected.³ Lack of detection is not believed to be due to lack of use. An NCAA study found that 3.5% of athletes had used HGH in the previous year, and a survey of 10th graders found that 5% were using HGH.⁴

Such use is based on stories of extraordinary gains in strength and muscle mass among serious athletes. These claims influence

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younger athletes who dream of competing at the highest level. At the same time, recreational athletes are exposed to advertisements that HGH will increase energy, build muscle strength, improve sex, and delay (if not prevent) aging.⁵ Advertisers allege that scientific studies support their claims and conclude, "Anyone over 35 who wants to have good health and longevity will need to be on an HGH program."⁶ Many of these claims relate to oral supplements that allegedly stimulate endogenous hormone production. More and more, however, physicians are being asked to provide the authentic material: prescriptions for injectable HGH. One-third of all HGH sales worldwide are estimated to be for unapproved uses.⁵ The evidence for and against its use by athletes will be reviewed here.

Background

Recombinant DNA technology has made available an abundant supply of HGH. Children and adults who are naturally deficient in HGH, and those who have the clinical syndrome of pituitary dwarfism, respond favorably to HGH replacement therapy. Such therapy increases growth, and is accompanied by anabolic effects including increased lean body mass and decreased fat mass.³

Pharmacology and Production

Growth hormone is a relatively small polypeptide secreted by the anterior pituitary gland in pulses several times a day.⁷ Normal HGH secretion is highest during slow-wave sleep. HGH production decreases dramati-

cally after puberty. This decline underlies popular claims that HGH therapy will overcome aging—reminiscent of claims that the fountain of youth lies in supplements of various other hormones that decline with age.

Endogenous production is intricately regulated by neural control, metabolic and hormonal feedback mechanisms, and circulating levels of various biochemicals.⁸ HGH production can be increased by exercise, stress, fever, fasting, and ingestion of amino acids like leucine and arginine.⁹ Particular drugs, like clonidine, L-dopa, gamma-hydroxybutyrate (GHB), and corticosteroids, increase HGH production by acting directly on the pituitary. Secretion is reduced by hyperglycemia, obesity, and hypothyroidism.

Exercise increases HGH production dramatically. Prolonged moderate exercise can increase HGH levels 10-fold.⁹ Anaerobic, intense exercise can naturally lead to extremely high HGH concentrations in some non-doping athletes.² With intense exercise, peak production usually is attained 15-30 minutes after exercise is completed. To mimic this, athletes usually inject HGH shortly after training. Elevated levels return to baseline 8-16 hours after intramuscular injection and 11-20 hours after subcutaneous injection.³ This contributes to the difficulty of identifying athletes who are doping.

Mechanism of Action

HGH binds to specific membrane receptors and binding proteins throughout the body.⁸ The hormone increases the uptake and incorporation of amino acids into muscle.⁷ HGH has acute, transient insulin-like effects that stimulate glucose uptake into muscle and adipose tissue.⁸ However, its chronic effects are antagonistic of insulin, leading to fatty acid mobilization, inhibition of glucose uptake, and reduced insulin sensitivity.⁹ HGH also has indirect effects mediated primarily by insulin-like growth factor-I (IGF-I) produced by the liver, although its mechanism of action is poorly understood.⁸

Clinical Studies

The results of controlled studies differ greatly from anecdotal reports from underground users. Such use often involves several anabolic drugs at very high doses and in complex regimens specific to each sport. Controlled studies are few and usually involve HGH alone at lower doses. Therefore, the effectiveness and safety of HGH usage is difficult to evaluate.

A prior review in this publication included five studies with untrained men.¹⁰ These found that HGH administration produced physiological changes, but muscle mass and strength did not change significantly compared to control groups.

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An early study with athletes enrolled seven experienced weight-lifters (average age 23 years).¹¹ Each athlete continued his customary training schedule (3-6 days/week) and injected 40 mcg/kg/d HGH for 14 days. Fasting serum IGF-I levels doubled ($P = 0.002$). The rate of skeletal muscle protein synthesis did not change significantly during the trial, nor did whole body protein breakdown, suggesting no ergogenic benefit from HGH supplementation.

Twenty-two male power athletes (average age 23 years) were randomly assigned to either placebo or 0.09 U/kg/d injected subcutaneously at bedtime.¹² Three HGH subjects dropped out because of carpal tunnel compression and/or fluid retention in the hands. The HGH subjects had significantly greater increases in HGH ($P < 0.01$) and IGF-I levels ($P < 0.001$). Other serum hormone and steroid levels did not change. Changes in fat-free mass, lean body mass, and skeletal muscle strength were identical between the two groups.

Eleven male endurance athletes (average age 32 years) were randomized to either placebo or 0.067 mg/kg HGH injected subcutaneously at bedtime.¹³ Radio-labeled leucine (an amino acid) was infused into the athletes to provide three different methods of measuring protein metabolism. HGH administration led to a significantly greater anabolic effect among athletes both at rest ($P < 0.01$) and during or after exercise ($P < 0.05$). The increase was visible after one week of HGH injections and accentuated after four weeks. The placebo group did not change compared to baseline.

Thirty healthy active subjects, none of whom were professional athletes, took part in the most recent controlled study.¹⁴ An equal number of men and women participated. All were randomly assigned to receive either HGH 0.033 mg/kg, HGH 0.067 mg/kg, or placebo daily for 28 days. Exercise measurements were made before and after the 28 days using a bicycle ergometer with automatic load increase. The maximum power output and maximum oxygen uptake did not vary significantly between the three groups. No significant differences were found for muscle mass, heart rate, blood pressure, or ECG readings. Total body weight was significantly higher for the higher HGH dose compared to placebo ($P = 0.028$), with calculations showing that this was primarily due to increased water retention.

Adverse Effects

Acromegaly is a syndrome in which people produce higher than normal levels of HGH.¹³ People with this condition have abnormal protein remodeling in skeletal muscle and other organs. While muscle mass is increased, physical strength and endurance are reduced.

Concerns have been raised that sustained elevated HGH from exogenous sources will lead to similar problems.

Acromegaly is also associated with cardiac pathology.¹⁵ In one small study, 15 body builders were self-selected to take either testosterone and anabolic steroids along with 0.15-0.30 IU/kg HGH, to take HGH alone, or to join a control group.¹⁶ After six weeks, the supplementing group had significantly lower HDL-cholesterol and apolipoprotein A-1 levels ($P < 0.001$), both of which are associated with higher risks of coronary disease.

Carpal tunnel compression, arthralgias, and fluid retention are common complaints in controlled studies.¹⁷ Chronic administration of HGH can lead to insulin resistance and suppression of endogenous HGH production.² Increased morbidity and mortality has been observed in severely ill patients given HGH, but the reasons for this association were unclear.¹⁸ Other serious adverse effects have occurred because cadaveric HGH of questionable quality has been available on the black market.¹⁹ In the early 1980s, several cases of Creutzfeldt-Jakob disease developed because of contaminated cadaveric HGH.

Formulation

HGH-deficient adults usually take 1-2 IU/d by subcutaneous injection every evening. Athletes sometimes take as much as 10-25 IU/d, three or four times a week.³ It is often taken in 4-6 week cycles and in combination with other performance-enhancing agents, especially anabolic steroids. An athlete's regimen can cost about \$5,000 per month.⁴ Because of this cost, many HGH advertisements actually promote supplements containing amino acids, most commonly arginine, ornithine, lysine, and tryptophan.³ These allegedly increase endogenous HGH production.

Conclusion

The most recent randomized controlled trial with athletes concluded that HGH administration has demonstrated no beneficial effects and that only untoward effects can be expected.¹⁴ A limitation with such studies is that in practice athletes often take larger, varying doses, and cycle on and off HGH and other anabolic agents. All or some of these may have synergistic effects, but are also likely to put athletes at greater risk. In addition, HGH is part of an intricate web of natural hormones and growth factors. Manipulating one part of the system will lead to counter-balancing changes in other metabolites, thus increasing the risk of unexpected adverse effects.

The favorable changes in body composition described anecdotally can be explained by increased fluid

Hormones and (Anti-)Aging

IN THE LATE 1980S, AT VETERANS ADMINISTRATION HOSPITALS IN Milwaukee and Chicago, 12 men age 60 and older began receiving injections three times a week that dramatically reversed some signs of aging. The injections increased their lean body (and presumably muscle) mass, reduced excess fat, and thickened skin. When the injections stopped, these changes reversed, and the signs of aging returned. What the men were taking was recombinant human growth hormone (HGH), a synthetic version of the hormone that is produced in the pituitary gland and plays a critical part in normal childhood growth and development.

At the same time, evidence was accumulating that menopausal hormone therapy with estrogen (alone or in combination with a progestin in women with a uterus) could benefit postmenopausal women by reducing cardiovascular disease, colon cancer, and other diseases of aging. Further studies have indicated that, although estrogen remains an effective way to control hot flashes, long-term use of these hormones may increase risk for several major age-related diseases in some women, especially when treatment is started years after menopause. The finding that levels of testosterone in men decreased with aging raised the question of whether they too might benefit from sex hormone treatment.

As a result of these preliminary observational findings, the National Institute on Aging (NIA) launched a series of research initiatives to clarify what influence hormone replacement therapy might have on the aging process. So far, most of these studies have been inconclusive, but have led many investigators to question whether the risks of hormone replacement may outweigh any benefit. Supplements of HGH, for instance, can promote diabetes, joint pain, carpal tunnel syndrome, and pooling of fluid in the skin and other tissues, which may lead to high blood pressure and heart failure. Studies in mice have raised other concerns about the hormone. Investigators have found that mice deficient in growth hormone production live substantially longer than normal mice, while mice overproducing growth hormone live shorter than average lives. This finding suggests that even if hGH replacement therapy is initially beneficial, ultimately it may be harmful and actually might curtail longevity.

Similarly, there is scant evidence that testosterone supplementation has any positive impact in healthy older men. In fact, some studies suggest supplementation might trigger excessive red blood cell production in some men. This side effect can increase a man's risk of stroke.

Estrogen is perhaps the most well studied of all hormones. Yet results from the Women's Health Initiative, the first major placebo-controlled, randomized clinical trial of estrogen therapy with or without progestin to prevent some chronic diseases of aging, surprised the medical community. There were more cases of stroke, blood clots, heart disease, and breast cancer in postmenopausal women using estrogen and progestin in the study, and more cases of possible dementia in women older than age 65, than in those using the placebo. But, there were also fewer bone fractures and cases of colon cancer. In postmenopausal women using estrogen alone, there were more cases of stroke and fewer bone fractures than in those women on placebo. Other studies indicate that menopausal hormone therapy is effective in controlling moderate-to-severe menopausal symptoms, so research is ongoing to evaluate benefits and risks in menopausal and younger postmenopausal women.

As research continues, the pros and cons of hormone replacement may become more precisely defined. These hormonal supplements appear to increase risk and provide few clear-cut benefits for healthy individuals and do not seem to slow the aging process.

In fact, normal physiological aging is quite variable, according to investigators involved in the Baltimore Longitudinal Study of Aging, a long-term NIA study begun in 1958 that has tracked the lives of more than 1,000 people from age 20 to 90 and beyond. Not only do individuals age overall at vastly different rates, it is quite likely that age-related changes in various cells, tissues, and organs differ as well. For instance, kidney function may decline more rapidly in some individuals. In others, bone strength may diminish faster. The organs that age fastest in one person may not age as rapidly in another. This suggests that genes, lifestyle, and disease can all affect the rate of aging and that several distinct processes are involved. ❖

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retention.¹⁴ Such changes can be enough to lead athletes to believe they can compete better which may in fact improve actual performance. However, water retention and other adverse effects can interfere with athletic per-

formance. More serious adverse effects also can occur. Particular concerns exist about the quality of HGH available on the black market, especially given the hormone's expense.

Recommendation

Use of HGH by athletes is banned by most sports organizations because of both ethical and medical concerns. Clinical trials with exogenous HGH injections have produced none of the gains sought by athletes, and point to many risks. Athletes, whether serious or recreational, who are considering this drug should be strongly urged to avoid its use completely. ❖

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Spirituality and Health

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PART 1 OF A SERIES ON SPIRITUALITY

A LARGE BODY OF OBSERVATIONAL RESEARCH HAS BEEN published on the role of religious belief and practice on physical and mental health.^{1,2} The consensus appears to be that there is some beneficial effect of religion on health, but this conclusion comes with numerous conditions and assumptions. The purpose of this article is to summarize some of this work and introduce the most salient issues. A second article will address attempts to expand on the positive observational findings with experimental studies.

Religiosity or Faith?

A foundational problem in all research on spirituality and health is the definition and measurement of spirituality. Like many other traits, it can be difficult to measure directly, and the use of surrogate measures is common. One way of beginning to come to grips with this

issue is to divide measures into behavioral and subjective as described by Chatters.¹

Behavioral measures may include a study participant's faith tradition and denomination, frequency of church attendance and/or other religious devotions, and the size and programmatic offerings of his/her religious community. Certain parts of the substantive content of faith that might motivate behavior, such as fear of the consequences of sin and adherence to the religious community's moral norms, might also be included under this heading.

The subjective dimension addresses the metaphysical aspects of faith. These may include a view of the nature of the divine (god as a distinct being or a universal life force), a sense of the degree of divine awareness of and intervention in the world, and the presence or absence of a sense of having a personal relationship with the object of worship.

These two categories influence and interpenetrate each other, but neither is sufficient to describe the complete religious experience. For instance, health status may influence one's ability to participate in public religious life, but may also intensify private, inner devotion. Potential confounding relationships of this kind mean that the results of studies of religiosity/spirituality and health should be approached with caution, especially when an attempt is made to generalize from one population to another. It should also be noted that, as will become apparent in the discussion of potential mechanisms, the operational definition of faith has great influence on the nature and explanation of study findings.

A second issue with research on spirituality and health is the measurement and nature of the outcomes under study. From the biomedical perspective, it might seem that the goal of studies of spirituality and health should be to show measurable improvements in objective dimensions of health. Numerous studies have taken this approach.³⁻⁶ However, because spirituality is at least in part a means to apply values and explanations to experience, the use of objective measures may not be the only appropriate strategy.

Other research has considered the relationship of spirituality and the subjective assessment of health.^{7,8} These studies showed evidence that spirituality had a positive effect on participants' assessment of their own health that was independent of other measures of health.

Mechanisms of Action

In considering the potential mechanisms by which spirituality might influence health, it is useful to consider a lesson learned in the study of dietary supplements.

Once a potential health benefit is identified in a natural substance, considerable effort may be devoted to identifying the critical ingredient(s) so that they may be extracted and delivered more efficiently. However, when these are tested in isolation, their effects often fail to meet expectations. There is something lost when the total context is not considered. The same is true of spirituality. Many of the potential explanatory mechanisms involve psychological and/or social factors. These are often highly correlated with one another and difficult to tease out into distinct strands, with consequent difficulties in measurement. For ease of presentation, however, the most commonly proposed mechanisms can be divided into several broad categories.

Healthy Behaviors

Considerable research has been done with denominational groups (Mormons, Seventh Day Adventists, and Orthodox Jews) that are known to have specific dietary and health practices, and other behaviors that might be associated with positive health states.⁹⁻¹² Some of these factors, such as the Adventist preference for a vegetarian diet, Mormons' abstention from tobacco and alcohol, or many faiths' discouragement of sexual promiscuity, may have direct benefits.

Other factors may be more subtle. If the culture of a religious community frowns on risk-taking, this may translate into avoidance of behaviors with potentially negative health consequences, such as injuries or sexually transmitted infections.² This may even extend to non-health dimensions, such as business and personal ethics, with potential benefit in the form of avoidance of conflict and stress. However, it may also be the case that religious communities preferentially attract people who are already risk-averse. Regardless, there appears to be some value in religious sanction of behaviors that have the concurrent (or in some cases subsequent!) blessing of medical science.

Social Support

Religious groups are natural communities from which members can draw material and moral support.¹³⁻¹⁵ There is evidence that those belonging to religious communities report having more, and richer, resources and support to draw upon than those who do not belong.¹⁶ At a practical level, this may translate into transportation and/or childcare for doctors' visits and other appointments, a reliable supply of prepared food after childbirth or bereavement, periodic visits to the homebound, and a variety of kinds of help in times of crisis or household disruption. At a psychological level, the principal benefit likely is a ready source of familiar

and sympathetic people with whom to share one's troubles. However, it is important not to overlook the psychological value of knowing that resources are available if needed.

There also is some benefit to being in the helping role. The perception that one is needed and valued can have a positive impact on mood and one's sense of self-worth. It may also encourage other desirable health behaviors (nutrition, rest, exercise) as ways of ensuring "fitness for duty."

Self-worth and Self-efficacy

The previous potential mechanisms deal mainly with concrete influences on health. However, there is also evidence that less tangible factors may be associated with health outcomes.^{17,18} Elements of both religiosity and spirituality can serve to boost self-image. As already mentioned, participation in a religious community can engender a sense of being needed. Long association brings with it the prestige of being a keeper of institutional memory. Spiritual practice, whether public or private, can create a sense of solidarity with the divine and a feeling of responsibility for enacting the divine will in one's life and in the world.

Any of these factors may increase consciousness of the need for self-care, including seeking medical attention as needed. They may also raise confidence in the faithful person that he or she can adhere to medical treatment and/or make and sustain needed lifestyle changes. The messages of strength through faith ("giving problems to God") and of the body as the temple of God, which are especially characteristic of the African-American church and appear to resonate with particular power among women, are good examples of how this mechanism might be seen to work.¹⁹

Coping and Emotional Support

A further twist in the potential relationship between faith and health is the possibility that faith does not so much improve health as alter the ways in which the faithful person views his or her health and the values that he or she assigns to specific health and life events.

Religion provides powerful resources for coping.²⁰⁻²² Most religious traditions offer examples of faithful people who found strength in adversity through their religious devotion. The modern believer is offered the opportunity to identify with and emulate them. In this way, negative health or life events (such as bereavement) may be re-evaluated as opportunities to show stoicism. This, in turn, may raise the sufferer's standing in the eyes of others in the faith community, bringing emotional and material support.

Finally, to the extent that the believer understands his or her relationship with the divine to transcend specific actions (such as structured prayers, ritual acts, or corporate public worship), periods of disability may result in an intensification of spirituality and a deeper belief and trust to compensate for other religious expressions that are temporarily or permanently not available. In this situation, the roles are reversed, with health a promoter of certain aspects of spirituality.

Negative Effects

For balance, it is important to bear in mind that the avenues by which spirituality and religious practice might benefit health may each also involve potential harms.

The healthy behavior model presumes that the faith community will support the believer in seeking the medical care that he or she needs, or that his or her physician recommends. This may not always be the case. Some religious groups discourage or prohibit specific kinds of treatments, from blood transfusions, immunizations, and various types of intensive care interventions, to medical care of any kind.

The social support model is built on an implicit assumption of reciprocity—those in the community help one another. However, those who are the neediest may not be able to participate as fully in the giving role as in the taking, and may have consequent difficulty—either internally, from feelings of guilt, or externally, from compassion fatigue among their fellow believers.

The self-efficacy model depends on the assumption that the believer will use the empowerment gained from faith to engage in the kinds of behaviors and seek the kinds of medical care that are judged by mainstream medicine to be sound. This may or may not be the case.

Finally, the sort of adaptation described by the coping model may become overdeveloped, leading to fatalism and inaction.

Conclusion

The range of proposed mechanisms for the spirituality-health connection makes clear the lack of unanimity as to the "active ingredient" in religious faith. All models, and the research on which they are based, must contend with the complex and interconnected reasons why and how people express their faith. Inward faith (spirituality) and outward expression (religiosity) influence and motivate each other. Their individual and joint impact on the health of a person is both unique and changing over time. Also, like many other factors affecting health, religious faith can have both positive and negative impacts.

To return to the dietary supplement example, perhaps the best way to imagine faith is as a whole substance, with some identifiable and some unknown components, only the sum of which should be credited with any noticeable effect.

Recommendation

For many clinicians, discussion of faith with their patients is difficult at best. Indeed, direct interaction may be most comfortable if directed mainly toward the impact of religion in the patient's life (meaning, comfort, peace) rather than to specific religious beliefs. It also should be emphasized that there is no evidence to support physicians who might encourage patients to take up religion for their health. In any case, it is unclear whether entering into as complex an undertaking as religious faith for so instrumental a reason would have much chance of success.

With these cautions in mind, however, there are positive steps that the clinician can take. First, know the ethics and health-related religious beliefs of the cultures from which your patients come. Second, where appropriate, be ready to suggest that a patient seek needed resources and services from his or her faith community. Third, be open to patients' need to express health-related concerns in spiritual terms. In such situations, a clinician may even suggest that a patient seek to deepen or enrich his or her spiritual practice as part of a strategy to restore and maintain health. Finally, be aware of the religious ideas and values (either present or past) that you bring to patient encounters. These steps will not empower anyone to improperly prescribe or proscribe faith, but they will help to clarify the role it may play in the clinician-patient interaction. ❖

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Clinical Briefs

With Comments from Russell H. Greenfield, MD

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U.S. CAM Kids

Source: Wilson KM, et al. Use of complementary medicine and dietary supplements among U.S. adolescents. *J Adolesc Health* 2006;38:385-394.

Goal: To determine the prevalence and patterns of use of complementary and alternative medicine (CAM) therapies and dietary supplements among adolescents.

Study design: Online self-administered survey with questions taken from prior research on CAM use, and including a variety of CAM modalities.

Subjects: A total of 1,280 teens aged 14-19 years drawn from a national sample of approximately 200,000 Harris Poll Online (HPOL) and Harris Youth Query members who completed the online survey.

Methods: A stratified random sample was drawn from the HPOL database consistent with known age and gender divisions. E-mail invitations, together with a unique password, were sent to more than 12,000 teens to participate in a survey "about your thoughts and experiences with various health and medical care issues." Focus groups were also held with a convenience sample of teens to explore their knowledge and under-

standing of, as well as experience with, CAM. Data obtained were weighted with respect to U.S. demographics.

Results: More than three-quarters of respondents had used CAM during their lifetime, with an average of 2.2 modalities experienced, and with girls more likely than boys to have used CAM. Nearly 50% of respondents reported having used CAM during the past month. Approximately 46% of the teens reported lifetime use of at least one of the dietary supplements listed (not including vitamins), with the most commonly used including herbal or green teas, ginseng, zinc, St. John's wort, weight-loss supplements, and creatine.

CME Questions

CME Instructions: Physicians participate in this continuing medical education program by reading the articles, using the provided references for further research, and studying the CME questions. Participants should select what they believe to be the correct answers, then refer to the list of correct answers to test their knowledge. To clarify confusion surrounding any questions answered incorrectly, please consult the source material.

After completing this activity, participants must complete the evaluation form provided at the end of each semester (June and December) and return it in the reply envelope provided to receive a credit letter. When an evaluation form is received, a credit letter will be mailed to the participant.

After completing the program, physicians will be able to:

- present evidence-based clinical analyses of commonly used alternative therapies;
- make informed, evidence-based recommendations to clinicians about whether to consider using such therapies in practice; and
- describe and critique the objectives, methods, results and conclusions of useful, current, peer-reviewed clinical studies in alternative medicine as published in the scientific literature.

31. The effectiveness of HGH injections to increase muscle strength in athletes is supported by:

- well-controlled clinical trials.
- anecdotal reports from athletes.
- large epidemiological studies.
- All of the above

32. Testing for illegal use of HGH by athletes is controversial because:

- questions have been raised about the reliability and accuracy of currently available tests.
- athletes do not like to be tested.
- the International Olympic Committee does not ban the use of HGH.
- HGH cannot be detected in body fluids.

33. The large body of observational research on the role of religious belief and practice on physical and mental health appears to show some beneficial effect.

- True
- False

34. The most commonly proposed mechanisms of action by which spirituality might influence health include:

- healthy behaviors.
- social support.
- self-worth and self-efficacy.
- coping and emotional support.
- All of the above

Answers: 31. b, 32. a, 33. a, 34. e.

Nearly 30% of respondents reported use of a supplement within 30 days of completion of the survey tool, while 46% were currently using a vitamin. Within the prior month, almost 10% of teens reported using a prescription aid together with supplements. Caucasian teens were more likely to have used herbal remedies, African-Americans more likely to have used faith healing or prayer, and Hispanic adolescents to have experienced spinal manipulation. Teens living in the West were more likely to have used CAM than those living elsewhere in the United States. A positive attitude towards CAM significantly impacted lifetime use. Of note, most respondents believed that “doctors don’t like CAM.”

Conclusion: Nationally, many adolescents use CAM, and not in a manner limited by geography or specific sub-population. This includes a high prevalence of use of herbs and supplements.

Study strengths: Employed weighted variables as gleaned from information from prior adolescent survey trials, including likelihood of response and propensity to be on-line; survey was not advertised as dealing specifically with CAM, thus eliminating some bias.

Study weaknesses: Poor response rate; inherent weaknesses related to survey/incentive model, especially in adolescents; lack of generalizability.

Of note: Studies evaluating use of CAM therapies among adolescents that focused primarily on local samples or special populations reveal that 54-70% of teens have used CAM; respondents were offered incentive points for completing the survey that could be redeemed for merchandise; use of herbs and supplements were grouped together in the analysis; 66% of respondents were in middle or high school, 24% were enrolled in post-high school education, and 10% were not in school; 19.5% of respondents had been involved in counseling, group therapy, or psychotherapy; level of parent education was not associated with CAM or supplement use; teens who viewed themselves as belonging to a lower socioeconomic group were more likely to use CAM and supplements; middle adolescence (age 16-17) was found to be the period of most intense CAM/supplement use.

We knew that: Prior studies have shown that a significant number of children are exposed to and use CAM thera-

pies; teens, like many adults, often do not disclose use of CAM therapies to their doctors; people who are homeless or relatively poor exhibit a high use of CAM therapies and/or supplements; parental use of CAM and supplements often predicts use by adolescents.

Comments: Whether the results of this study can be readily translated to our own locales or not, the same tone of prudent precaution is sounded that has been heard when addressing CAM and supplement use in adults—odds are, our patients are not sharing everything with us. Not only to help deepen the professional healing relationship between patient and health care provider, but also to appropriately help people of any age navigate the maze that sometimes is CAM and supplement use, practitioners must consistently inquire about the use of such therapies in a manner non-judgmental. Many issues arise during the adolescent years, notably those revolving around body image for young girls, and a health care partner who can help evaluate various CAM therapies is invaluable. Even if we don’t know the supplement or therapy in question, we can offer to evaluate in partnership any information the patient brings to us.

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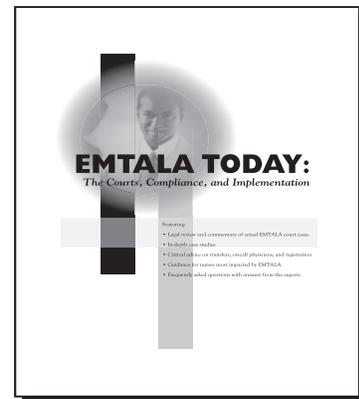
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THOMSON
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Indeed, the basis of health care is not in encyclopedic knowledge—it has always been in creating a relationship based in mutual respect and trust.

What to do with this article: Keep a copy on your computer. ❖

First Do No Harm: Iron Supplements and Pregnancy

Source: Casanueva E, et al. Weekly iron as a safe alternative to daily supplementation for nonanemic pregnant women. *Arch Med Res* 2006;37:674-682.

Goal: To compare effectiveness and safety of daily vs. weekly iron, folic acid, and vitamin B₁₂ supplementation in healthy, non-anemic pregnant women.

Study design: Prospective randomized comparison trial.

Subjects: Women with singleton pregnancies more than 20 weeks gestation (n = 116).

Methods: Subjects were randomized to receive daily supplementation with one tablet containing 60 mg elemental iron (ferrous sulfate), 200 mcg, and 1 mcg vitamin B₁₂, or two of the same tablets once a week. Food frequency questionnaires were completed by the women, and maternal hemoglobin and ferritin concentrations were measured every four weeks from 20 to 36 weeks gestation.

Results: Hemoglobin levels were significantly higher in the daily supplementation group from weeks 28 to 36, resulting in lower frequency of anemia during weeks 32-36, but a significantly higher incidence of hemoconcentration at 28-36 weeks. Hemoconcentration occurred at gestational week 28 or later in 18% of women receiving daily supplementation as compared with only 7% receiving supplementation weekly. Low ferritin levels were more prevalent than anemia at every time point in both groups, but ferritin levels decreased

more in the weekly supplementation group than in those receiving supplements daily. Assessment of pregnancy outcomes revealed that hemoconcentration at gestational week 28 was associated with a significantly higher relative risk of low birth weight (RR = 6.23) and premature delivery (RR = 7.78).

Conclusion: In non-anemic women receiving iron supplementation after 20 weeks gestation, daily administration is more successful than once a week administration at preventing mild anemia, although both regimens prevent severe anemia associated with perinatal risk. However, daily supplementation significantly increases the risk of hemoconcentration at 28 weeks, and to levels associated with low birth weight and premature delivery.

Study strengths: Regular evaluation and blood sampling; strong subject adherence to protocol.

Study weaknesses: Dose employed (60 mg elemental iron) is twice that typically recommended; does not address supplementation prior to gestational age 20 weeks, as often utilized in the United States (standard practice in Mexico is to begin iron supplementation at gestational age 20 weeks); compliance determined via supplementation diaries and pill counts.

Of note: Participants were women mainly from middle and low socioeconomic classes in Mexico City (17% were younger than age 16 years, but participants were “fairly well educated by Mexican standards”); subjects had not received any form of supplementation prior to gestational age 20 weeks; supplements were supplied at no cost to participants and were to be taken at least one hour after meals; the mucosal lining of the small intestine turns over every 5-6 days, and new cells may be programmed to absorb iron according to bodily iron stores; high intraluminal intestinal concentrations of iron actually result in decreased iron absorption; the present study was not fully blinded because the nutritionist dispensed tablets to the women and later judged adherence to supplement regimen;

because the trial took place in Mexico City, altitude-adjusted norms for hemoglobin during pregnancy as put forth by the Centers for Disease Control and Prevention were utilized; compliance was only slightly higher in the weekly supplementation group; the total amount of iron ingested by the weekly supplementation group was only 28% of that taken by the daily supplementation group.

We knew that: Iron-deficiency anemia is common during pregnancy (iron requirements increase during pregnancy, mostly due to increased blood volume); iron-deficiency anemia early in pregnancy is associated with low birth weight and premature delivery; severe anemia near term also puts the expectant mother at significant health risk; epidemiological data suggest that daily and weekly iron supplementation programs are equally efficacious with respect to preventing iron-deficiency anemia; previous epidemiological and clinical studies have also shown that hemoconcentration is associated with an increased risk of low birth weight and premature delivery; ferritin levels typically decrease during pregnancy even in the face of iron supplementation, and can increase secondary to inflammatory conditions.

Comments: The results of this longitudinal trial would be disquieting were it not for the fact that the iron dose employed was quite high, but it is good to know that in select circumstances less frequent administration of iron can be effective at safely preventing iron-deficiency anemia. That said, some trials suggest that routine iron supplementation for non-anemic women during pregnancy does little more than improve hematologic parameters. The routine use of iron supplementation during pregnancy in at-risk populations is important, but what about in low-risk populations receiving good prenatal care? Certainly, significant anemia must be identified and treated, but perhaps not every non-anemic pregnant woman requires iron supplementation throughout her pregnancy. At this time, little would suggest harm in low-dose iron

supplementation across the board, but it is at least a point of interest.

What to do with this article: Remember that you read the abstract. ❖

Work Can Kill Us: Stress and the Metabolic Syndrome

Source: Chandola T, et al. Chronic stress at work and the metabolic syndrome: Prospective study. *BMJ* 2006;332:521-525. Epub 2006 Jan 20.

Goal: To investigate the association between chronic work stress and the metabolic syndrome.

Study design: Prospective cohort study using the job strain questionnaire.

Subjects: Men and women aged 35-55 years at baseline who were employed in 20 London civil service departments (n = 10,308 from the Whitehall II Study).

Methods: The Whitehall II study recruited participants from 1985 to 1988, then collected survey data through postal questionnaires in 1989, in 1991-1993, in 1995 (no questions about work stress or health behaviors), and again in 1997-1999. Data regarding cumulative exposure to work-based stress were taken from four of the five survey periods, and biological measures of the metabolic syndrome were obtained in 1997-1999. Data on health behaviors were also examined, including smoking, alcohol use, exercise, and regular ingestion of fruits and vegetables.

Results: A dose-response relationship was found between exposure to chronic job stress and the risk of metabolic syndrome independent of other relevant risk factors. Those with chronic work stress were more than twice as likely to develop metabolic syndrome than those without significant work stress (odds ratio 2.25). Both men and women from lower employment grades were more likely to have metabolic syndrome. While men experiencing chronic job

stress were more likely to develop the syndrome compared to their relatively unstressed colleagues, women in similar circumstances were more than five times as likely to have the syndrome (however, their numbers were quite small). Especially among men, exposure to chronic job stress was also associated with health-damaging behavior. Multivariate analysis that combined data for both men and women and adjusted for age, employment grade, health behaviors, and baseline obesity revealed the same association between work stress and increased risk of developing metabolic syndrome.

Conclusion: Greater exposure to job stress over 14 years is associated with a greater risk of metabolic syndrome in a linear manner. A social gradient exists with respect to risk for metabolic exposure that can in part be explained through work stress.

Study strengths: Prospective nature of the trial; multiple measures of work stress; analysis that excluded obesity at baseline.

Study weaknesses: High dropout rate (by the last phase of the study participation rate was 75%), but potentially ameliorated through statistical analysis.

Of note: Components of the metabolic syndrome were not measured at baseline, though obesity, defined as BMI > 30 kg/m², was used as an indicator of risk for the syndrome; chronic work stress was defined as experiencing iso-strain on three or more surveys during the 14 years of follow-up; relatively few participants, overall, had chronic work stress as defined in this study; the “social gradient,” as noted by the authors, is important—those in the lowest employment grades had double the odds of the syndrome compared with those in the highest employment grades; there was little evidence that participation in unhealthy behaviors mediated or confounded the effect of work stress on risk of developing metabolic syndrome; as noted by the authors, overweight people may be more socially isolated at work and find working conditions more stressful; it is interesting to note the rela-

tively low rate of significant job stress experienced by women in the study.

We knew that: While a precise definition of the metabolic syndrome has yet to be fully agreed upon, most experts agree that the syndrome represents a cluster of risk factors that increases risk of heart disease and Type 2 diabetes, including abdominal obesity, hypertension, insulin resistance with or without glucose intolerance, prothrombotic and pro-inflammatory states, and atherogenic dyslipidemia (elevated triglycerides, small LDL particle size, low HDL); work stress has been tied to development of heart disease in both prospective and retrospective studies, though the biological mechanisms remain unclear; the iso-strain model is based in the hypothesis that socially isolated (little support, high demands, little control, low reward) job strain puts people at the highest risk for heart disease; chronic job stress may impact the autonomic nervous system (increased sympathetic activity) as well as neuroendocrine activity, thereby impacting cortisol levels, lipoprotein metabolism, and insulin sensitivity, as well as heart rate variability.

Comments: Data have been accumulating for some time linking psychosocial stressors and risk for cardiovascular disease. Some, but importantly not all of the findings, can be tied to an increase in unhealthy behavior patterns in those under chronic stress. Results of this well-done, prospective trial add fuel to the fire. Although many employers are now paying attention to stress at work, many of those same employers are still seeking solutions (one need only examine corporate employee health expenditures on antidepressants to understand why). For all the data, for the sheer common sense of it all, it remains a mystery why more practitioners have not partnered with corporations to help ameliorate this situation. After all, if one thing is clear, stress management can no longer be considered optional; rather, it must be deemed an integral part of any health promotion program.

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ALTERNATIVE MEDICINE ALERT™

A Clinician's Evidence-Based Guide to Alternative Therapies

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Taking a Spiritual Assessment

DISCUSSIONS OF SPIRITUAL BELIEFS AND PRACTICES CAN BE UNCOMFORTABLE AND AWKWARD for the practicing physician. However, a growing body of evidence points to spirituality as an important coping tool for patients. Consider the following research results:

- In a national survey on prevalence and patterns of use, 35% of respondents reported using prayer for health concerns; 75% prayed for wellness, 22% prayed for specific medical conditions.¹
- Another recent study reports that 33% of people would welcome a discussion of their spiritual beliefs in a routine office visit; this number surges to 70% in an end-of-life setting.²

What Patients Want

A 2004 study published in the *Annals of Family Medicine* examined when patients feel a discussion about spirituality is appropriate, what patients want their physicians to know about their spiritual beliefs, and what they want physicians to do with this information.³ The results help shape a framework for when to take a spiritual assessment. Of the nearly 800 people who completed the survey:

- Seventeen percent said they never want to be questioned about spiritual beliefs; 63% wanted to be asked depending on the nature of the situation; and 20% always wanted their physician to know about their beliefs.
- Of those who sometimes or always wanted to discuss their spiritual beliefs, 87% wanted their physicians to understand how their beliefs influence how they deal with being sick; 85% wanted their physician to understand them better as a person; and 83% wanted their physicians to understand their decision making.
- Among the more than 50% who wanted to talk, providing compassion, encouraging realistic hope, advising how to take better care of oneself when ill, changing treatment, and referral to a spiritual counselor were the actions most commonly endorsed.
- Praying with their physician and having the physician “just listen” were the least preferred courses of action.

Table 1

The HOPE questions for a formal spiritual assessment in a medical interview

H: Sources of hope, meaning, comfort, strength, peace, love, and connection

O: Organized religion

P: Personal spirituality and practice

E: Effects on medical care and end-of-life issues

Source: Anandarajah G, Hight E. Spirituality and medical practice: Using the HOPE questions as a practice tool for spiritual assessment. *Am Fam Physician* 2001;63:81-88.

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- The most acceptable scenarios for spiritual discussion were life-threatening illnesses, serious medical conditions, and loss of loved ones.

Spiritual Assessment Tools

Several tools exist that can guide a physician in taking a spiritual assessment. Tables 1 and 2 outline the HOPE tool, developed by Anandarajah and Hight.⁴

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Table 2
Examples of questions for the HOPE approach to spiritual assessment
<p>H: Source of hope, meaning comfort, strength, peace, love, and connection</p> <p>We have been discussing your support systems. I was wondering, what is there in your life that gives you internal support?</p> <p>What are your sources of hope, strength, comfort, and peace?</p> <p>What do you hold on to during difficult times?</p> <p>What sustains you and keeps you going?</p> <p>For some people, their religious or spiritual beliefs act as a source of comfort and strength in dealing with life's ups and downs; is this true for you?</p> <p>If the answer is "Yes," go on to O and P questions.</p> <p>If the answer is "No," consider asking: Was it ever? If the answer is "Yes," ask: What changed?</p> <p>O: Organized religion</p> <p>Do you consider yourself part of an organized religion?</p> <p>How important is this to you?</p> <p>What aspects of your religion are helpful and not so helpful to you?</p> <p>Are you part of a religious or spiritual community? Does it help you? How?</p> <p>P: Personal spirituality/practices</p> <p>Do you have personal spiritual beliefs that are independent of organized religion? What are they?</p> <p>Do you believe in God? What kind of relationship do you have with God?</p> <p>What aspects of your spirituality or spiritual practices do you find most helpful to you personally? (e.g., prayer, meditation, reading scripture, attending religious services, listening to music, hiking, communing with nature)</p> <p>E: Effects on medical care and end-of-life issues</p> <p>Has being sick (or your current situation) affected your ability to do the things that usually help you spiritually?</p> <p>As a doctor, is there anything that I can do to help you access the resources that usually help you?</p> <p>Are you worried about any conflicts between your beliefs and your medical situation/care/decisions?</p> <p>Would it be helpful for you to speak to a clinical chaplain/community spiritual leader?</p> <p>Are there any specific practices or restriction I should know about in providing your medical care? (e.g., dietary restrictions, use of blood products)</p> <p><i>If the patient is dying:</i> How do your beliefs affect the kind of medical care you would like me to provide over the next few days/weeks/months?</p> <p>Source: Anandarajah G, Hight E. Spirituality and medical practice: Using the HOPE questions as a practice tool for spiritual assessment. <i>Am Fam Physician</i> 2001;63:81-88.</p> <p>Reprinted with permission from: © American Academy of Family Physicians.</p>

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