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Chromium Supplementation for Weight Loss

By Dónal P. O'Mathúna, PhD

YET ANOTHER INDICATION OF THE SERIOUS OBESITY PROBLEM IN the United States was the selection of obesity for the April 9, 2003, thematic issue of the *Journal of the American Medical Association (JAMA)*. Women in particular struggle with this issue, as Table 1 demonstrates. The proportion of women categorized as overweight or severely obese has increased similarly over the same years.

Pharmaceutical responses to the problem received setbacks with the 1997 withdrawal of fenfluramine and dexfenfluramine (both associated with valvular regurgitation and primary pulmonary hypertension) and the 2000 withdrawal of phenylpropanolamine, present in popular over-the-counter weight-loss medications and associated with stroke.[1] Diets remain perennially popular; however, the *JAMA* obesity theme issue included a review of popular low-carbohydrate diets that concluded there was insufficient evidence to recommend for or against their use.[2]

Frustrated by diets and concerned about the adverse effects of pharmaceuticals, many are turning to nonprescription weight-loss products, including dietary supplements. Such products are especially popular with young women.[3] One of these is chromium, which generates more than $100 million in sales annually.[4] The most popular formulation is chromium picolinate, available in pills, chewing gum, sports drinks, and nutrition bars. Products are marketed as "fat burners" both for those who want to lose weight and athletes who want to build muscle. Other claims made for these supplements are that they increase energy, curb addictions, cure acne, prevent insomnia, relieve depression, and increase life span.

Biochemistry

Chromium is an essential trace element and part of the insulin metabolic pathway. The U.S. Department of Agriculture estimated safe and adequate daily dietary intake of chromium is 50-200 micrograms (mcg) for adults (1 mcg = 0.001 mg).[5] The Institute of Medicine (IOM) 2001 report on Dietary Reference Intakes set the Adequate Intake (AI) level for chromium at 35 mcg/d for young

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men and 25 mcg/d for young women. The AI is the amount expected to meet or exceed the daily requirements in essentially all healthy people.[6] Establishing these levels, and measuring them clinically, is hampered by the extremely low levels of chromium in body fluids. There currently is no simple, reliable test for chromium deficiency.

Pharmacology

Chromium deficiency first was reported in 1977 when patients on long-term total parenteral nutrition developed classic diabetic symptoms that were reversed with the addition of chromium to their diets.[7] The potentially beneficial role of chromium in treating certain patients with Type 2 diabetes (those who are chromium deficient) currently is receiving much attention.[8] Because of the role of insulin in managing body weight, and given that chromium's mechanism of action involves glucose and insulin metabolism, interest has arisen on the potential role of chromium in weight-loss strategies.

Mechanism of Action

Chromium deficiency leaves cells less sensitive to insulin (or "insulin resistant").[9] As a result, glucose is less able to enter cells for energy production and instead is stored as fat. Insulin resistance also hinders the passage of amino acids into muscle cells, reducing protein synthesis.[10] Chromium supplementation allegedly reverses these effects, leading to the "burning" of excess fat, weight loss, and increased muscle mass.

Clinical Studies

A meta-analysis of controlled clinical trials of chromium picolinate for weight loss was published in April 2003.[11] Seventeen trials met the inclusion criteria of being randomized, placebo-controlled, and double-blind. However, seven could not be used in the meta-analysis because of incomplete data. None of these trials found significantly greater body weight loss in those taking chromium compared to placebo.

Data from the remaining 10 trials were pooled with the meta-analysis finding an overall significant reduction in body weight for those taking chromium picolinate compared to placebo. However, the mean difference in body weight loss was only 1.1 kg over 10-13 weeks (95% confidence interval [CI] of -1.8 to -0.4 kg). The reviewers questioned whether this was clinically significant, especially given that a 1,200 kcal/d diet achieves a mean weight loss of 0.5-0.6 kg/week.[11] A similarly small but significant reduction (-1.2%) in body fat was found and a nonsignificant effect on lean body mass.

A general concern with meta-analyses is whether significant overall findings are real or an artifact of the statistical pooling. This is of particular concern with this meta-analysis because, individually, only two trials had statistically significant results favoring chromium. One method of checking the validity of the robustness is to remove from the analysis the data from the most positive trial. When these data were removed from this chromium meta-analysis, the significant reduction in body weight and percent body fat was eliminated. Such a finding requires that the overall result of the meta-analysis be interpreted with caution.[11]

Further examination of the two trials with positive effects from chromium supplementation reveals important methodological weaknesses. In the first, 154 adults were divided into three groups and received placebo, 200 mcg, or 400 mcg chromium picolinate daily.[12] Subjects were instructed to consume "at least two servings" of a protein drink containing their assigned chromium dose. After 72 days, underwater displacement testing showed significantly reduced body fat in the chromium groups compared to placebo, but no significant difference between the two chromium groups. Mean weight

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Table 1

Increase in obesity (body mass index > 30) prevalence among U.S. adults (ages 20-74) by racial/ethnic group and gender

	Men		Women	
	Prevalence (%)		Prevalence (%)	
Racial/Ethnic Group	**1988 to 1994**	**1999 to 2000**	**1988 to 1994**	**1999 to 2000**
Black (non-Hispanic)	21.3	28.8	39.1	50.8
Mexican American	24.4	29.4	36.1	40.1
White (non-Hispanic)	20.7	27.7	23.3	30.6

Source: CDC, National Center for Health Statistics, National Health and Nutrition Examination Survey. Health, United States (Table 70) 2002.

loss difference was 1.0 kg on 200 mcg (95% CI of -2.4 to 0.4 kg) or 1.3 kg on 400 mcg (95% CI of -2.3 to -0.3 kg). Amount of drink consumed, overall diet, and exercise frequency were not controlled (whereas diet and exercise were monitored in all other studies included in the meta-analysis).

In the second positive study, the same researchers randomly assigned 130 new subjects to take capsules containing either 400 mcg chromium picolinate or placebo.[10] After 90 days, body composition was measured using dual energy X-ray absorptiometry. Changes in actual weight, percent body fat, and fat-free mass did not differ between the two groups, but the chromium group showed significantly reduced fat mass ($P = 0.023$). After statistical adjustments to control for dietary and exercise differences, significant differences were calculated for actual weight ($P < 0.001$), percent body fat ($P < 0.001$), and fat mass ($P < 0.001$). However, the significant differences were found only in calculated estimates of weight and fat loss based on energy expenditure, not the measured values. The measured mean weight loss difference was 1.1 kg (95% CI of -2.3 to 0.1 kg).

Adverse Effects

Chromium supplements are believed to be safe, with no clinical studies reporting adverse reactions. The IOM report found insufficient evidence to set an Upper Limit.[6] Rats given several thousand times the equivalent of 200 mcg/d chromium in humans showed no adverse effects.[13] However, a small number of cases of liver toxicity and other adverse effects have recently been reported.[8,14] The FDA has received several hundred adverse event reports involving chromium supplements, though most involve dietary supplements containing numerous herbs and other agents.[9]

In vitro studies have demonstrated that chromium picolinate can produce chromosomal damage in hamster ovary cells[15] and can cleave DNA in solution.[16] Although the former study used doses vastly in excess of normal physiological levels, the latter occurred within physiological ranges. Chromium picolinate's unique stability gives it good absorption, but also allows accumulation in body tissues, leading to concerns about long-term side effects.

Drug Interactions

No adverse drug interactions have been reported. However, ascorbic acid, aspirin, and indomethacin markedly increase chromium absorption, while antacids lower absorption.[5] Diets high in complex carbohydrates, not simple sugars, increase chromium absorption.[5] Potential interactions may occur with drugs affecting glucose or cholesterol levels, or with corticosteroids.[17]

Formulation

Trivalent Cr^{3+} is the natural form of chromium found almost exclusively in foods, especially brewer's yeast, liver, American cheese, cereals, and wheat germ. However, chromium content in foods is highly variable, and processing can either increase or decrease the level.[6] The search for the biologically active form of chromium led to the extraction of glucose tolerance factor (GTF) from yeast.[18] This complex contains chromium, nicotinate, and amino acids and has led to several new chromium complexes being tested for efficacy and safety. Chromium picolinate is the form most commonly used in supplements, usually 200 mcg capsules. Many products contain smaller amounts of chromium picolinate along with numerous herbs and minerals.

Conclusion

Chromium's essential role in insulin metabolism is well-established. Supplementation in chromium-deficient diabetics may offer some benefits, including improved weight management.[8] However, the majority of controlled trials of chromium picolinate as a weight-loss supplement found no significant benefit for weight loss or percent body fat reduction. A meta-analysis of these trials found a small, but statistically significant benefit. Two trials contributed heavily to this benefit and both had serious methodological weaknesses. However, both were also larger than any of the other trials. Research is lacking on the long-term effects of consuming chromium picolinate.

Recommendation

Chromium supplementation offers very little, if any,

benefit to women attempting to lose weight. Although some controversy exists over the possibility of serious harmful effects, these have not been observed in clinical trials. Diabetic patients should not take chromium without first consulting their physicians and monitoring their blood glucose closely. For those attempting to lose weight, lifestyle changes continue to offer most benefit. For example, reducing the amount of prolonged sedentary activities, especially hours watching TV, could potentially reduce the number of women with obesity by 30%.[19] Other lifestyle changes more likely to produce weight loss than dietary supplements include reducing caloric intake, increasing exercise, modifying eating behaviors, and enlisting others' support. These remain the foundations of successful weight-loss programs. ❖

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Less TV, More Exercise Are First Steps Toward Achieving Weight Loss

Source: Hu FB, et al. Television watching and other sedentary behaviors in relation to risk of obesity and type 2 diabetes mellitus in women. *JAMA* 2003;289:1785-1791.

Abstract: Current public health campaigns to reduce obesity and Type 2 diabetes have largely focused on increasing exercise, but have paid little attention to the reduction of sedentary behaviors. The authors examined the relationship between various sedentary behaviors, especially prolonged television watching, and risk of obesity and Type 2 diabetes in women. This prospective cohort study was conducted from 1992 to 1998 among women from 11 states in the Nurses' Health Study. The obesity analysis included 50,277 women who had a body mass index (BMI) of less than 30, and were free from diagnosed cardiovascular disease, diabetes, or cancer, and completed questions on physical activity and sedentary behaviors at baseline. The diabetes analysis included 68,497 women who at baseline were free from diagnosed diabetes mellitus, cardiovascular disease, or cancer. During six years of follow-up, 3,757 (7.5%) of 50,277 women who had a BMI of less than 30 in 1992 became obese (BMI 30). Overall, the researchers documented 1,515 new cases of Type 2 diabetes. Independent of exercise levels, sedentary behaviors, especially TV watching, were associated with significantly elevated risk of obesity

and Type 2 diabetes, whereas even light to moderate activity was associated with substantially lower risk. This study emphasizes the importance of reducing prolonged TV watching and other sedentary behaviors for preventing obesity and diabetes.

Source: Irwin ML, et al. Effect of exercise on total and intra-abdominal body fat in postmenopausal women: A randomized controlled trial. *JAMA* 2003;289:323-330.

Abstract: The increasing prevalence of obesity is a major public health concern. Physical activity may promote weight and body fat loss. The authors examined the effects of exercise on total and intra-abdominal body fat overall and by level of exercise in a randomized controlled trial conducted from 1997 to 2001. A total of 173 sedentary, overweight (BMI ≥ 24.0 and > 33% body fat), postmenopausal women ages 50-75 years who were living in the Seattle area. Participants were randomly assigned to an intervention consisting of exercise facility and home-based moderate-intensity exercise (n = 87) or a stretching control group (n = 86). Twelve-month data were available for 168 women. Women in the exercise group participated in moderate-intensity sports/recreational activity for a mean (SD) of 3.5 (1.2) d/wk for 176 (91) min/wk. Walking was the most frequently reported activity. Exercisers showed statistically significant differences from controls in baseline to 12-month changes in body weight (-1.4 kg; 95% confidence interval [CI], -2.5 to -0.3 kg), total body fat (-1.0%; 95% CI, -1.6% to -0.4%), intra-abdominal fat (-8.6 g/cm^2; 95% CI, -17.8 to 0.9 g/cm^2), and subcutaneous abdominal fat (-28.8 g/cm^2; 95% CI, -47.5 to -10.0 g/cm^2). A significant dose response for greater body fat loss was observed with increasing duration of exercise. Regular exercise such as brisk walking results in reduced body weight and body fat among overweight and obese postmenopausal women.

■ COMMENTS BY MARY L. HARDY, MD

Attempts to meet a major goal of Healthy People 2000 public health initiative (a prevalence of overweight adults of less than 20% of the total population) have failed and failed badly. As of 2000, the majority of Americans are overweight, with 56% reporting a body mass index (BMI) greater than 25.[1,2] Sadly, our rate of weight gain has been increasing in the last decade. Obesity, defined as a BMI greater than 30, has increased 65% from 1991 so that now 19.8% of the American population have a BMI greater than 30.[1] It has been estimated that the costs of obesity, both in financial terms as well as in development of health problems, is higher than those for either smoking or excessive drinking.[3]

Perhaps of greatest concern are the effects on our children, who are themselves alarmingly overweight and developing metabolic illnesses not previously seen in children. According to the 1999 National Health and Nutrition Examination Survey (NHANES), 13% of children and adolescents are seriously overweight and are displaying increasing rates of diseases, such as Type 2 diabetes. This bodes poorly for our children in the future. Fontaine and his group reported a loss of years of expected life related to obesity, which was higher the worse the obesity and the earlier it was present.[4] Adverse effects also were worse for blacks than whites. For young, severely obese black men (BMI > 45) this translated into 20 years of life lost.

Not only do obese patients have an increased risk of significant illnesses (including hypertension, diabetes, dyslipidemia, syndrome X, coronary artery disease, and certain cancers) and a concomitant decrease in life expectancy, they also suffer from a reduced quality of life.[5-7] The higher the degree of obesity, the greater the impairment of health-related quality of life (HLQOL); weight reduction improves HRQOL in the short term.[4]

Despite the fact that physicians are worried about the adverse effect on the health status of patients, it appears that pain may be the symptom that drives patients' immediate sense of impaired health.[8] This decrease in QOL may be even more severe in children. In fact, children and adolescents with severe obesity report a quality of life that is similar to that of children with cancer.[9] Certainly, it is neither medically desirable nor socially acceptable to be overweight. Despite the fact that millions of Americans are dieting, our population just keeps getting fatter. What's going on?

Recently much attention has been given to adverse changes in our diet, especially the increased consumption of high fructose corn syrup (236% in last 20 years), increased amounts of food consumed away from home, and increased plate and portion sizes at restaurants.[10] However, we don't always pay as much attention to the other side of the energy equation—not the increased intake of energy, but the rate of use of calories. The two articles we are examining today investigate exercise as a factor in creating and modifying obesity and its attendant risks.

Hu and associates followed a very large cohort (n = 50,277) of non-obese women from the Nurse's Health Study for more than six years. During the six years in which they were observed, 7.5% of the women became obese and 40% of these obese women developed Type 2 diabetes. Sedentary behavior was strongly correlated with an increase in both weight gain and risk of diabetes. The risk of sedentary behavior was paradoxically independent of exercise, although in women who exercised, the rate of weight gain and diabetes was less. All kinds of sedentary activities were not equivalent in their negative impact.

Watching television (TV) was most strongly negatively correlated with weight gain and risk of diabetes

and was associated with higher risk of adverse outcome than other sedentary activity at home or at work. For each 2 hr/d increase in TV watching, subjects showed a 5% increase in weight gain and 7% increase in risk of diabetes. Further, those who watched more TV were also more likely to smoke and drink alcohol and were less likely to exercise. They also took in more total calories and made less desirable food choices (higher in fat, meat, and sweets; lower in fish, vegetables, fruit, and whole grains).

The authors offered interesting comments about why TV watching was such a pernicious type of sedentary behavior. First, if you are watching TV you generally are not doing something active—thus substituting a passive for an active activity. TV watchers also tend to eat while watching TV, thus increasing calorie intake, and tend to follow a less healthy eating pattern, which has been shown to be directly related to the types of advertisement and food cues present on TV. Which one of us hasn't seen the food ads for pizza, burgers, and other fast, high-fat food aired during the dinner hour? Finally, TV watching uses even less calories than other sedentary activities, such as reading a book, sewing, or doing office work. In conclusion, the study authors felt that 30% of the obesity cases and 43% of the Type 2 diabetes cases were potentially preventable if subjects would have followed a relatively active lifestyle characterized by watching TV less than 10 hrs/wk and walking at least 30 min/d.

However, the question remains—can exercise decrease weight and modify the health risks of obesity in women? The second article, by Irwin and colleagues, examines the effect of moderate-intensity exercise on 173 sedentary, obese (mean BMI = 30.9) postmenopausal women—a group that has notorious difficulty losing weight. All of these women had significant amounts of total body fat (47.6% on average) with large stores of intra-abdominal fat (147.6 g/cm^2). Patients were randomly assigned to an exercise group (45 min of moderate-intensity exercise for 5 d/wk) or to a stretching control group (similar time).

Support for the exercise group was robust. For the first three months of this year-long trial, women were required to attend exercise classes three times per week, under the supervision of an exercise physiologist, followed by a nine-month at home program. Additional attention was given to the experimental group to ensure continued adherence to the exercise regimen, including behavior change education, phone calls, and individual meetings. Disappointingly, the total weight loss in this study of the experimental group was small (0.5 kg) and barely significantly different than the control group, which gained 0.7 kg. However, significant decreases were seen in percentage of total body fat and amount of intra-abdominal fat in the exercise group vs. the control group. Interestingly, the BMI of the groups were not significantly different at the end of the intervention, highlighting the weakness of BMI as a sole indicator of changes in obesity status.

But is the change in abdominal fat a clinically significant outcome? It probably is because not all fat is created equal when it comes to cardiovascular risk. The presence of abdominal body fat has been correlated more highly with an increased risk of heart disease and insulin resistance than fat in other locations. Likewise, intra-abdominal fat is highly active, secreting intermediary agents, such as cytokines, which promote inflammation. The Diabetes Prevention Program has reported that loss of 5% of total body weight is necessary for a decline in risk of heart disease and diabetes. But, there may be benefits to be realized by a change in distribution of body fat as well as by a decrease in total body fat. A randomized clinical trial of 120 sedentary, postmenopausal women showed that a lifestyle intervention, consisting of dietary advice, exercise training, and support, lead to healthy changes in dietary habits and significant weight loss. In addition, the weight loss was associated with a decrease in inflammatory markers, including cytokines, interleukin 6, and C reactive protein.[11] No direct measurement of intra-abdominal body fat was made, but the decrease in the hip-to-waist ratio (a surrogate measure for changes in abdominal fat) was greater in the treatment group than in the control group. Decreases also were seen in blood pressure, insulin sensitivity, and serum glucose. Serum lipids also were influenced favorably with a decrease in triglycerides and low-density lipoprotein with an increase in high-density lipoprotein. So, in fact, the change in body fat distribution reported by Irwin et al likely could represent a significant gain in health for these previously sedentary, postmenopausal women, even without a large weight loss.

How can clinicians use the research results summarized here to help patients? First, we must be willing to address the weight issues of patients. Only 42% of obese people reported that their doctor recommended weight loss when they were asked by researchers.[12] Encourage patients that even relatively small changes in weight (5% of total body mass) or decrease in inches around the waist can confer significant health benefits. Measure hip-to-waist ratios, lipids, blood pressure, insulin sensitivity, etc. so that you will be able to point to other things besides just a drop on the scale as a measure of success. Physicians also can let patients know that their quality of life will go up as their weight comes down, and for

patients who suffer from pain as a result of weight, quality of life improvement will be especially noticeable to them.

Don't just focus on the food denial message, also stress exercise as a positive intervention to aid health. Set a goal of 30 minutes most days of moderate intensity exercise. This reasonable goal should be a relief to patients who feel overwhelmed by attempting a huge change. Remind them that any increase in activity at home or at work pays off and steer them away from especially risky behavior like excessive TV watching. Increase the likelihood of a successful intervention by recommending that patients take a class, join a gym, or get a trainer for at least the first 3-4 months. Finally, for patients with children who are overweight, the emphasis on exercise, if it extends to the whole family, can be especially beneficial to the children as they are exposed to positive health choices that may last a lifetime. ❖

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1. evaluate alternative medicine and complementary therapies for women's health concerns;
2. identify risks and interactions associated with alternative therapies;
3. discuss alternative medicine options with patients; and
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CME Questions

17. Theoretically, chromium supplementation should lead to:
a. weight loss.
b. weight gain.
c. decreased muscle mass.
d. buildup of fat cells.

18. Chromium's essential role is well-established for:
a. weight loss.
b. insulin metabolism.
c. increased muscle mass.
d. Both a and b

19. A recent study examining the relationship of sedentary behaviors with obesity and Type 2 diabetes found that those who watch television:
a. had increased weight gain and higher risk of diabetes.

Answers: 17.a, 18.b, 19.d.

b. were more likely to smoke and drink alcohol.
c. took in more calories and made less desirable food choices.
d. All of the above

Integrative Medicine Service, Memorial Sloan-Kettering Cancer Center, New York

The driving force behind the Integrative Medicine Service at Memorial Sloan-Kettering Cancer Center in New York is Barrie R. Cassileth, PhD. Cassileth became interested in complementary and alternative medicine (CAM) more than 25 years ago when she was an assistant professor at the University of Pennsylvania School of Medicine and director of the university's psychosocial programs. Cassileth found that cancer patients were using a variety of CAM therapies, some more useful than others. She began to focus much of her research on complementary therapies that would reduce symptoms and improve quality of life for cancer patients and family members.

She established the Integrative Medicine Service at Memorial Sloan-Kettering in 1999 to complement mainstream medical care and to address the emotional, social, and spiritual needs of patients and families. The Service has two main focus areas: individual patients and clinical research.

Programs for Individuals

Memorial Sloan-Kettering's Integrative Medicine Service offers a variety of CAM services for individuals, including inpatient and outpatient care. Specifically, these services include:

- **Individual therapies.** The Service offers touch, mind-body, and creative therapies; acupuncture; and nutrition and herbal counseling, consultation, and education.
- **Fitness, movement, and spiritual/energy classes.** These classes can be taken in either a group or private setting. Current classes are: yoga; the Alexander Technique; Qi Gong; T'ai Chi; back in shape through movement, music, and motivation; lengthen and strengthen with Pilates Mat; chair aerobics; focus on healing; and strong bones. All therapies and classes are fee-for-service and payable by cash, check, or credit card.
- **Web-based information resources about herbs, botanicals and other products.** This web site provides information for oncologists and health care professionals, including a clinical summary for each agent and details about constituents, adverse effects, interactions, and potential benefits or problems. Evaluations of alternative or unproved cancer therapies are also provided. The site is updated continually.
- **Workshops and educational programs.** The Service offers programs for patients, caregivers, and professionals, including a range of written and consultation information about CAM, including herbs and other over-the-counter remedies, herb-drug interactions, and toxicities associated with unproved cancer therapies. In addition, the Service offers training programs for licensed massage therapists and for family members who want to learn how to provide safe and gentle massage to patients. It also offers visiting professorships and graduate student internships for health care professionals.

Research and Clinical Trials

The Integrative Medicine Service research program has two major components:

- **Quality of life studies.** Current and proposed research includes studies of acupuncture for fatigue, shortness of breath, hot flashes, nausea, and pain. The program also includes a study on music therapy for reducing depression and anxiety in patients undergoing bone marrow transplant. A project studying music therapy in the recovery room is expected to begin soon. In addition, in conjunction with the Pain and Palliative Care Service, the Service is constructing a controlled trial on massage therapy for terminally ill patients.
- **Botanical therapies.** The botanicals research program is studying several Asian herbs and combination products in preliminary laboratory trials. This research is expected to expand into clinical trials.

Both components of research are conducted in collaboration with senior laboratory and clinical scientists at Memorial Sloan-Kettering Cancer Center and the Sloan-Kettering Institute. The Service has received 15 grants to study the benefits of various CAM therapies and to investigate botanicals that may have anti-tumor effects.

In Future Issues:

Acupuncture and Labor

Biofeedback and Pelvic Exercises for Incontinence