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One of the goals of integrative medicine is to provide clinicians with practical and reliable information so that they are able to offer each individual clear guidelines to improve patient health outcomes. This integrative approach also emphasizes treatment modalities to improve a patient's overall health and well-being that are the least invasive, least toxic, and least costly.¹ With this method in mind, we present nutrition-food, mind-body, and exercise interventions that focus on diet and lifestyle modifications as the first line of treatment in order to prevent and/or treat a specific disease state.

Diabetes and Chromium

Diabetes Overview

UW HEALTH

In this issue, we present recent clinical research on Diabetes mellitus Type 2 (DM) with a particular focus on chromium supplementation. This integrative approach is particularly pertinent when patients present with a recent DM diagnosis. A wide range of integrative modalities exists to improve a recently diagnosed DM patient. We have elected to present current data on chromium supplementation as one of many possible adjuvant therapies. Although there is no Recommended Daily Allowance for chromium, recent research suggests that it is an essential nutrient that potentiates insulin action and therefore influences carbohydrate, lipid, and protein metabolism.²

PREVALENCE AND TREAMENT

Diabetes is a worldwide epidemic that is especially prevalent in India, China, and the United States.³ Within the US, diabetes is one of the most common chronic diseases with more than 7% of the adult population affected. It is even more common in the elderly, Latino, African-American, Asian and Pacific Island-American, and Native-American populations.⁴ The cornerstone of diabetes management therapy consists of introducing a regular exercise routine along with a diet that emphasizes increased consumption of complex carbohydrates, and a reduced consumption of saturated and trans-fatty acids.^{5,6,7,8,9, 10, 11, 12, 13}

ADJUVANT TREATMENTS

Along with diet and exercise regimes, there are a wide range of adjuvant integrative therapies based on nutrients alone. In addition to chromium, research demonstrates that many nutrients exhibit possible beneficial effects for the treatment of different stages of diabetes. These nutrients include biotin, carnitine, coenzyme Q10, essential fatty acids, inositol hexaniacinate, alpha-lipoic acid, magnesium, manganese, n-acetyl cysteine, vanadyl sulfate, vitamin B12, vitamin B6, vitamin C, vitamin E, and vitamin K. In addition, individual plants, traditional plant formulations, and single phytonutrients increase the number of treatment options available to the practitioner. For this issue, however, our focus is on chromium.

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Chromium Status

There is not a specific biochemical measure of chromium status. Chromium concentrations in tissues are 10 to 100 times higher than those in blood. Tissue stores are not in equilibrium with blood stores so a change in fasting plasma or serum chromium is not a good indicator of slight changes in chromium levels. Serum chromium levels are generally an indicator of excessive exposure to chromium. Hair chromium levels may reflect endogenous chromium levels but analysis is confounded due to environmental exposures such as hair bleach or dyes. It appears that urinary chromium excretion is indicative of excessive chromium status also.14 Chromium serum and urinary levels help diagnose an excess of chromium but there is no reliable test to detect a deficiency.

Chromium Function

According to Higdin at the Linus Pauling Institute, a biologically active form of chromium participates in glucose metabolism by enhancing the effects of insulin. The precise structure of the biologically active form of chromium is not known. Researchers hypothesize that a low-molecularweight chromium-binding substance (LMWCr) may enhance the response of the insulin receptor to insulin. It is thought that the inactive form of the insulin receptor is converted to the active form by binding insulin. The binding of insulin by the insulin receptor then stimulates the movement of chromium into the cell and results in binding of chromium to apoLMWCr, a form of the LMWCr that lacks chromium. Once it binds chromium, the LMWCr binds to the insulin receptor and enhances its activity. The ability of the LMWCr to activate the insulin receptor is dependent on its chromium content. When insulin

levels drop due to normalization of blood glucose levels, the LMWCr may be released from the cell in order to terminate its effects.¹⁵ Chromium appears to increase insulin receptor sensitivity.

Chromium Studies

Individuals with DM have been found to have higher rates of urinary chromium loss than healthy individuals, especially those with diabetes of more than 2 years duration.¹⁶ Prior to 1997, well-designed studies of chromium supplementation in individuals with DM showed no improvement in blood glucose control, though they provided some evidence of reduced insulin levels and improved blood lipid profiles.17 The following more recent human clinical studies (three randomized controlled clinical studies, one clinical study) demonstrate the possible benefits of introducing chromium supplementation above the adequate intake levels. These studies are now presented.

In this first randomized controlled trial, individuals being treated for DM (180 men and women) were divided randomly into three groups and supplemented with a placebo, 1.92 micromol (100 µg BID or 200 μ g/d) Cr as chromium picolinate two times per day, or 9.6 micromol (500 µg BID or 1000 µg/d) Cr two times per day. Subjects continued to take their normal medications and were instructed not to change their normal eating and living habits. HbA1c values improved significantly after 2 months in the group receiving 19.2 pmol (1,000 µg) Cr per day and was lower in both chromium groups after 4 months. Fasting glucose was lower in the 19.2-µmol group after 2 and 4 months. Two-hour glucose values were also significantly lower for the subjects consuming 19.2 µmol supplemental Cr after both 2 and 4 months. Fasting and 2-h insulin values decreased

significantly in both groups receiving supplemental chromium after 2 and 4 months. Plasma total cholesterol also decreased after 4 months in the subjects receiving 19.2 mol/day Cr. Supplemental chromium had significant beneficial effects on HbA1c, glucose, insulin, and cholesterol variables in subjects with DM. The beneficial effects of chromium in individuals with diabetes were observed at levels higher than the upper limit of the Estimated Safe and Adequate Daily Dietary Intake. **Daily effective dose: 200 µg/day chromium.**¹⁸

In the second randomized controlled clinical trial, the effects of supplementation with organic and inorganic chromium on glucose tolerance, serum lipids, and drug dosage in DM patients were studied. Seventy eight DM patients were divided randomly into two groups and given Brewer's yeast (23.3 µg Cr/d), and CrCl3 (200 µg Cr/d) sequentially with placebo in between, in a double blind cross-over design of four stages, each lasting 8 weeks. Both supplements caused a significant decrease in the means of glucose, fructosamine, and triglycerides. The means of HDL-cholesterol, and serum and urinary chromium were all increased. The mean drug dosage decreased slightly (and significantly in the case of Glibenclamide-an oral sulphonylurea hypoglycemic agent) after both supplements, patients no longer required insulin. No change was noted in dietary intakes or Body Mass Index. A higher percentage of subjects responded positively to Brewer's yeast chromium, which was retained more by the body, with effects on fructosamine, triglycerides, and HDL-cholesterol maintained in some subjects when placebo followed it, and mean urinary chromium remaining significantly higher than zero. The authors concluded that chromium supplementation gives better control

of glucose and lipid variables while decreasing drug dosage in DM patients. Daily effective dose: 23.3 µg Cr/d (brewers yeast) or 200 µg/d chromium.¹⁹

The aim of this clinical study was to determine the effects of combined zinc and chromium supplementation on oxidative stress and glucose homeostasis of people with DM. Adult subjects with HbA1c > 7.5%were supplemented for 6 months with 30 mg/day of zinc gluconate or 400 µg/day of chromium pidolate (tris(2-pyrrolidine-5-carboxylato) chromium III) or combined zinc/ chromium supplementation of placebo. Although no significant change was noted in HbA1c, these data suggest the potential beneficial antioxidant effects of the individual and combined supplementation of Zn and Cr in people with DM. These results are particularly important in light of the deleterious consequences of oxidative stress in people with diabetes. Daily effective dose: 30 mg/day zinc and/ or 400 µg/d chromium.²⁰

In a third randomized controlled trial to determine the effects of chromium supplementation on oxidative stress of DM and euglycemic (EU) subjects, adults having HbA1c values of <6.0% (EU), 6.8-8.5% (mildly hyperglycemic, MH), and >8.5% (severely hyperglycemic, SH) were supplemented for 6 months with 1000 µq/day of Cr (as Cr yeast) or with a placebo. The data results suggest that Cr supplementation was an effective treatment strategy to minimize increased oxidative stress in DM patients whose HbA1c level was >8.5%, and the Cr in EU groups might act as a pro-oxidant. Daily effective dose: 1000 μ g/d chromium for those with HbA1c values > 8.5%.²¹

Conclusions

Overall the three randomized controlled trials and one clinical study completed since 2000 demonstrated the potential blood glucose-lowering effect of chromium supplementation. A recently diagnosed DM patient has several lifestyle options in order to improve his or her health. The importance of diet and exercise modification to help control diabetes can not be emphasized enough. Evaluating chromium levels in a recently diagnosed DM patient may be a practical and sound starting point. In the above trials the chromium dosage ranged from 23.3 to 1000 µg/day. In some instances elevated doses in euglycemic individuals lead to a possible pro-oxidant effect. To determine the proper dosage, the health care practitioner needs to assess the daily chromium intake from dietary sources for their DM patients. Once this level is evaluated, dietary modifications to increase certain foods high in chromium should be encouraged, especially whole grains. In conjunction with these changes, supplemental chromium may be advised with a dosage range from 25-400 µg/day.

Clinical Steps

- Assess chromium levels based on 24-hour food recall or request a food diary. A food diary allows the patient to asses at the end of each day their dietary intake, and provides the physician or nutritionist with a concrete dietary regimen to assess chromium level intake.
- 2. Encourage patients to eat foods rich in chromium such as whole grain cereals, broccoli, and grapes.
- 3. Assess patient glycemic values at next visit (HbA1c, lipids). If patient has difficulty in controlling blood sugar or evidence of the

metabolic syndrome, chromium supplementation may enhance insulin receptor sensitivity while also improving the lipid profile.

 Advise chromium picolinate or chromium nicotinate supplementation between 200-400 µg/d, if the diet is low in chromium-rich foods and blood sugars are difficult to control.

Types of Chromium

Chromium (III) is available as a supplement in several forms: chromium chloride, chromium nicotinate, chromium picolinate, and highchromium yeast. They are available as stand-alone supplements or in combination products.²² Chromium nicotinate and chromium picolinate may be more bioavailable than chromium chloride.23, 24 A more recent formulation, in development by scientists with USDA's Agricultural Research Service (ARS), is a complex of chromium and the amino acid histidine. It is absorbed at least 50 percent better than chromium picolinate, according to chromium researcher and developer, Richard Anderson, with ARS' Beltsville (MD) Human Nutrition Research Center.²⁵ Although this formulation is not yet available on the market, clinicians may find it useful in the future.

The Food and Nutrition Board has set an Adequate Intake level based on chromium content in normal diets. For adults (19-50 years) females require 25 μ g/day and males require 35 μ g/day; for adults (> 51 years) females require 20 μ g/day and males require 30 μ g/ day.²⁶

The amount of chromium found in food sources varies. Furthermore, there is no single large database on chromium content in food. Processed meats, whole grains products, bran cereals, green beans, broccoli, and spices tend to be relatively high in chromium. Overly processed foods that are high in simple sugars such as sucrose and fructose are not only low in chromium but have been found to promote chromium loss.²⁷

Cereals, particularly bran cereals, are among the top sources of chromium, according to state-of-the art analyses of 40 foods. Of the seven cereals analyzed, five contained between 10 and 20 percent of the minimum suggested chromium intake in a one- or twoounce serving. But a slice of whole wheat bread or an ounce of toasted wheat bran provides only about one percent of the minimum, suggesting that much of the chromium in foods is contributed by other factors and is not intrinsic to the food itself. The high levels in cereals are probably inadvertently added during fortification with other minerals or vitamins.

Chromium also may be introduced as a result of processing or handling. For example, one cup of canned mushrooms had more than 10 percent of the suggested minimum chromium intake, as did one teaspoon of cocoa powder. But chocolate syrup had only half as much per serving. Canned whole tomatoes and pineapple slices scored highest in chromium content in this study, with one cup providing 33 to 43 percent of the minimum suggested intake. Many canned and processed foods are prepared in stainless steel vessels, which have a high chromium content. This appears to be a case of good contamination because the body can convert inorganic chromium to a usable form. 28

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Food	Serving	Chromium (mcg)
Broccoli	1/2 cup	11.0
Turkey ham (processed)	3 ounces	10.4
Grape juice	8 fl. ounces	7.5
Waffle	1 (~2.5 ounces)	6.7
English muffin	1	3.6
Potatoes	1 cup, mashed	2.7
Bagel	1	2.5
Orange juice	8 fl. ounces	2.2
Beef	3 ounces	2.0
Turkey breast	3 ounces	1.7
Apple w/ peel	1 medium	1.4
Green beans	1/2 cup	1.1
Banana	1 medium	1.0

Because chromium content in different batches of the same food has been found to vary significantly, the information in the table should serve only as a guide to the chromium content of foods.²⁹

A Role for Mindfulness? PREVENTION AND MANAGEMENT OF DIABETES

Mindfulness intervention studies on diabetes are limited in general. Although there are numerous studies that investigate the role of stress reduction or relaxation training on glycemic control, the results are inconsistent. Many studies demonstrate that stress reduction training is able to improve patient mood. Interestingly, a subset of these studies provides evidence that stress reduction training may improve diabetic control.

Stress has been associated with poor glycemic control.¹ Stress negatively affects mood which can disrupt an effective self-care regimen. Stress can also stimulate insulin antagonists,^{2,3} thereby disrupting blood glucose stability. The introduction and training of stress reduction techniques, such as Mindfulness-Based Stress Reduction (MBSR), may help individuals better manage diabetes.

For example, a recent review of methodological issues related to studying stress and metabolic control in diabetes concluded that the "strength and direction of the relationship between stress and blood glucose control varies considerably between individuals."4 There are a variety of differences among individuals that may account for this conclusion, including psychological variables. Another recent study reported that cognitive distortions were associated with higher stress levels, less adherent self-management behavior, and poorer glycemic control.⁵ Mindfulness-Based Cognitive Therapy (MBCT), a variant of MBSR, reduces cognitive distortions in depressed patients. Among a particular

subgroup of patients (e.g., those with higher levels of cognitive distortions), it appears that stress reduction and mindfulness training may improve health outcomes related to glycemic control.⁶

To demonstrate the possible link between stress reduction and glycemic control, a recent study found that chronic stress increased the incidence of diabetes in genetically vulnerable rats⁷ while another study suggested that stress-induced production of proinflammatory cytokines represents one possible mechanism.⁸ These data imply that reducing acute and/or chronic stress can decrease the incidence of diabetes in genetically vulnerable individuals, though longitudinal research studies designed to test this possibility are clearly needed. Since MBSR has been proven effective in reducing stress and improving mood across a variety of studies.^{9, 10, 11} and has also been shown to reduce the inflammatory process associated with psoriasis,¹² MBSR may be useful for glycemic control.

Among a subset of patients suffering with DM, MBSR training may prove beneficial by providing a practical tool to reduce stress. Once an individual is able to better manage stress, better glycemic control may just follow.

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Clinical Pearl

Stress worsens blood sugar control but more importantly, the number of cognitive distortions (chaotic noncentered thought) is related to both stress and abnormal blood sugar.

A Gentle Yet Effective Therapy

Yoga is a practice that developed and expanded in the South Asian sub-continent where many schools and traditions exist. Some of these yoga traditions have spread to other parts of the world and continued to develop especially in the United States. According to basic yoga philosophy, yoga practice includes eight distinct stages. In most yoga classes two stages, in particular, are taught and practiced: asanas (physical postures) and pranayama (breath expansion).

Asanas are a series of physical postures to improve flexibility of body and mind. Pranayama is usually reserved for the end of a class to facilitate a more relaxed state of mind in order to prepare for meditation. Recent medical research on the efficacy of a daily yoga practice has demonstrated beneficial effect for a wide range of ailments such as psychopathological (depression, anxiety), cardiovascular (hypertension, heart disease), respiratory (asthma), diabetes, and a variety of others.¹ We present the results of a study that tested the efficacy of daily yoga practice that included asanas and pranayama for patients with Non-insulin Dependent Diabetes *mellitus* (NIDDM).

Twenty-four patients (30-60 years) with NIDDM underwent yoga training in a particular sequence for 30-40 min/day for 40 days. At baseline, the patients were on antihyperglycemic and dietary regimens. After 40 days of yoga training, results indicate that there was a significant decrease in fasting blood glucose levels from basal 190.08 +/- 18.54 in mg/dl to 141.5 +/- 16.3 in mg/dl. The post prandial blood glucose levels decreased from 276.54 +/- 20.62 in mg/dl to 201.75 +/- 21.24 in mg/dl, glycosylated hemoglobin showed a decrease from 9.03 +/- 0.29% to 7.83 +/- 0.53%. The pulse rate, systolic and diastolic blood pressure decreased



significantly. In this small sample these findings suggest that better glycemic control and stable autonomic functions can be obtained in NIDDM patients with yoga training. The exact mechanism as to how these postures and controlled breathing exercise interact with somato-neuro-endocrine mechanism remains to be worked out.² Based on this small study, an adjuvant yoga practice may be a practical option for those NIDDM patients on antihyperglycemic and dietary regimes who prefer a more gentle yet effective exercise routine.

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RESEARCH

BEYOND THE BOX

Rísing Anger: Rísing Fats and Sugars ANGER, AND PLASMA LIPID, LIPOPROTEIN, AND GLUCOSE LEVELS IN HEALTHY WOMEN

Siegman AW, Malkin AR, Boyle S, Vaitkus M, Barko W, Franco E., University of Maryland, Baltimore County, USA. Anger, and plasma lipid, lipoprotein, and glucose levels in healthy women: the mediating role of physical fitness. J Behav Med. 2002 Feb;25(1):1-16.

SUMMARY:

A study of 103 healthy middle aged women showed a correlation between the outward expression of anger and elevations of serum glucose, total cholesterol, LDL cholesterol, and triglyceride levels. This correlation was apparent only in physically unfit women. Those women, who had high scores in the expression of anger but were physically fit, did not have the same rise in these serum markers.

The moral of the study: If you are angry, go for a jog!

Or as Martin Luther King Jr. said, "I have decided to stick with love. Hate is too great a burden to bear."

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A ROLE FOR MINDFULNESS

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