

The Role of the Optimal Healing Environment in the Care of Patients with Diabetes Mellitus Type II

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ABSTRACT

An optimal healing environment (OHE) can include both general and specific physical, medical, behavioral, psychological, social and spiritual components. Type 2 diabetes mellitus, primarily a disease of lifestyle, provides an excellent opportunity to investigate the potential impact of this broader model of care on a chronic illness. This paper proposes a strategy for studying the application of the OHE model to the care of patients with type 2 diabetes. It provides a brief review of the current literature on prevention of type 2 diabetes in patients at high risk, and then discusses the evidence for and against a variety of interventions for established diabetes mellitus including nutritional, herbal, mind-body and exercise strategies. The essential elements of a protocol for an integrative medicine or OHE approach to diabetes are then outlined, followed by a discussion of the research issues that would emerge from an effort to test the effectiveness of such an approach.

BACKGROUND/STATEMENT OF THE PROBLEM

Diabetes mellitus is currently the number one cause of blindness, end-stage kidney failure, and circulatory problems leading to amputation in the United States.¹ Type 2 diabetes mellitus, once referred to as non-insulin-dependent or adult-onset, is present in approximately 16 million persons in the United States.² Its incidence is increasing rapidly concurrent with the epidemic of obesity in this country, which contributes to insulin resistance, and has approximately tripled over the past three decades. Even more alarming is the steady demographic shift in type 2 diabetes to younger populations in whom the incidence of diabetes has increased almost 40% for those under 50 years of age and almost 70% for those under 40.² This earlier age at onset allows for a much longer duration of illness in a large segment of the diabetic population, with an associated increased probability of comorbidities such as coronary artery disease, cerebrovascular disease, and renal failure, also of great concern.

THE OPTIMAL HEALING ENVIRONMENT FOR PATIENTS WITH DIABETES

Jonas et al.³ have defined the optimal healing environment (OHE). Type 2 diabetes is primarily a disease of lifestyle, and thus provides an excellent opportunity to investigate the potential impact of this broader model of care on a chronic illness. This paper proposes a strategy for studying the application of the OHE model to the care of patients with type 2 diabetes.

Relevant research to date

Most research on the treatment of type 2 diabetes has focused on the use of pharmaceutical agents including oral hypoglycemic agents, angiotensin-converting enzyme (ACE) inhibitors, and insulin. Oral agents, insulin, and both in combination are effective in reducing hyperglycemia and in preventing or delaying the onset of complications of diabetes. A small reduction in hemoglobin A_{1c} (HgbA_{1c}) of less than 1% has been clearly associated with improvement in outcomes, including a reduced incidence of microvascular com-

plications. This occurs regardless of whether this reduction is due to pharmaceutical agents or lifestyle change.⁴ ACE inhibitors reduce the likelihood of progression from microalbuminuria to renal failure in diabetics.⁵

There are considerable epidemiologic data on risk factors for type 2 diabetes, and at least three large-scale trials of lifestyle-oriented approaches to prevention as discussed below. There is surprisingly little well-done published research on the effectiveness of lifestyle intervention, dietary modification, exercise, and weight loss for treatment of established diabetes. The published research on complementary and alternative approaches to diabetes, mind-body therapies, nutritional supplements, botanical medicines, and traditional therapies is scanty and does not usually provide adequate follow-up data. There are a number of small published trials of specific nutritional, botanical, and mind-body interventions for diabetes that may help define the important components of the OHE for this condition.

Risk factors for type 2 diabetes are now well defined and include obesity (body-mass index [BMI] over 25), family history of diabetes, lack of physical activity, poor diet (excessive calories, low fiber intake, high intake of saturated and trans fats, high glycemic load, high glycemic index), cigarette smoking, and abstinence from alcohol consumption.^{6,7} These risk factors often manifest as impaired glucose tolerance prior to the development of frank diabetes in those at high risk for the disease.

The Finnish trial is the most important study of lifestyle-oriented prevention trials. This intervention consisted of individualized counseling aimed at weight reduction, reduction of total fat and saturated fat intake, increased intake of fiber, and increased physical activity studied in a cohort of 522 subjects with impaired glucose tolerance. At 4 years of follow-up, the cumulative incidence of diabetes in the intervention group was 11% versus 23% in the control group, a 58%-reduction in risk. Average weight loss in persons with a mean of BMI of 31 in the intervention group in the first 2 years was only 3.5 kg. This suggests that even modest weight loss can have a substantial impact on diabetes risk.⁸ Earlier nonrandomized studies of similar interventions in high-risk populations in China⁹ and Sweden¹⁰ found similarly decreased incidences of new-onset diabetes.

The Finnish trial model may be particularly useful for the OHE project, because the interventions were relatively modest, consisting of seven sessions with a nutritionist during the first year, and one session every 3 months thereafter, as well as individualized guidance on how to increase physical activity (Table 1). It is not known if the results of this trial might have been even more impressive if other dimensions of the OHE such as family and community support, mind-body or spiritual practices, and active focus on the therapeutic relationship with a provider of care had been incorporated into the model. At this writing, not even the "conventional" lifestyle interventions of this prevention trial have

TABLE 1. ELEMENTS OF LIFESTYLE INTERVENTION IN THE FINNISH DIABETES PREVENTION STUDY

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- Total fat intake < 30% of total energy
 - Saturated fat < 10% of total energy
 - Fiber intake > 15g per 100 kcal
 - Moderate exercise for at least 30 minutes per day
 - Frequent ingestion of whole grain products, vegetables, fruits, low-fat milk and meat products, soft margarines and vegetable oils rich in monounsaturated fats
-

been adequately tested in a treatment trial of patients with established disease.

Group versus individual care

The concept of group care is a new approach gaining popularity in diabetes care. This approach addresses issues of community and social support and of adherence to a trial protocol, and may be particularly relevant to the implementation of the OHE approach to diabetes care. Researchers in Italy have recently shown that the use of interactive group visits for following lifestyle intervention in patients with diabetes is more effective, and not significantly more expensive, than individual care.¹¹ This study followed participants for an average of 51 months and found interactive group care resulted in significantly better outcomes in terms of sustained changes in BMI, glycosylated hemoglobin, quality of life, and dosages of hypoglycemic agents compared to traditional individual diabetes care.

Specific nutritional interventions

Specific dietary interventions that have been studied for treatment of established diabetes include low glycemic index (LGI) diet,^{12,13} increased fiber intake,^{14–18} magnesium supplementation,¹⁵ chromium supplementation,^{16–20} and soy supplementation.¹⁷ Although clear evidence of an impact on long-term morbidity and complications is lacking for all of these, preliminary evidence suggests they all may have a role in a nutritional approach to the treatment of diabetes. Increased intake of whole grains versus refined grains may also be an important intervention, although this has not been studied prospectively in established disease.^{18,19}

Botanical medicines

A number of botanical medicines have been tested for their role in the treatment of diabetes. Herbs that appear promising include American ginseng (*Panax quinquefolius*),^{20,21} fenugreek (*Trigonella foenum-graecum*),²² and gymnema (*Gymnema sylvestre*).²³ All have significantly lowered HbA_{1c} in at least some studies. Bilberry (*Vaccinium myrtillus*), an herb rich in anthocyanoside flavonoid antioxidants, may have a role in preventing progression of diabetic retinopathy.^{7,8,24}

Exercise

Lack of exercise is clearly established as a risk factor for development of diabetes in susceptible individuals.⁷ The Finnish, Chinese, and Swedish intervention/prevention trials all included exercise as a critical component. In the Finnish trial, achieving the target of 4 hours of moderate physical activity per week was associated with a significant decrease in risk of diabetes even in those patients who were not successful in losing weight.⁸ Similarly, a meta-analysis of 14 studies evaluating the impact of exercise on established diabetes found that exercise resulted in a significant decrease in HgbA_{1c} from 8.3% to 7.6%, even without a significant decrease in BMI.²⁸

Mind–body interventions

Although the impact of stress on the hypothalamus–pituitary axis, cortisol production, and neuroendocrine signaling is well established, this has not been the case in the sketchy and equivocal literature on the connection between mind–body therapies for stress reduction and glycemic control in type 2 diabetes. Small studies of relaxation training, some with electromyography biofeedback,^{26,27} and of cognitive–behavioral therapy²⁸ have thus far failed to establish a significant impact on glycemic control despite a demonstrable positive effect on anxiety level. One noncontrolled study of yoga for people with diabetes ($n = 149$) did demonstrate a significant improvement in hyperglycemia in response to oral glucose challenge after 40 days of yoga therapy.²⁹ *Qigong* training has also shown promise.³⁰

Despite this lack of evidence, designing an OHE for diabetes care would benefit from a mind–body therapy component. It should be tailored more toward overall experience of wellness and management of habit change as opposed to glycemic control *per se*.

DESCRIBING THE OHE FOR DIABETES

Best-case series

The best-case series approach might be an effective first strategy in developing a model of the OHE for diabetes. This approach would select approximately 100 patients who have successfully managed excellent control of diabetes, and survey them regarding what dimensions of their lives have been most important in facilitating that control. Patients could be recruited from a wide spectrum of settings such as conventional private practices, integrative medicine settings and hospital based clinic settings to provide the most widely generalizable set of data on potentially effective interventions. The survey tool would need to be constructed as amenable to qualitative analysis to capture information on the specific types of family and community support, spiritual practice, personal beliefs, provider relationships, and workplace fac-

tors that might bear on the person's experience. The data from this analysis would then be used to design an OHE protocol with the set of multidimensional, lifestyle-oriented interventions most likely to be effective in the real-life treatment of this condition.

The following brief descriptions illustrate how a best-case series might inform the design of a prospective trial of the OHE for diabetes:

JM, a 45-year-old man with a history of ankylosing spondylitis and in recovery from substance abuse, was diagnosed 18 months ago with type 2 diabetes and an HgbA_{1c} of 8.4%. Over the subsequent 6 months, JM saw an integrative nutritionist 4 times, and was able to significantly revise his diet and increase his exercise. His HgbA_{1c} lowered to 6.2%. He attributed his successful lifestyle change to a marked increase in the frequency of his sessions with his Buddhist prayer group to 4–5 times weekly. He felt that this change, combined with revisiting the spiritual/psychologic process of his recovery from cocaine addiction, had provided the “centered-ness” required to change his lifestyle.

LR, a 60-year-old retired bus driver, with history of mild hypertension and significant obesity, was diagnosed with type 2 diabetes 15 months ago, HgbA_{1c} 8.1%. He declined nutrition consultation, and opted to educate himself on the Internet regarding LGI diet weight loss options. He proceeded to lose 75 pounds over the 6 months after his diagnosis, lowering his HgbA_{1c} to 6.4%. He attributes his success to his partnership with his wife and his decision to “do this on his own.”

Neither of these patients' success was the result of a “medical” intervention. In one, it was because of a renewal of a spiritual practice, and in the other to a unique quality of the family constellation and the patient's personal style and orientation. In both, the most important factors in the treatment would not have been identified without a specific inquiry into the question of what dimensions of the larger “healing environment” were most influential.

BASIC ELEMENTS OF A PROTOCOL FOR ASSESSING THE OHE FOR DIABETES

Separate from a “best case series,” it is possible to propose a number of components for an OHE-oriented research protocol for this disease based on published research and on the current working definition of the OHE. Such a protocol would assume that up-to-date, high-quality conventional care is already being provided, and that management of pharmaceuticals, weight loss counseling, and access to exercise

counseling and facilities are already available to the patients. The following would be considered integral components of this approach:

1. A collaborative, healing relationship between the patient and the primary provider of care; this relationship could be examined in the setting of group care, individual care, or both
2. An integration of the patient's family and/or social support network into the treatment program
3. An intervention (mind-body and/or "energy practice"-oriented) that will facilitate the patient's belief in their ability to "heal" in this area and to succeed with lifestyle change
4. Dietary intervention, including regular meetings with a nutrition educator during the course of the study; family members involved in food purchasing and preparation should be included in the nutritional counseling intervention
5. Group involvement of some sort, whether in the "group care" model described above or through participation in a support group; this group portion of the protocol allows the patients' families to be explicitly brought into the OHE.

A number of other interventions could be included in the design of the OHE, although extensive research to date to support these is not available. These interventions might include nutritional supplementation with chromium, magnesium, soy, and a fiber supplement, and the possible use of botanical medicines including gymnema, fenugreek, American ginseng, and/or bilberry. However, introduction of herbals into a protocol introduces significant complexity because of issues of product purity and consistency and the potential for herb-drug interactions in patients on medication.

It is tempting to consider the use of a traditional system of care such as Chinese medicine or Ayurvedic medicine. However given that each entails its own program of dietary change, exercise and herbal medicines, they might be better studied unto themselves as "OHEs." In addition, the question of applying a traditional healing system as a model of an OHE has not been systematically assessed. In a review of the literature on Ayurvedic approaches to diabetes, for example, the RAND Foundation concluded that although there are a number of published trials of herbal and other interventions for diabetes from the Ayurvedic tradition, there are no trials that examine Ayurveda as a systematic, holistic multimodal healing approach to this condition. This fact hinders the assessment of efficacy.³¹

Another approach is to test the importance of an "integrator" of care in the OHE model. That is, a health care provider/partner for the patient with specific training in how to facilitate healing and the OHE approach. This person need not, and perhaps should not, be a physician. A nursing pro-

fessional, a health educator, or a nutritionist could potentially fill this role as well as a physician at a significantly lower cost. If a protocol was designed to deliver care in group settings, the training for the professionals in these "integrator" roles could be standardized to provide all with an in-depth understanding of the OHE concept, and with the core skills to implement it in their setting. This approach could be compared to a group in which the primary locus of care is in individualized interaction between patients and study physicians where the impact of the healing relationship is subject to variability based on the styles and/or skills of the participating practitioners. The importance of the therapeutic alliance between patient and provider of care, and of finding ways to describe and measure this, cannot be overemphasized in the research design, as this is integral to enhancing the patient's empowerment in handling their health issues.

An area that needs investigation is the question of whether mind-body approaches such as hypnotherapy, biofeedback, visualization, and others actually can be used to successfully facilitate long-term lifestyle change as is required in the treatment of diabetes. There are very few published data on this question; preliminary data are suggestive of the potential for such a role, especially for hypnotherapy.^{32,33} Because the OHE approach requires lifestyle change as a key component of the treatment of almost every condition, research on this question would be relevant not only for the treatment of diabetes, but also for cardiovascular disease, pain conditions, digestive disorders, and many other chronic conditions.

INCLUSION/EXCLUSION CRITERIA

Study participants should meet the current criteria for the diagnosis of type 2 diabetes. Those with significant comorbidities, such as advanced coronary artery disease, renal disease, or other chronic diseases making survival for 4 or more years unlikely, would be excluded. Those patients with other conditions that would preclude an ability to actively participate in the program, such as significant psychiatric illness, would also be excluded.

In addition, given the level of patient participation and active involvement that an OHE protocol would require, investigators might choose to develop a measure of patient "hardiness"³² as a criterion for inclusion in the study. Without some baseline assessment of this quality in potential study participants prior to randomization, it is possible that a high dropout rate would affect the study conclusions. Alternatively, the OHE intervention could be designed to provide support to enhance the "hardiness" of those lacking this quality at baseline to prevent a high dropout rate. Either way, some baseline measure of this quality will be important in order to allow later interpretation of which populations of patients might benefit from this type of OHE intervention.

It may also be possible to use such a baseline measure to stratify for this quality of “hardiness” in the final analysis.

RESEARCH DESIGN/ANALYSIS ISSUES

The design and analysis for this study must incorporate both quantitative and qualitative dimensions in order to capture the diverse potential outcomes of a multifaceted OHE-type of intervention. Some of the outcomes, such as improvement in glycosylated hemoglobin or a decrease in BMI, will be readily captured in a quantitative analysis. Others such as the impact of the healing relationship between patient and provider, or the success of a mind–body or energy intervention in promoting intention, self-awareness, and wholeness in subjects, will be impossible to describe accurately with only quantitative measures. Miller et al.³³ have proposed a double-helix trial design for the study of the impact of healing relationships in which a qualitative and a quantitative analysis are intertwined in the study protocol. Such a nested qualitative approach may be useful here, as well as in studies of the impact of the OHE on other disease conditions. It is important to note that many experienced medical investigators lack experience or expertise in qualitative analyses, and successful implementation of a qualitative analysis may require coinvestigators in sociology, psychology, and nursing for collaboration in study design.

The study should be randomized and controlled, although blinding either of investigators or of participants is not impossible in this type of approach. The control group could be provided with standard nutrition (American Diabetic Association diet), an exercise program and conventional medical care.

A long duration of follow-up is essential. The dual questions of whether a complex lifestyle-oriented healing intervention will be successful in controlling diabetes, and of whether such an approach will lead to durable change, will need to be addressed in the study design. An intervention that is successful in the short term, but not sustainable will not be a significant contribution to the field at this point. At minimum, detailed follow-up should continue for at least 1 year, and ideally for 2. Maintenance of BMI changes should ideally continue for 3 to 5 years. This need for sustained follow-up will pose one of the largest challenges to investigators given the cost of maintaining study infrastructure over such a long period.

It will be important to find ways in the research design to incorporate an adequate description of the influence of family and social support, spiritual practice, the physical environment of the home, and the workplace environment on the experience of the patient in adapting to his or her condition. It will probably not be possible to design an intervention to actively incorporate all of these diverse influences on health, but information regarding how these domains of the OHE influence for better or worse the patients ability to

eat properly, to exercise, to cultivate a positive attitude and to monitor blood sugar effectively are pertinent to the conclusions related to the outcomes of the project.

OUTCOME VARIABLES: QUANTITATIVE ANALYSIS

There is a set of well-established and defined physiologic markers that should comprise one dimension of the quantitative outcome assessment for this program. Glycosylated hemoglobin and measure of fasting glucose and 24-hour euglycemia would be the primary objective outcome measures. Other outcome measures that could be considered include:

- Weight/BMI
- Fasting insulin
- Area under insulin curve (24 hours)
- Lipid profiles, including high-density lipoprotein (HDL), low-density lipoprotein (LDL), very low-density lipoprotein (VLDL), triglycerides
- Dosage of hypoglycemic medications
- Progression of retinopathy as measured on ophthalmologic examination
- Changes in blood pressure
- Progression of renal disease/microalbuminuria.

A quality-of-life measure such as the Short-Form-36 should be included as part of the analysis, as could quality-of-life instruments more specifically aimed at patients with diabetes as well.

OUTCOME VARIABLES: QUALITATIVE ANALYSIS

A number of dimensions of the patients’ experiences of healing in this study require a qualitative approach to analysis. The experiences of the providers also are an integral part of the quality of the OHE experience and will need to be assessed. Periodic interviews with care providers during the course of the study could be analyzed for recurrent themes using a qualitative approach to obtain on how providers experience this type of care process and on what type of training might more effectively prepare them for delivering care in the OHE model.

Similarly, some measure of the degree to which the providers of care in this study succeeded or failed in developing a “healing relationship,” a critical component of the OHE, with each study participant will need to be assessed. This could be accomplished through recurrent interviews with study participants followed by a qualitative analysis. Alternatively, a set of initial interviews or focus groups could be used to develop a quantitative analysis tool for re-

peated assessment of the patients' and/or their families' perceptions of the "healing quality" of their relationship with their providers.

COMPOSITION OF INVESTIGATOR TEAM

The team will require a skilled administrator given the complexity of coordinating a multifaceted lifestyle-oriented treatment approach. Diabetes educators will play a key role, and each center should have at least one such person on the study staff. If this person has appropriate skills, they could potentially also serve as the mind-body intervention coordinator for the program. Each center should also have access to an exercise expert with appropriate training to provide either group or individual-oriented exercise advice depending on study design. At least one physician investigator will be needed at each site to provide medical oversight. As discussed above, the inclusion of investigators with expertise in qualitative data collection and analysis will be critical. Depending on whether investigators choose to test the concept of an "integrator," the challenging question of how this newly described health care role will integrate with other members of the existing healthcare team will need to be considered.

CONCLUSION

There are many ways in which the design of an OHE for the treatment of patients with type 2 diabetes resembles and overlaps with that for a wide variety of other conditions such as obesity and cardiovascular disease. It may be that the most practical approach is to design a set of interventions which address such issues as the therapeutic alliance, the role of the family, and the influence of spiritual practice as well as proper nutrition, exercise, and mind-body health. All of these can be uniformly applied and tested across a variety of conditions. For example, the question of whether and how mind-body practices can enhance durable lifestyle change could be researched for a number of conditions simultaneously. This general OHE framework could then be refined in further trials to be more specifically tailored to diabetes and to other specific conditions of interest.

REFERENCES

- DeFronzo R. Pharmacologic therapy for type 2 diabetes mellitus. *Ann Intern Med* 1999;131:281-303.
- Harris MI, Flegal KM, Cowie CC, et al. Prevalence of diabetes, impaired fasting glucose, and impaired glucose tolerance in U.S. adults. The Third National Health and Nutrition Examination Survey, 1988-1994. *Diabetes Care* 1998;21:518-526.
- Jonas WB, Chez RA, Duffy B, et al. Investigating the impact of optimal healing environments. *Altern Ther Health Med* 2003;9:58-64.
- Genuth S, Eastman R, Kahn R. et al. American Diabetes Association. Implications of the United Kingdom prospective diabetes study. *Diabetes Care* 2003;26(Suppl 1):S28-S32.
- Pahor M, Psaty BM, Alderman MH, et al. Therapeutic benefits of ACE inhibitors and other antihypertensive drugs in patients with type 2 diabetes. *Diabetes Care* 2000;23:888-892.
- Manson JE, Spelsberg A. Primary prevention of non-insulin-dependent diabetes mellitus. *Am J Prev Med* 1994;10:172-184.
- Hu FB, Manson JE, Stampfer MJ, et al. Diet, lifestyle, and the risk of type 2 diabetes mellitus in women. *N Engl J Med* 2001;345:790-797.
- Tuomilehto J, Lindstrom J, Eriksson JG, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med* 2001;344:1343-1350.
- Pan XR, Li GW, Hu YH, et al. Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance: The Da Qing IGT and Diabetes Study. *Diabetes Care* 1997;20:537-544.
- Eriksson KF, Lindgarde F. Prevention of type 2 (non-insulin dependent) diabetes mellitus by diet and physical exercise: The 6-year Malmo feasibility study. *Diabetologia* 1991;34:891-898.
- Trento M, Passera P, Bajardi M, et al. Lifestyle intervention by group care prevents deterioration of Type II diabetes: A 4-year randomized controlled clinical trial. *Diabetologia* 2002;45:1231-1239.
- Kabir M, Oppert JM, Vidal H, et al. Four week low-glycemic index breakfast with a modest amount of soluble fibers in type 2 diabetic men. *Metabolism* 2002;51:819-826.
- Heilbronn LK, Noakes M, Clifton PM. The effect of high- and low-glycemic index energy restricted diets on plasma lipid and glucose profiles in type 2 diabetic subjects with varying glycemic control. *J Am Coll Nutr* 2003;21:120-127.
- Anderson JW. Fiber and health: An overview. *Am J Gastroenterol* 1986;81:892-897.
- Rodriguez-Moran M, Guerrero-Romero F. Oral magnesium supplementation improves insulin sensitivity and metabolic control in type 2 diabetic subjects: A randomized double-blind controlled trial. *Diabetes Care* 2003;26:1147-1152.
- Anderson, RA, Cheng N, Bryden NA, et al. Beneficial effects of chromium for people with diabetes. *Diabetes* 1997;46:1786-1791.
- Jayagopal V, Albertazzi P, Kilpatrick ES, et al. Beneficial effects of soy phytoestrogen intake in postmenopausal women with type 2 diabetes. *Diabetes Care* 2002;25:1709-1714.
- Fung TT, Hu FB, Pereira MA, et al. Whole-grain intake and the risk of type 2 diabetes: A prospective study in men. *Am J Clin Nutr* 2002;76:535-540.
- Montonen J, Knekt P, Jarvinen R, et al. Whole-grain and fiber intake and the incidence of type 2 diabetes. *Am J Clin Nutr* 2003;77:622-629.
- Vuskan, V, Sievenpiper JL, Koo VY, et al. American ginseng (*Panax quinquefolius L*) reduces postprandial glycemia in nondiabetic subjects and subjects with type 2 diabetes mellitus. *Arch Intern Med* 2000;160:1009-1013.

21. Vusjan V, Sievenpiper JL, Xu Z, et al. Konjac-Mannan and American ginseng: Emerging alternative therapies for type 2 diabetes mellitus. *J Am Coll Nutr* 2001;20(5 Suppl):370S–380S; discussion 381S–383S.
22. Gupta A, Gupta R, Lal B. Effect of *Trigonella foenum-graecum* (fenugreek) seeds on glycaemic control and insulin resistance in type 2 diabetes mellitus: A double blind placebo controlled study. *J Assoc Physicians India* 2001;49:1055–1056.
23. Baskaran K, Kizar Ahamath B, Radha Shanmugasundaram K, et al. Antidiabetic effect of a leaf extract from *Gymnema sylvestre* in non-insulin-dependent diabetes mellitus. *J Ethnopharmacol* 1990;30:295–300.
24. Cohen-Boulakia F, Valensi PE, Boulahdour H, et al. In vivo sequential study of skeletal muscle capillary permeability in diabetic rats: Effect of anthocyanosides. *Metabolism*. 2000;49:880–885.
25. Boule NG, Hadda E, Kenny GP, et al. Effects of exercise on glycaemic control and body mass in type 2 diabetes mellitus: A meta-analysis of controlled clinical trials. *JAMA* 2001;286:1218–1227.
26. Aikens JE, Kiolbasa TA, Sobel R. Psychological predictors of glycaemic change with relaxation training in non-insulin-dependent diabetes mellitus. *Psychother Psychosomatic* 1997;66:302–306.
27. Jablon SL, Naliboff BD, Gilmore SL, et al. Effects of relaxation training on glucose tolerance and diabetic control in Type II diabetes. *Appl Physiol Biofeedback* 1997;22:155–169.
28. Henry JL, Wilson PH, Bruce DG, et al. Cognitive-behavioral stress management for patients with non-insulin dependent diabetes mellitus. *Psychol Health Med* 1997;2:109–118.
29. Jain SC, Uppal A, Bhatnagar SO, et al. A study of response pattern of non-insulin dependent diabetics to yoga therapy. *Diabetes Res Clin Pract* 1993;19:69–74.
30. Tsujiuchi T, Kumano H, Yoshiuchi K, et al. The effect of Qi-gong relaxation exercise on the control of type 2 diabetes mellitus: A randomized controlled trial. *Diabetes Care* 2002;25:241–242.
31. Ayurvedic Interventions for Diabetes Mellitus: A Systematic Review. Summary, Evidence Report/Technology Assessment: Number 41. AHRQ Publication No. 01-E039, June 2001. Agency for Healthcare Research and Quality, Rockville, MD. Online document at: www.ahrq.gov/clinic/epcs/sums/ayurvsum.htm. Accessed December 26, 2003.
32. Jonas WB, Chez R, Duffy B, et al. Investigating the impact of optimal healing environments. *Altern Ther Health Med* 2003;9:58–64.
33. Miller WM, Crabtree BF, Duffy B, et al. Research guidelines for assessing the impact of healing relationships in clinical medicine. *Altern Ther Health Med* 2003;9(3 Suppl):80A–95A.

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