ARE THIAZOLIDINEDIONES FIRST-LINE AGENTS?

TO THE EDITOR:

In the "Clinical Inquiries" section of the May 2002 issue of *the Journal of Family Practice*, Drs Culhane and Graves[1] summarized their opinion on the "glitazones" by saying that the ". . . thiazolidinediones are not generally considered for first-line therapy." They followed that immediately with, "These agents may be most beneficial in patients with insulin resistance . . . ." The problem is that all individuals with type 2 diabetes have insulin resistance. Insulin resistance is the underlying problem. In medicine we try to always treat the underlying problem and not just symptoms. Elevated glucose and insulin levels are mere symptoms of the problem, and using sulfonylureas and insulin merely treats symptoms. Metformin also treats only the symptom of hyperglycemia. Therefore, the thiazolidinediones should be used as the very first-line agent (after exercise and diet) in type 2 diabetes unless contraindicated. All other agents are second-line therapy. Although insurance companies may agree with Drs Culhane and Graves because the thiazolidinediones are more expensive, in this case the best medical practice is clear cut.

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DR CULHANE RESPONDS:

I thank Dr Weldy for his comments regarding the role of thiazolidinediones in the treatment of diabetes mellitus. It is true that most patients with type 2 diabetes mellitus are insulin resistant and that sulfonylureas and insulin do not treat the underlying insulin resistance seen in these individuals. However, these agents do treat the hyperglycemia and offer a relatively safe and inexpensive approach to the treatment of type 2 diabetes mellitus. In addition, the sulfonylureas, insulin, and metformin are the only agents proven to decrease microvascular complications in patients with type 2 diabetes mellitus.[2] Also, metformin is the only medication that has been shown to reduce macrovascular complications and mortality in obese patients with type 2 diabetes mellitus.[3] Although the primary mechanism of action of the thiazolidinediones is to improve insulin sensitivity, there are no randomized controlled trials demonstrating that their novel mechanism of action leads to a reduction in morbidity and mortality. In addition, the thiazolidinediones cost considerably more than metformin and sulfonylureas, and liver enzymes of patients on thiazolidinediones must be monitored every 2 months because of the potential risk of hepatotoxicity. Therefore, based on available evidence, metformin should be used as initial drug treatment in obese patients with type 2 diabetes mellitus. In nonobese patients, sulfonylureas or metformin may be used first-line treatment and thiazolidinediones should be reserved for patients who cannot tolerate or have a contraindication to sulfonylureas or metformin.

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HOMEOPATHY OR ISOPATHY?

TO THE EDITOR:

I would like to point out a major flaw in the article by Dr McCarter,[1] which appeared in the "Patient-Oriented Evidence that Matters" section of the July 2002 issue of *the Journal of Family Practice*, and similarly in the study Dr McCarter reviewed. Essentially, the study by Lewith and colleagues[2] was not truly an evaluation of homeopathy per se, but of isopathy. The medication used was not prescribed according to the fundamental principles of homeopathy and therefore would not be expected to work.

Isopathy (derived from "isos pathos" or "equal suffering") refers to the use of the exact substance that causes an illness as a therapeutic tool for that same illness. Isopathy is the principle underlying conventional immunotherapy, eg, vaccinating with measles in an attempt to prevent measles, injecting pollen extract to try to subdue pollen allergies, etc.

Homeopathy (derived from "homoios pathos" or "similar suffering") is founded on the principle of similars. A medicinal substance that can produce a certain set of symptoms in healthy persons in a clinical investigation, can be used to stimulate a curative response in individuals experiencing a similar set of symptoms in an innate disease process.

To select the correct homeopathic medicine, one must elicit the totality of characteristic physi-

cal, emotional, and mental symptomology, making a careful analysis of the symptom picture. The homeopathic medicine possessing the ability to induce the most similar symptom picture to that being experienced by the patient is the one chosen for therapeutic intervention and has the greatest probability of cure in a given case. Using the true homeopathic approach is of utmost importance when treating complex diseases such as asthma and allergic diatheses, as well as autoimmune disorders, colitis, migraines, etc, if one is to achieve genuine therapeutic benefit.

In isopathic immunotherapy, none of the fundamental steps of case taking and case analysis, which are critical to the selection of the clinically appropriate homeopathic medicine, are undertaken. It is no small wonder that isopathic immunotherapy, as that used in the study by Lewith and associates,[2] would be ineffective in some cases.

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DR MCCARTER RESPONDS:

As Dr Fleisher indicates, isopathy is not synonymous with homeopathy. Isopathy is 1 of 4 basic types of homeopathy. Homeopathy as described by Dr Fleisher is considered by some authorities to be "classical homeopathy," another of the 4 basic types of homeopathy.[3] Lewith et al[2] were indeed using the isopathic form of homeopathy in their study. They were attempting to validate the method used in a smaller pilot study that showed a benefit to isopathic homeopathy.[4] However, their results in this larger well-done study did not show a benefit.

The real issue is not the specific form of homeopathy used or even the proper definition of homeopathy; the article by Lewith and colleagues was not chosen for review because of the negative findings for homeopathy. It was selected because they studied the treatment of a common problem encountered by family physicians every day and measured patient-oriented outcomes. Ultimately, whether the treatment studied was homeopathy, isopathy, acupuncture, or a new pharmaceutical is immaterial. When a physician makes a treatment decision with a patient, he or she should have evidence of benefit before substituting a new therapeutic modality for an already effective treatment.

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INFLUENZA VACCINE DOES NOT PRODUCE MYOPATHY IN PATIENTS TAKING STATINS

TO THE EDITOR:

Influenza is an acute febrile illness caused by infection with influenza virus A&B. Clinical manifestations are fever, myalgia, and cough. Myositis (symptomatic or laboratory confirmed) and rhabdomyolysis have also been reported.[1] Influenza vaccine is recommended for populations at increased risk for developing complications.

Myopathic syndromes are one of the major adverse effects of HMG-CoA reductase inhibitors ("statins"). Only 1 case of rhabdomyolysis after influenza vaccine in a patient using statins has been reported.[2] We attempted to determine if influenza vaccine given to patients treated with statins causes asymptomatic or symptomatic myopathy.

Our study was conducted in outpatient rural clinics of Clalit Health Services in north Israel, during October 2001. Patients were eligible if they were at least 50 years of age and had received an influenza vaccine. A 5-mL blood sample for creatine phosphokinase (CPK) and aldolase levels was obtained before and 5 to 7 days after vaccination. Clinical and demographic data as well as reactions after the vaccination were recorded. We studied 98 patients: 52 who received statins and 46 controls. Their mean age was 69.7 years (range, 50–91 years). Clinical and demographic characteristics were similar in both groups.

Local reactions (rubor, pain, mild swelling) were reported in 20 patients (20.2%): 7 in the statin group and 13 in the control group (P = NS). These reactions improved after a few days without treatment. Only 2 patients (2%) (1 in each group) had myalgia. CPK and aldolase levels were measured before and after influenza vaccination for the entire study population and were analyzed separately by sex (because of sex differences in total muscle mass and normal ranges). CPK levels increased slightly, but not significantly, after influenza vaccination in both groups of female patients, and in male patients only in the control group. The only significant change observed was an increase in aldolase levels after influenza vaccine in female control subjects (P = .013). All CPK and aldolase values before and after vaccination were within normal ranges.

Thus, we found no indication in this pilot study that influenza vaccination causes clinical or laboratory evidence of myopathy in patients taking statins.

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—Laura Dowden, Publisher, 10/9/02