found that sTNF-R1 is independently associated with albuminuria in type 2 diabetic patients (4). To the best of our knowledge, however, it is not clear whether serum homocysteine is associated with TNF receptor in type 2 diabetic patients. The aim of the present study was therefore to investigate the relationships between serum homocysteine and TNF receptor in patients with type 2 diabetes.

Fifty nonobese Japanese type 2 diabetic patients were studied. Their BMI, HbA_{1c}, and serum creatinine were 22.6 ± 0.3 kg/m2 (range 17.6–26.2), 7.8 ± 0.2% (5.5–12.3), and 0.70 ± 0.02 mg/dl (0.46–0.98), respectively. They had not been treated with insulin or any medications known to alter homocysteine level. In conjunction with homocysteine, systolic and diastolic blood pressure, HbA_{1c}, glucose, lipids, serum creatinine, TNF-α, sTNF-R1, and sTNF-R2 were measured after an overnight fast.

With univariate analysis, serum homocysteine was positively correlated with age ($r = 0.361$, $P = 0.012$), diabetes duration ($r = 0.292$, $P = 0.045$), serum creatinine ($r = 0.623$, $P < 0.001$), sTNF-R1 ($r = 0.415$, $P < 0.005$), and sTNF-R2 ($r = 0.371$, $P < 0.01$). Other variables including TNF-α, however, were not associated with homocysteine. Multiple regression analyses showed that serum homocysteine was independently associated with serum creatinine ($F = 20.1$) and sTNF-R1 ($F = 6.9$), which explained 49.3% of the variability of homocysteine. Thus, TNF system activity may be responsible for the evolution of atherosclerosis induced by homocysteine in nonobese Japanese type 2 diabetic patients.

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Phenformin-Induced Lactic Acidosis in an Older Diabetic Patient

A recurrent drama (phenformin and lactic acidosis)

Editor's note: The authors had the following statement in their letter to me, with which I agree, "Most physicians are aware of the risk of lactic acidosis in patients taking phenformin. However, this side effect is continuously observed because phenformin is still used in Italy, Brazil, and China. We believe that the publication of our observation in an important journal like Diabetes Care *may help to prompt governments of these countries to ban phenformin, just like in the rest of the world. This is the only way to prevent further cases of this avoidable, unacceptable and life-threatening complication."*

A 73-year-old man with diabetes presented with upper-abdominal pain and nausea. He also had a history of hypertension, a pace-maker implant, and peripheral arterial disease treated with amputation of his left leg. His therapy included ticlopidine, enalapril, omeprazole, and 2 mg glibenclamide/30 mg phenformin b.i.d. The patient was alert and cognitively intact. Blood pressure and heart rate were 120/70 mmHg and 70 bpm, respectively. Radiographs of the chest and abdomen and an abdominal ultrasound study were normal. Laboratory tests disclosed a severe lactic acidosis (pH 6.8, pCO_2 14.1 mmHg, pO_2 108 mmHg, HCO_3 4.9 mmol/l, lactate 21 mmol/l, and anion gap 31 mmol/l). After phenformin discontinuation, the patient's conditions rapidly improved. He was treated with intravenous insulin and glucose (1) and discharged 7 days later in good condition.

This report confirms that phenformin-induced lactic acidosis (PLA) is still a public health problem (1,2). To our knowledge, phenformin is still used in Italy, China, and Brazil. In a Medline search, we found 12 cases that occurred in Italy between 1981 and 1998 (2). In two patients phenformin was even brought back into use soon after, thereby questioning the belief that PLA is adequately recognized (2). More importantly, according to data by Intercontinental Marketing Services (www.imshealth.com), 838,000 preparations of phenformin and a sulfonylurea have been sold in Italy between January and October 2005. Because PLA occurs in 1 of 4,000 patients (3) with a mortality rate of ~50%, these data raise worrying health care considerations. In fact, diabetic patients often have comorbid conditions known to favor PLA.

Phenformin was removed from the U.S. market in 1977, but, surprisingly, cases of patients who have been prescribed the drug abroad are continuously reported (1). Phenformin can also be illegally obtained online or through mail orders to replace metformin, which is more costly. Furthermore, herbal medicines containing phenformin are also consumed in developed countries. In February 2000, the Food and Drug Administration recalled five Chinese herbal medications containing phenformin (4), while Health Canada is currently warning consumers not to take "Shortclean," a phenformin-based Chinese "natural" medicine (5).

Phenformin can always be replaced by metformin, which should not be associated with a higher risk of lactic acidosis compared with nonbiguanide therapies (6). Despite most clinicians being aware of PLA, the only way for preventing further cases is to forbid phenformin in countries where it is still used.

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COMMENTS AND RESPONSES

Patient Self-Management of Insulin Doses in the Hospital

This letter may seem "far out," but in my experience and that of some of my colleagues, with select patients, usually type 1's, patient self-management (with physician oversight) yields better glycemic results (and less patient and physician anxiety) than if insulin dosing is left to the vagaries of the busy floor staff. Getting the hospital administration to allow this is often the biggest challenge.

Reading the exchange of letters in the December 2005 issue regarding the management of inpatient hyperglycemia made me reflect on personal experiences as a hospital patient (1,2). In past years, as surgeons and cardiologists tended to their more immediate tasks, my diabetes was often relegated to a secondary and sometimes seemingly nonexistent concern. I was frustrated and angered by substitution of the sliding-scale for my normal insulin regimen, especially as my blood glucose spiraled out of control. It is encouraging that this critical issue is receiving increased attention.

My own bouts with surgeries at the University of Pittsburgh Medical Center this past winter highlight the benefits of focusing on inpatient diabetes management. Not only did I demand a consult with my endocrinologist and her staff to develop and implement a treatment plan for my hospital stay, I requested intravenous insulin infusions during surgery and in the recovery room and intensive care unit. The growing evidence supporting the value of infusions is overwhelming.

It is sometimes easy, however, to overlook another effective tool for in-hospital diabetes management— the patient. Undoubtedly, the most helpful step for me was continuing to manage my own insulin pump therapy while in the hospital. Clearly, every patient demonstrating proficiency, whether using a pump or multiple insulin injections, should be encouraged to continue self-management on the nursing floor. For me, this alleviated the anxieties often felt by patients when their diabetes management routines have been disrupted. And the results were phenomenal. My blood glucose stayed within normal ranges almost the entire time! With the help and oversight of my consulting endocrinologist and certified diabetes educators, self-management presented few difficulties for me and relieved the surgical staff of this additional responsibility. Many of the nurses and other hospital staff were actually curious to learn more about insulin therapy and, particularly, pump therapy.

I kept my own glucose monitor and a supply of strips with me, as well as replacement batteries and other pump supplies. While staff would routinely check my blood glucose levels, the timing was somewhat irregular and did not always correlate with meals. I carefully recorded monitor readings, food intake, and insulin dosing to review with my consulting diabetes specialists. I also maintained a cache of glucose tablets and fruit juice to treat inevitable lows. Although these were available on the hospital floor, I was concerned about getting the immediate attention of the nursing staff during a sudden hypoglycemic episode. Nevertheless, I reported every incident and the actions taken for entry into my medical records.

In addition, I reminded every hospital staff member about my diabetes and my treatment plan, and I always had a family member available to do this when I was unable to speak for myself. While this information was contained in my chart, it is unreasonable to expect that everyone remembers every detail all the time. These approaches kept my diabetes in the forefront and dramatically enhanced each hospitalization.

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Acute Neuropathic Joint Disease: A Medical Emergency?

Response to Tan et al.

We read with some interest the commentary by Tan et al. (1) on the management of the Charcot foot in diabetes. While we agree entirely that this condition should be ranked as a medical emergency, because failure to act quickly can lead to irreversible adverse consequences, we do not agree that the evidence is available to support uncritical use of bisphosphonates. The only blinded trials conducted so far did not demonstrate any overt improvement in long-term prognosis (2,3). There is much suggestive evidence to favor the consideration of bisphosphonate use, but it is not currently accepted by all authorities that this therapy is essential.

A number of other treatments also deserve consideration (4,5). For example, intranasal calcitonin and tumor necrosis factor-α antagonists may prove useful, although the efficacy of both has yet to be established in controlled trials. In the absence of evidence to support the use of