

## OBSERVATIONS

## Probing the Validity of the Probe-to-Bone Test in the Diagnosis of Osteomyelitis of the Foot in Diabetes

The ability to probe the base of a wound to periosteum or bone (the “probe-to-bone” test) is increasingly used to indicate the likelihood of underlying osteomyelitis. The original study (1) reported sensitivity, specificity, and positive (PPV) and negative (NPV) predictive values of 66, 85, 89, and 56%, respectively. However, this work has been criticized on the grounds of the high pretest probability of the disease (2), since the prevalence of osteomyelitis in the chosen sample (in-patients with clinically overt infection) was 66%. It follows that the usefulness of the test may be very different in less-selected populations. We have therefore determined the validity of the probe-to-bone test in a consecutive series of outpatients attending our own multidisciplinary service.

A total of 81 patients (with a total 104 foot ulcers) attended the clinic over a 5-week period in May–June 2005. Ulcers were probed by one of two specialist podiatrists following debridement. The diagnosis of osteomyelitis was determined by one of two expert diabetologists, who were blind to the results of the probe to bone test. The diagnosis of osteomyelitis was based in each case on the presence of clinical signs of infection (inflammation with or without serous or purulent discharge) in association with radiologic evidence of bone destruction with interruption of the cortex (either at presentation or at any stage over the ensuing 8 weeks), supported when necessary by magnetic resonance imaging and microbiologic analysis of deep tissue samples. Those who were diagnosed with osteomyelitis included those in whom the diagnosis had already been made at the time of probing and those in whom the diagnosis was made later. Nineteen (23.5%) patients were diagnosed with osteomyelitis complicating foot ulcers, in two of whom bone infection complicated two

separate nonadjacent ulcers. Three patients had two or more nonadjacent ulcers, of which only one was associated with osteomyelitis. A total of 14 patients had osteomyelitis complicating a single ulcer. A total of 21 ulcers (20.2% of 104) were associated with osteomyelitis. The probe-to-bone test was positive in 8 of these 21 ulcers and in 7 of 83 without associated bone infection (sensitivity 38%, specificity 91%). While the NPV was 85%, the PPV (the probability that a patient with a positive test would have osteomyelitis) was only 53%. It is possible that the calculation of both sensitivity and NPV might be in part explained by the fact that some cases of osteomyelitis may already have been responding to treatment at the time of probing, but this would not have affected the calculation of either the specificity or the PPV.

These data emphasize that the predictive value of a positive probe-to bone test in the original report was influenced by the high prevalence of osteomyelitis in the population studied. The prevalence of osteomyelitis in the present population was still high at 23.5% patients (20.2% ulcers) but was only approximately one-third of that in the earlier study, and the PPV was correspondingly lower. It is likely that the PPV would be lower still in patients managed in a less-specialized service.

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## An Exploratory Study Into the Effectiveness of a Combination of Traditional Chinese Herbs in the Management of Type 2 Diabetes

While a range of drugs are used to ameliorate the effects of type 2 diabetes and its complications, they tend to slow rather than stop the progression of the disease (1). Many herbs have been used traditionally by different cultures in the management of type 2 diabetes (2); however, in general there is little scientific evidence to support their efficacy. The aim of this project was to conduct a small-scale trial to examine the effects of a commercial combination of *Trichosanthes kirilowii*, *Polygonatum sibiricum*, *Dioscorea opposita*, *Panax ginseng*, and *Stevia rebaudiana* and chromium nicotinamide (Glucostat; Health World Limited, Eagle Farm, Australia) on type 2 diabetic subjects who are not yet taking orthodox medication.

Four male and six female subjects aged between 33 and 70 years who had been diagnosed with type 2 diabetes and were on a low glycemic diet participated in this study. They were administered a 3.2-g dose three times a day over a 90-day period. Fasting blood glucose (FBG) data were collected daily using handheld glucometers, and HbA<sub>1c</sub> (A1C), cholesterol, and BMI were recorded at the start and end of the trial. This study was approved by the human ethics committee at the University of New England.

The mean FBG for all patients at the start of the study was  $9.4 \pm 1.1$  mmol/l and ranged from 7.6 to 11.3 mmol/l. Nine patients responded to the treatment showing a significant, though moderate, decrease ( $10 \pm 4\%$ ) in FBG; however, while A1C, cholesterol, and BMI also declined, this did not reach significance. When treatment stopped, FBG rose rapidly over 15–20 days to pretreatment concentrations; however, when treatment was resumed ( $n = 5$ ) FBG again declined by 14.3% (range 8–21) over the following 6 weeks.

This herbal combination may have some benefit in the treatment of type 2 diabetes, particularly perhaps in the early stages of the disease. The effects, while significant, took time to become appar-

ent, and the herbal combination appears to slowly improve the FBG concentrations over a period of continuous use. Surprisingly, this effect was rapidly reversed when the treatment ceased, as blood glucose returned to pretreatment levels within 15–20 days. Those subjects who started to take the herbal remedy again after the withdrawal period showed a more rapid decline in their FBG concentrations than when they first started the treatment. It is unclear from this study whether the FBG would return to euglycemia over a longer period of time, but it appears that the rate of decline slows and may plateau before this was reached.

This study strongly suggests that this combination of traditional Chinese herbs, together with chromium, may be effective in improving glycemic control in people diagnosed with type 2 diabetes. The mechanism of action remains unclear and may be a combination of an increase in insulin responsiveness and glucose uptake. The relative importance of the individual component herbs is also unknown, and we are undertaking further studies to investigate this.

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## Severe Injection Site Reaction to Insulin Detemir

Insulin detemir is a new long-acting insulin analog. Though generally well tolerated, injection site reactions have been reported in 2% of insulin detemir users (1). Most commonly, these untoward reactions manifest as mild injection

site erythema or discomfort and seldom lead to discontinuation of the product. Herein, I report the case of a patient with a severe local reaction to insulin detemir necessitating its withdrawal.

A 37-year-old Caucasian woman with a 25-year history of type 1 diabetes was switched from NPH (Humulin N; Eli Lilly) to insulin detemir (Novo Nordisk) because of poor glycemic control characterized by undue variability of her blood glucose readings and an elevated HbA<sub>1c</sub>. She was also being treated with insulin lispro (Eli Lilly), which she remained on. She had no previous history of injection site problems. With both the previous and the new insulin, she maintained the same proper injection technique and injected, as was her custom, into her abdominal wall.

The patient developed injection site problems within hours of her very first injection of insulin detemir with a characteristic and reproducible pattern occurring with all subsequent injections, ultimately necessitating withdrawal of the insulin within a few days of its institution. Within 6 h of an injection of insulin detemir she would develop a slightly raised, indurated, nonerythematous, minimally uncomfortable, nonpruritic, nontender lesion of ~3 cm. Over the subsequent 6 h, a lesion would expand in size reaching a diameter of 5–6 cm and become erythematous (without central sparing), warm, and moderately tender. Over the subsequent 12 h, a lesion would enlarge further, reaching a diameter of 10 cm, and become markedly indurated, hot, and extremely painful. Over the subsequent 12 h, a lesion would gradually and spontaneously resolve. No fever, chills, rigors, or sweats were experienced. Rotating her injection site around various parts of her abdomen was of no benefit, and a trial injection into the thigh resulted in the identical sequence of events. Insulin detemir was discontinued, and the patient reverted back to her former insulin with no further injection site problems.

Recently, a patient was described who was thought to have experienced a type III allergic reaction to insulin detemir (2); however, unlike the current patient, in this previous report, the lesions encountered were said to be “small” and only “slightly painful” as well as being nonerythematous. Whether the patient described in this case report reacted to the insulin detemir per se or one of its excipients is not known.

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## A Case of Fulminant Type 1 Diabetes Associated With Painless Thyroiditis

Type 1 diabetes is classified as type 1A and type 1B diabetes, which are considered to be caused by autoimmune and nonautoimmune (idiopathic) mechanisms, respectively (1). Fulminant type 1 diabetes is characterized by a rapid-onset diabetic ketoacidosis within a short period of time, normal to near-normal HbA<sub>1c</sub> level at onset, and complete  $\beta$ -cell destruction and was originally reported as a subtype of type 1B diabetes (2). Recently, the involvement of viral infections has been suggested to be the triggering mechanism of fulminant type 1 diabetes (3,4). The involvement of T-cell autoimmunity in this disease, however, has also been reported (5–8). Thus, its etiology is still unclear. Here, we report a case of fulminant type 1 diabetes and painless thyroiditis that presented simultaneously.

A 47-year-old woman was admitted to our hospital in a diabetic ketoacidotic coma. She suffered from fatigue and fever 2 days before admission. One day before admission, she visited a clinic and was given drugs for the common cold. On the day of admission, however, she became comatose and was transferred to our emergency room. Her arterial blood pH was 6.9 and bicarbonate was 1.5 mmol/l. She had markedly increased levels of ketone bodies and serum potassium (7.6 mEq/l). Computed tomography of the brain showed no abnormal findings. After admission, she went into cardiac arrest

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