diate-acting insulin (NPH and lente) in normal (3–5) and diabetic (6–8) subjects. Other reports on the miscibility of regular with long-acting insulin are available (9,10).

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Ice-Water Addiction Complicating Painful Diabetic Neuropathy in Childhood

Acute painful diabetic neuropathy, a rare syndrome in childhood (1), can have incapacitating symptoms. Adequate pain management is difficult to achieve in these patients, and depression and anorexia frequently accompany the clinical picture (2). No medications, including narcotics, consistently relieve the pain, but some patients have found immersion of the painful extremity in cold water to be effective analgesia (2). Prolonged exposure to this wet and cold environment, however, may result in the insidious development of cold injury that is ignored because of the accompanying anesthesia (3). We report the occurrence of acute painful neuropathy in a pediatric diabetic patient whose dependence on ice-water immersion for pain relief resulted in deep-seated cold injury (immersion foot).

CASE HISTORY

A 14 yr-old boy with insulin-dependent diabetes mellitus was referred for evaluation of severe bilateral foot pain of 2 wk duration. The patient complained of a continuous burning sensation punctuated by brief stabbing pains, exacerbated by walking and worse at night. Aspirin had been ineffective, but immersion of his feet in cold water gave significant relief. The patient, who lived on a farm, denied exposure to lead, pesticides, or other toxins. He always wore shoes and felt that a localized cutaneous exposure to an allergen or toxin could not have occurred.

After the initial diagnosis of diabetes 5 yr earlier, the patient received NPH insulin twice a day at a maximum dose of 13 U each morning and 3 U each evening (~0.4 U/kg). Glycosylated hemoglobin had not been measured. Three months before referral, after hospitalization for diabetic ketoacidosis, his dose of insulin was increased to 46 U NPH and 10 U regular each morning and 17 U NPH and 15 U regular each evening (~1.9 U/kg) over 4–6 wk. On this regimen, he had experienced several mild hypoglycemic episodes.

Physical examination revealed a thin adolescent in extreme pain: height 158 cm, weight 46 kg, blood pressure 102/80 mmHg, pulse 90 beats/min. Funduscopic exam was normal. The feet were red and swollen, and sparse petechiae and small vesicles were noted on several toes. Arterial pulsations were easily palpable. Strength, proprioception, and sensation to light touch and pinprick were normal. Deep tendon reflexes were present and symmetric. The patient walked with a shuffling gait, refusing to bear weight on either forefoot.

Diagnostic studies included an erythrocyte sedimentation rate of 35 mm/h (normal range 0–15 mm/h), glycosylated hemoglobin 7.7% (normal range 5–8%), normal levels of erythrocyte lead, and undetectable levels of mercury and arsenic. Cultures of vesicular fluid were negative. Nerve-conduction studies revealed absent sural nerve responses bilaterally and slowing of conduction velocity in both peroneal nerves, indicative of a sensorimotor polyneuropathy. Ophthalmologic examination revealed no evidence of diabetic retinopathy. A nerve biopsy was not performed.

Various medications including naproxen, amitriptyline hydrochloride, meperidine hydrochloride, and morphine sulfate failed to relieve his discomfort. He insisted on nearly constant immersion of his feet in ice water; withdrawal of this therapy

was followed by rebound pain of increased severity. This pattern and the appearance of the patient's feet suggested the presence of cold injury (immersion foot), a diagnosis supported by a burn specialist. Heavy sedation was required as the ice water was withdrawn. When the patient was discharged, he was taking carbamazepine and ibuprofen and was able to walk with the support of a walker. Within 3 wk, these medications were discontinued. Absence of pain and normal ambulation were documented 2 mo later.

DISCUSSION

Painful (hyperalgesic) neuropathy is a debilitating, transient complication of diabetes mellitus. More common in males, it may develop in insulin-dependent or non-insulin-dependent patients regardless of the duration or control of their diabetes. Depression, anorexia, and weight loss commonly precede or are associated with neuropathy (2). Motor abnormalities are absent, and sensory changes are usually slight compared with the magnitude of pain, which may be cramp-like, burning, or lancinating and characteristically intensifies at night. Nerve biopsy reveals recent axonal degeneration (in some cases associated with demyelination) in most affected patients (2). That the onset of neuropathy frequently occurs 2–4 wk after an abrupt improvement in metabolic control (as occurred in our patient) raises the possibility that the pain may arise from regenerating axonal sprouts (4). Severe manifestations are transient, lasting from 2–10 mo, and recurrences are unusual.

Like all diabetic neuropathies, this painful variety is rare in children. Occurrences in adult patients after stressful events, e.g., surgery, acute myocardial infarction, or prompt improvement in metabolic control (5), suggest a causal relationship to acute changes in the metabolic state. The young patient described above clearly experienced a rapid increase in insulin dosage after several years of inadequate control before the onset of neuropathic symptoms. Although early anecdotal reports implicated insulin as a toxic agent in this setting (6), it is now clear that other modes of hypoglycemic therapy may precipitate painful neuropathy (7), and continued treatment with insulin does not impede its resolution.

The term *immersion foot* refers to cold injury of the feet resulting from prolonged exposure to water at temperatures <50°F. This gradual cooling of the extremity leads first to a reduction in skin sensitivity often followed by neuralgiform pains that increase in intensity until total anesthesia of the limb develops. Edema of the foot is accompanied by muscular stiffness and rigidity, which is reversible and disappears in the course of rewarming (3). Rewarming is painful while the anesthesia gradually disappears; characteristically, the edema resolves completely, although varying degrees of deep neurovascular and bone injury may persist.

The predictable effect of cold-water immersion on reducing skin sensitivity has led to its use by adult diabetic patients with painful neuropathy (2). The severity of our patient's symptoms required prolonged immersion in very cold water for adequate pain relief, leading to the development of early immersion cold injury. Pain associated with rewarming of his feet became indistinguishable from symptoms of his painful diabetic neuropathy; reimmersion was then required to prevent the recurrence of intolerable pain. Enforced withdrawal from this cycle prevented permanent cold injury.

Whereas the presence of pain is actually considered a good prognostic sign in diabetic neuropathy, the requirement of narcotics to control pain has resulted in addiction in some diabetic patients (6). It is not surprising, therefore, that dependence on any form of effective pain relief may occur during the course of this syndrome. Awareness of the potential for injury from cold-water immersion may prevent long-term consequences from this exquisitely painful but transient complication of diabetes mellitus.

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Lessons From Glucose Monitoring at Night

The recent editorial by Sherwin et al. (1) was an excellent summary of studies relating to elevated fasting blood glucose in insulin-dependent diabetic (IDDM) patients. I take issue, however, with their concluding suggestion that "it may sometimes be helpful to switch patients from human to animal insulin." We have been using intensive insulin therapy with two daily doses of long-acting insulin and preprandial doses of regular insulin plus corrective doses of regular insulin as needed for >15 yr. At various times, we have used NPH, protamine zinc, ultralente, and lente insulins. We have used beef-pork, pure pork, and human versions of several of these insulins. For several years, our favorite long-acting insulin