(2); the latter was the main bladder abnormality in our patient, presumably reflecting the brainstem atrophy. Previously, bowel dysfunction has only rarely been documented in WFS (3,4). In our case, loss of SPRCs and sphincter weakness were the main bowel abnormalities. The SPRCs are likely to reflect the intrinsic neuronal activities of the pacemaker cells in the myenteric plexus, which can be damaged in peripheral neuropathies that involve small fibers. Sphincter tone is maintained by the extrinsic somatic nerve for the external sphincter and sympathetic nerve for the internal sphincter, respectively, which can also be damaged in peripheral neuropathies. These bowel dysfunctions need specific management to maximize the quality of life in patients with WFS.

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Objective Evidence for the Reversibility of Nerve Injury in Diabetic Neuropathic Cachexia

Diabetic neuropathic cachexia is an acute complication of diabetes marked by such extreme pain and weight loss that, although exceptionally rare, it imparts major challenges in management and diagnosis. Little is known of the fundamental pathophysiologic features of the peripheral nervous system in this condition; for example, the symptomatic resolution that is classically observed may arise from either complete destruction of pain-transmitting nerve fibers or from their repair. To reconcile this issue, we report the first case to our knowledge that the nerve dysfunction is reversible. A 36-year-old woman presented with subacute hyperglycemic symptoms. Soon after initiation of insulin therapy and the decline of HbA_{1c} from 14.9 to 5.5%, she developed severe lancinating pain and profound weight loss associated with anorexia, amenorrhea, insomnia, and dehydration. On examination, allodynia was so pronounced that a light touch to her shoulder would cause her to weep. Profound loss of subcutaneous adipose tissue and loss of muscle bulk was evident, such that her weight had decreased from a baseline of 58.3 to 41.8 kg (corresponding to a decrease in BMI from 21 to 15.7 kg/m^2). Pain, temperature, and light touch sensation were abnormal in the hands and feet.

Blood count, chemistries, and thyroid and cortisol levels were normal. Further tests for malignancy and malabsorption, including serum immunoelectrophoresis, computed tomography, bone scan, and endoscopy with biopsies, were normal. Titers for antinuclear antibodies and viral etiologies were negative. Nerve conduction studies demonstrated impaired conduction velocity (indicative of impaired myelin sheath function) and impaired amplitude potentials (indicative of impaired nerve axon function) of both sensory and motor nerves.

Hydration, oral nutritional support, and opiate therapy were provided during an 8-week hospitalization. She subsequently received symptomatic therapy with amitriptyline and gabapentin; a year later these analgesic therapies were discontinued, and her weight had returned to baseline. The aberrations in nerve function had normalized; most dramatic was the improvement in nerve axon function, represented by a doubling of amplitude potentials. For example, in the sural nerve the conduction velocity improved by 30% (from 36 to 47 m/s) and the sensory amplitude potentials doubled (from 3.4 to 7.5 μV) from baseline. Similar changes were seen in the median and peroneal nerves for these parameters and also for F-wave latencies and vibration perception thresholds.

The profound weight loss, the symmetrical sensorimotor polyneuropathy associated with dramatic painful paresthesias devoid of weakness, the temporal relation with insulin therapy, and the chronic course are in complete accordance with the diagnosis of diabetic neuropathic cachexia (1). This report emphasizes the need for vigilant symptomatic therapy of diabetic neuropathic cachexia while expediting investigations for eliminating alternate causes. Unique to this report, however, is the objective finding of nerve dysfunction that was dramatically reversed after symptomatic recovery; it supports the proposed hypothesis that paradoxical hypoxic injury occurs at the initiation of insulin therapy (2,3). This case fundamentally suggests that the reversal of painful symptoms is associated with repair of functional aberrations in nerve fibers induced by hypoxia rather than their irreversible ischemic destruction.

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COMMENTS AND RESPONSES

Influence of Glycemic Index/Load on Glycemic Response, Appetite, and Food Intake in Healthy Humans

Response to Alfenas and Mattes

In their recent article, Alfenas and Mattes (1) conclude that the glycemic index values of individual foods do not predict glycemic response to mixed meals, nor influence measures of hunger. Because the observed glycemic response did not differ between diets, the lack of effect on appetite is not surprising. Thus, the potentially important aspect of the study pertains to the prediction of glycemic index in mixed meals.

The authors' approach was to validate published glycemic index values in a pretest, selecting 48 of 79 foods with consistent glycemic responses. However, their methods do not conform to standard procedures (2–4). Only 3 subjects were used for each food instead of the recommended minimum number of 10 (3). Blood glucose was measured by glucometer, a device that is not sufficiently accurate in the normal range for research purposes (4). With such a small subject number, CIs around the mean would likely overlap for most foods on both diets. From a statistical perspective, the selection of foods with an underpowered pretest using inaccurate methods would produce regression to the mean.

It is important to emphasize that published values for specific foods cannot be used for a study such as this without careful validation because published values may not have been determined correctly, the composition or manufacturing procedures of individual products may change over time, and shelf life and preparatory methods may also affect glycemic index. Such concerns are not unique to studies of glycemic index. One cannot assume, for example, that a published value for vitamin C content of Valencia orange will apply to every piece of fruit, at all times of year, from any location.

Major categories of food differ in glycemic index with reasonable consistency; most fruits, legumes, minimally processed grain products, and pasta prepared from hard wheat have low– to moderate–glycemic index, whereas highly processed grains products and pasta previously prepared and canned have a high–glycemic index. Most of the foods used by Alfenas and Mattes for the low–glycemic index diet included highly processed grain products (quick pizza, quiche, pita, bagel, etc.).

There are many studies demonstrating that the glycemic index of individual foods predicts a response to mixed meals when appropriate methodology is utilized (5–7). With regard to the authors' description of our study, two of the test meals did have identical macronutrient composition and solid food components, and the measured glycemic response corresponded closely with prediction (8).

Clearly, research into the relationship between glycemic index and glycemic response merits study. To advance the dialogue, adequately powered studies employing accepted methodology will be needed. A more fundamental question is whether diets comprised of low–glycemic index foods improve important clinical end points related to obesity, diabetes, heart disease, and cancer.

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Influence of Glycemic Index/Load on Glycemic Response, Appetite, and Food Intake in Healthy Humans

Response to Alfenas and Mattes

Recently, Alfenas and Mattes (1) concluded that the differential glycemic responses of foods tested in isolation are not preserved under conditions of chronic ad libitum consumption of mixed meals (1). This conclusion is unwarranted because of serious methodological problems that undermine the validity of their results.

Foods were classified as low– or high–glycemic index by the investigators; the glycemic index of each food was determined in three subjects by measuring glucose four times with a glucose meter and discarding means with inconsistent values. Since white bread was used as the reference, all glycemic index values discussed here are adjusted accordingly. We commend the authors for wanting to mea-