release from the pancreas in those who maintain at least some insulin reserve,[13,14] has not been discussed. Nor has it been emphasized that the centrally acting agents may indeed compound the problem of impotence, which already afflicts many diabetic patients.[15,16]

While it is understandable why the committee cannot discourage or advocate the use of specific antihypertensive agents in the diabetic population, I feel that, especially in treating the diabetic hypertensive patient, emphasis should be given to agents that have more favorable hemodynamic and metabolic profiles.[17–19]

I only wish to bring attention to a specific problem that may have been overshadowed by the general problem of hypertension in our population at large.

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Angioedematous Urticaria in a Diabetic Patient Successfully Treated with Nifedipine

Y. O., a female office worker, has had diabetes for the past 16 of her 22 yr. She presented to us for the first time on 5/26/84 for control of chronically elevated blood sugars and complained of nocturia, chronic fatigue, chronic constipation, and frequent nocturnal muscle spasms of her feet. She admitted to occasional cardiac "palpitations" associated with anxiety on running up stairs. She also admitted to chronically cold feet in winter, which do not rewarm readily when she returns indoors. She denied any allergic history, but noted that her father is allergic to penicillin and suffered an anaphylactic episode after a bee sting.

Daily medications consisted of beef-pork insulin (25 U NPH mixed with 3 U regular) each morning, a commercial vitamin mixture, and an "herbal laxative."

Physical examination disclosed the following positive findings. Background retinopathy, diplopia on lateral gaze, pustules on the left tonsil, a fine macular rash on the buttocks, reduced oscillometrics at both ankles, and a fungal infection of her toenails.

Laboratory findings included the following abnormalities: glycohemoglobin, 13.2% (normal 4.4–8.2%); ionized calcium, 3.62 meq/L (normal 2.25–2.95 meq/L) with a normal 24-h urine calcium; IgE, 161 U/ml (normal 0–150 U/ml); creatinine clearance, 80.5 ml/min. A throat culture yielded many non-group A beta hemolytic streptococci, sensitive to penicillin.

The patient was treated with 1% cicloperox olamine cream twice daily for her fungal toenails. She was asked to take Hydrocil (Rowell Laboratories, Inc., Baudette, Minnesota) (a high-fiber, sugar-free product) instead of the "herbal laxative." She was put on a very low carbohydrate diet, frequent self-monitoring of blood glucose (BG), and her insulin regimen was changed to 4 U of Monotard (lente) human insulin (Squibb-Novo, Princeton, New Jersey) in the morning and 4½ U at 11 p.m. In addition, she was asked to administer 3½–5½ U of Actrapid (regular) human insulin (Squibb-Novo) ½ h before each meal for a total of 21½ U of insulin daily.

On 5/30, we received the results of the throat culture and prescribed 500 mg oral potassium penicillin V every 6 h for 2 wk.

On 6/12, the patient phoned us complaining of swelling of her hands and itching all over her body. She admitted to having numerous insect bites and disclosed that a peacock

had invaded her home on the previous day (possibility of flea or tick bites?). She was instructed to discontinue the penicillin. A brief trial of diphenhydramine HCl (Benadryl, Parke Davis, Morris Plains, New Jersey) did not improve the symptoms. Later that day she developed chills and joint pains while the itching became even more severe. The itching exacerbated considerably 20 min after injecting one of her doses of Actrapid human insulin. This exacerbation lasted 1–2 h. A. O. was immediately started on oral prednisone, 40 mg/day, in spite of her diabetes. She was instructed to discard the vial of Actrapid she had been using and to use a fresh vial.

The symptoms vanished while she was on a 40 mg of prednisone but her BG, which had been virtually normal around the clock on the new insulin/diet regimen, now became very erratic. Therefore, we began to taper the prednisone on 6/16. On 6/17, she experienced another exacerbation of itching (20 min after injecting Actrapid insulin). Again it lasted 1–2 h. On 6/18, she returned to the office for a routine phlebotomy while on 30 mg/day of prednisone. Her body was now sparsely covered with 1 mm, pink, nearly flat papules. After the venipuncture, a number of scarlet streaks suddenly appeared on her skin. She claimed that these streaks occupied sites that she had previously scratched. A test for dermatographia was, therefore, performed and was strongly positive.

On 6/22, while on 10 mg prednisone/day she complained of new episodes of itching and occasional small hives, all unrelated to the time of insulin injections. Her BGs were now essentially normal. The prednisone was increased to 20 mg/day but a mild itching continued and her BGs again became erratic.

On 6/25, we again began to taper the prednisone but this time instructed the patient to take an oral calcium channel blocker, nifedipine (Procardia, Pfizer Laboratories, New York, New York), 10 mg, at the first sign of symptoms. This was tried at the next attack and successfully terminated all symptoms in less than ½ h. In the ensuing weeks she experienced fine hives or itching or both nearly every day, usually between the hours of 4:30 and 6 p.m. None of the episodes appeared related to insulin injections and all responded to oral nifedipine. In an effort to determine if these events were actually responding to the nifedipine or were terminating spontaneously, the patient was asked to treat subsequent episodes by biting open the nifedipine capsule and holding the liquid nifedipine sublingually for a few minutes. When she did this, the episodes terminated within 10 min. The episodes continued to occur in a progressively milder form until 7/13, about 1 mo after the initial event. Her BGs have been essentially normal throughout each day, except during menses.

Because of this benign outcome, we made no effort to establish a final diagnosis. The symptoms were characteristic of cholinergic urticaria, which is usually treated with antihistamines, specifically cyproheptadine or hydroxyzine. Differential diagnoses include delayed hypersensitivity reactions to insect bites, human insulin, or to penicillin.

Our choice of nifedipine for the treatment of dermatologic eruptions stems in part from its known action as an inhibitor of mast cell degranulation. In this role it prevents the release of histamine, serotonin, SRSA, prostanoids, etc., from mast cells that have migrated into the microvasculature and interstitium of the skin. The advantages of sublingual nifedipine relative to the aforementioned antihistamines reside in its relative freedom from significant adverse side effects and the rapid termination of its activity (about 3 h) after an onset of action within 5–10 min.

It is important to note that this medication should not be used prophylactically for the prevention of urticaria but only to treat an ongoing episode. Chronic usage for the treatment of asthma is known to cause spontaneous "breakthrough" exacerbation of asthmatic symptoms due to the excessive accumulation and resultant release of secretory granules by the mast cell population inhabiting bronchi (personal communication, Arye Rubenstein, M.D.).

To our knowledge, this is the first report of the use of a calcium channel blocking agent for the treatment of urticaria.

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Rhabdomyolysis Associated with Hyperosmolar Nonketotic Coma

Hyperosmolar nonketotic coma (HNKC) is not rare in the older diabetic population, accounting for 5–15% of all admissions for coma associated with diabetes.[1]

Complications associated with HNKC include severe electrolyte disturbances, phosphate depletion, cerebral edema, arterial thrombosis, myocardial infarction, cardiac dysrhythmia, and azotemia. This study demonstrates another complication of HNKC, rhabdomyolysis, manifested by extreme elevations of creatinine kinase (CK), with levels to 29,000 IU/L.

Case Report

C. J. is a 55-yr-old black man with a history of NIDDM of 10 yr duration. His diabetes had been well-controlled by diet alone. However, 7 days before admission, the patient noted progressive polyuria and polydipsia. Two days before admission, the onset of lethargy was noted by his family and he was brought to the emergency room. There was no history of trauma, seizures, or drug or alcohol abuse. He had no known cardiovascular, mental, or renal impairment before admission. He denied chest discomfort. He had been on hydrochlorthiazide for several years for treatment of hypertension. His serum potassium levels had always been normal. The dosage had not been changed.

Physical examination. On admission to the hospital, he was lethargic but arousable. Blood pressure was 80/40, pulse rate 120, respiratory rate 30, temperature 39°C. Physical exami-