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BP, BLOOD PRESSURE; NIDDM, NON-INSULIN-DEPENDENT DIABETES MELLITUS; BMI, BODY MASS INDEX; FBG, FASTING BLOOD GLUCOSE; sBP, SYSTOLIC BLOOD PRESSURE; dBP, DIASTOLIC BLOOD PRESSURE.

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Glucotoxicity and oxidative hemolysis in G-6-PD deficiency

Hemolysis in a G-6-PD–deficient subject may occur as a result of drug administration (1), infection (2), renal failure (3), insulin (4), diabetic ketoacidosis (5), and hypoglycemia (6). We report a 30-yr-old insulin-requiring diabetic individual who developed the complication in the absence of these conditions.

P.S., a 30-yr-old surgeon presented with polyuria, polydipsia, and a weight loss of 10 kg over the preceeding 3 mo. His appetite was normal, he had no major illnesses in the past, and he was not known to be G-6-PD deficient. He had no family history of diabetes mellitus. He was not on any medication.

On examination, he was 173 cm tall and weighed 61 kg (BMI 20 kg/m^2). His pulse was 90 bpm and BP was 120/80 mmHg. He had no pallor, jaundice, cyanosis, clubbing, or peripheral lymphadenopathy. On examination, cardiovascular, respiratory, alimentary, and neurological systems were normal.

The investigations were as follows: Hb 15.8 g/dl; WBC 8250 cells/mm^3; (P:42, L:56, E:2); erythrocyte sedimentation rate 2 mm/1st h; FPG 14.99 mM; postglucose plasma glucose 1 h :25.7 mM, 2 h :22.15 mM; serum insulin 0 h 27.6 pM; 1-h postglucose 60 pM; 2-h postglucose 21.6 pM; HbA_1 16.5%; cholesterol 4.34 mM; triglycerides 1.02 mM; blood urea 9.3 mM; serum creatinine 97.24 μM. Urinalysis revealed glycosuria. The chest (pa) X ray and electrocardiogram were normal.

The patient was treated with a meal plan of 1650 kcal/day (carbohydrate 55%, protein 20%, fat 25%) and a split dose insulin regimen (regular 12 and Lente 16 before breakfast and regular 8 and Lente 12 before dinner).

The patient presented with jaundice 3 days later. On examination he was pale and had icterus, however, the vital functions and systemic examination were normal. The Hb was 7.0 g/dl, WBC count was 6700 cells/mm^3, and the reticulocyte count was 14.4%. The G-6-PD activity was deficient. The serum bilirubin was 3.8 mg/dl; direct bilirubin 0.6 mg/dl; indirect bilirubin 3.2 mg/dl, serum glutamate pyruvate transaminase 71 U/L; serum alkaline phosphatase 50 U/L; blood glucose 10.06 mM; serum creatinine 97.24 μM; urinalysis revealed glycosuria. The Hb electrophoresis revealed an HbA fraction. Serum electrolytes were normal. The anti-nuclear antibody and the anti-DNA antibody were absent.

The patient was diagnosed with hemolysis in erythrocytes deficient in G-6-PD. The patient was managed conservatively on diet, intravenous fluids, and regular insulin. Hb gradually rose to 11.6 g/dl on 5/3/91, and the patient was discharged on a meal plan of 1700 kcal/day and a split-dose insulin regimen.

The patient as of today (9/28/92) has gained 7 kg and is well controlled on the prescribed regimen. He has had no further episodes of hemolysis.

Hemolysis in G-6-PD–deficient subjects is the result of oxidative damage to erythrocytes (7). Oxidative stress is observed in subjects with chronic hyperglycemia because of enhanced production of oxygen free radicals (8,9). These, in turn, produce cellular injury (10). Hyperglycemia appears to be the operative mechanism in precipitating hemolysis as other factors (1–6) were excluded.

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G-6-PD, GLUCOSE-6-PHOSPHATE DEHYDROGENASE; NIDDM, NON-INSULIN-DEPENDENT DIABETES MELLITUS; BMI, BODY MASS INDEX; BPM, BEATS PER MINUTE; BP, BLOOD PRESSURE; WBC, WHITE BLOOD CELLS; FPG, FASTING PLASMA GLUCOSE.

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Eye color and IDDM

It has been shown that a relatively large proportion of IDDM patients in southern Germany have a low-pigment eye color (blue or green) compared with nondiabetic control subjects (66 vs. 38%, $P < 0.01$) (1). Although no studies exist concerning the exact percentage, it is commonly accepted that dark eye colors prevail among Greeks.

The eye color of 42 randomly selected IDDM patients and 135 nondiabetic control subjects was evaluated in daylight by the same observer. Study subjects were all Greek in origin. They did not differ concerning mean age and sex (30.1 ± 11.2 vs. 32 ± 11.5 yr of age, $P = 0.44$; M/F 22/20 vs. 65/70, $P = 0.63$). Classification was done empirically into high-pigment eye color (brown or black iris) and low-pigment eye color (blue or green iris). The prevalence of low-pigment eye color was not significantly different among IDDM patients and control subjects (33.33 vs. 23.7%, $P = 0.21$).

In conclusion, we believe that the described finding of an increased frequency of low-pigment eye color in IDDM patients is not a unanimous observation. The discrepancy between the German study and this one is perhaps attributable to ethnic differences of the studied samples.

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Comments on "Prevalence of Carotid Atherosclerosis in Diabetic Patients" by Kawamori et al.

Kawamori et al. (1) give impressive data of their ultrasound measurements of the carotid artery wall. The results concerning the great majority of their patients (275 NIDDM patients) are evident. The number of the investigated IDDM patients, however, is very small, and we cannot agree with the statements concerning young diabetic patients.

The authors investigated 20 IDDM patients 21–66 yr of age (the NIDDM patients were >30 yr of age). Unfortunately, they do not mention how many patients were included in the group 20–29 yr of age. The number must be far lower than 20, because it is only a part of the group of 20 IDDM patients. In spite of the small number of patients the authors state that the IMT was significantly greater in diabetic than in nondiabetic subjects of this age-group. They conclude, that "young diabetic subjects were found to have advanced atherosclerosis of the carotid arteries." First, an increased IMT is believed to be a sign of early, not advanced atherosclerosis (2–4). Second, our experience would lead us to reject the major conclusion made by the authors.

For the past 2 yr, we have performed a prospective ultrasound study of the carotid artery wall (measuring IMT) in IDDM patients ≤40 yr of age. Initial results were presented at the 28th Annual Meeting of the EASD in Prague 1992 (5), including the data of 125 patients. We found alterations of the carotid artery wall (increased IMT and/or plaques) in 21% of our patients with diabetes duration >2 yr. Patients with an increased IMT more often showed nephropathy than patients with normal wall thickness, the difference was highly significant. Moreover, patients with additional plaques showed hypertension and hypercholesterolemia significantly more often than patients with normal carotid artery wall.

Our investigations suggest that the risk of early atherosclerotic lesions of the carotid artery wall in young IDDM patients is increased in the presence of some accompanying diseases, especially nephropathy. IDDM patients without late complications or accompanying dis-