OBSERVATIONS

Interferon-α and Development of Type 1 Diabetes

A case without insulin resistance

Interferon has been considered to contribute to the development of diabetes (1). In 1992, Fabris et al. (2) reported a case of type 1 diabetes with onset during interferon-α treatment for chronic hepatitis, concluding that interferon triggered the autoimmune destruction of β-cells. Because interferon also produces insulin resistance and impairs glucose tolerance, Koivisto et al. (3) have claimed that insulin resistance evoked by interferon therapy may indirectly accelerate autoimmune destruction of β-cells (4). We encountered a case of type 1 diabetes presenting 7 months after interferon therapy without development of insulin resistance.

A 53-year-old woman had a history of elevated serum aminotransferase activity since 1994. Hepatitis C virus antibodies were detected in serum; markers for hepatitis B virus were absent. The patient had not abused alcohol, and fasting plasma glucose was 5.7 mmol/l without glycosuria. Examination of a liver biopsy specimen revealed chronic active hepatitis. A 75-g oral glucose tolerance test (OGTT) performed before any treatment with interferon revealed normal glucose tolerance. In April, 1996, interferon-α was started at 10 MU daily for 4 weeks, and then three times weekly for 20 weeks. At 3 months after the beginning of interferon therapy, fasting plasma glucose transiently increased to 8.2–9.3 mmol/l, but returned to normal range (<7.8 mmol/l) within a month. Serum aminotransferase had become normal 4 months after interferon therapy.

At 7 months after cessation of interferon therapy, the patient experienced the sudden onset of polyuria accompanied by thirst and consulted our hospital. Fasting plasma glucose was 14.0 mmol/l, postprandial glucose was 27.4 mmol/l, and urinary C-peptide excretion was low, at 5.2 μg/day. Ketoacidosis was not present. In a 75-g OGTT, the plasma glucose concentration was 25.4 mmol/l at 60 min, and the peak insulin level was 6.6 μU/ml. Serum C-peptide increased from 2.1 to 4.8 ng/ml after intravenous administration of 1 mg of glucagon. The concentration of anti-GAD antibody was 48,800 U/ml. The HLA locus was typed as HLA DR4, 8; DQ1, 4 (DQB1* 0401, 0601). Insulin sensitivity was estimated by the steady-state plasma glucose (SSPG) method with the use of Sandostatin (5). SSPG at 120 min was 5.7 mmol/l, which indicated normal insulin sensitivity. Insulin (10 U/day) was started, and 3 weeks later, fasting plasma glucose had decreased to 7.0 mmol/l.

Our patient had a sudden onset of diabetes 7 months after cessation of interferon therapy. She showed low excretion of insulin, and a high titer of anti-GAD antibody, but no insulin resistance. How type 1 diabetes occurred after so long an interval following interferon treatment is not clear, but insulin resistance does not appear to be involved. More likely, interferon-α directly triggered autoimmune destruction of β-cells, leading to type 1 diabetes.

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Methionine Synthase D919G Mutation in Type 2 Diabetes and Its Relation to Vascular Events

Methionine synthase (N^5-methyltetrahydrofolate-homocysteine 5-methyltransferase) (MS) is a mammalian cobalamin-dependent enzyme catalyzing the production of methionine from homocysteine by remethylation, and deficiency of MS activity results in hyperhomocysteinemia (1). A common D919G (2756A → G) mutation at the human MS gene has recently been identified (2). There is now considerable evidence of an association between modest homocysteine elevation and vascular disease (3–5); to explore possible relationships between the MS genotypes and cardiovascular risk in diabetes, we studied 668 Australian type 2 diabetic patients aged 62.3 ± 0.5 years (mean ± SEM) with and without documented macro- and microvascular complications.

The genotype distribution was 3.7, 34.0, and 62.3% for GG, GA, and AA, respectively, and in Hardy-Weinberg equilibrium ($\chi^2 = 0.731$, $P > 0.05$), and did not differ between men and women ($\chi^2 = 3.511$, $P = 0.173$). The GG homozygote frequencies in the patients with angina pectoris, myocardial infarction (MI), stroke, and peripheral vascular disease (PVD) were 16.0, 4.0, 4.3, and 13.0%, respectively, and were not different from those in patients without these vascular events (angina pectoris: $\chi^2 = 0.229$, $P = 0.892$; MI: $\chi^2 = 3.686$, $P = 0.158$; stroke: $\chi^2 = 0.097$, $P = 0.953$; PVD: $\chi^2 = 3.269$, $P = 0.195$). There were also no significant associations between the MS D919G mutation and microalbuminuria ($\chi^2 = 2.846$, $P = 0.241$), neuropathy ($\chi^2 = 4.210$, $P = 0.122$), or retinopathy ($\chi^2 = 1.999$, $P = 0.368$).

We conclude that the MS D919G mutation is common in type 2 diabetes patients (an allele frequency of 20.7% in the present series), but that it is not associated with the occurrences of macro- or microvascular complications in these patients. These results suggest that the mutation is unlikely to be functional.

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Do Mobile Cellular Phones Interfere With Portable Insulin Pumps?

Medical devices may potentially suffer electromagnetic interferences generated by mobile cellular phones, especially when phones are used in close proximity to patients (1). Such interferences depend not only on the strength and frequency of the electromagnetic field, but also on the intrinsic susceptibility and protection of the medical equipment. Resulting functional abnormalities of medical devices may be hazardous for patients, especially those with cardiac pacemakers (2,3). To our knowledge, there are no available data about the electromagnetic compatibility between cellular phones and portable insulin pumps.

Our study was supported by the Centre National d'Etudes des Télécommunications. We have tested two different models of insulin pumps, the Microjet Quark and the Minimed 506, and three types of digital cellular phones, the Global System for Mobile Communications (GSM) Motorola International 2500 (900 MHz; maximum peak power, 8 W), the GSM Lisa P9026 (900 MHz; 2 W), and the Digital Cellular System (DCS) Flare B300 (1,800 MHz; 1 W). Pumps were filled with ^{125}I-labeled insulin and Velosulin U100 (Novo Nordisk, Bagsvaerd, Denmark) and were set to deliver a basal infusion of 2 U/h for 2 h, along with three boluses of 10 U. We measured successively the amount of insulin delivered in vitro under basal conditions and during two simulation tests, in which each phone, while transmitting at maximal power, was placed in 10-cm proximity to, and then in direct contact with, the pumps.

When the Microjet Quark was in direct contact with the 8-W GSM model, the latter activated the alarm and induced a large reduction of the basal infusion (80%), whereas the boluses were not modified. No effect was observed when the phone was placed 10 cm from the pump. Similar results were obtained with the 2-W GSM model, but only a modest (15%) reduction of the basal infusion was observed when the phone was set in direct contact with the pump. Conversely, neither alarm activation nor an effect on the bolus or basal infusion was observed with the 1-W DCS model, even when placed in direct contact with the pump.

With the Minimed 506, alarm activation did not occur, nor was there an effect on the bolus or basal infusion, regardless of the phone model or distance tested.

These preliminary data suggest that interferences between cellular phones and portable insulin pumps do not seem to represent a major problem in clinical practice, given that the majority of cellular phones used today have a maximum power of 1 or 2 W. Furthermore, those phones are reducing their transmission power according to the proximity of the base station. Therefore, in most cases, after 10 sec of emission, their power is far less than 2 W. Nevertheless, one should be cautious with some models of mobile phones, which may potentially induce functional abnormalities in some types of pumps when the two devices are used in very close proximity. In addition, further tests that include implantable pumps as well as other models of portable pumps are needed.

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Glycemic Control During Exercise in Type 1 Diabetes

Comparison of a new medical food bar with usual care

People without diabetes have a myriad of excuses for not exercising—lack of time, little immediate benefit, no energy, no money to join a gym, and the like. Many of these excuses are used, likewise, by patients with diabetes. Diabetes poses the added risk, however, of the development of hypoglycemia during exercise, which is reported to be common in many studies on exercising patients with diabetes (1–3). The purpose of this study was to investigate how a new med-

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