fair; the patient complained only of moderate itching, which did not lead her to drop out of the study.

These results show that short-term treatment with coenzyme Q10 and L-carnitine, while acting on mitochondrial muscle functions, were unable to restore insulin secretion and/or insulin sensitivity in our patient. This discrepancy in effectiveness of the treatment on these two tissues suggests that the impairment of muscle oxidative processes is probably not involved in the glucose intolerance in this disease. This therapeutic failure, however does not definitely mean that coenzyme Q10 is not of potential benefit in the management of diabetes secondary to mitochondrialriopathy. It is possible that pancreatic beta cells are less sensitive and in need of a higher dosage of coenzyme Q10 for a longer duration in order to improve mitochondrial functions. In addition, we can hypothesize that treatment was introduced too late in the natural course of the disease. Katagiri et al. [4] have shown that there is a progressive loss of insulin secretion in some subjects with the 3243 mutation. The insulin secretion in our patient was reduced to levels usually observed in classic insulin-dependent diabetes, suggesting that there was a profound loss of beta cells. It is probable that treatment applied at earlier stages, such as during either glucose intolerance or non-insulin-dependent diabetes, may improve insulin production. Because these drugs are well tolerated and their beneficial effect on other tissues such as muscle suggest extending such a clinical trial to patients with less severe pancreatic lesions.

Yours sincerely,

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Could differences in body mass index and/or insulin sensitivity explain the association between parental diabetic nephropathy and risk of diabetes in offspring?

Dear Sir,

McCance et al. [1] describe a population-based study of the association between parental diabetes, diabetic nephropathy and risk of diabetes in offspring. Diabetic nephropathy in a parent

was associated with an increased risk of diabetes in offspring, particularly among offspring under age 35 years. This association persisted after controlling for age, age at onset of parental diabetes and diabetes in the other parent using logistic regression. The authors conclude that "the present results provide support for parental diabetic nephropathy, independent of age at onset of parental diabetes, conferring an increased risk for diabetes in the offspring".

Nowhere in the paper do the authors mention data on the subjects' body mass index (BMI) or degree of adiposity, although such data would certainly have been available to the investigators. The associations between high BMI, insulin resistance, and increased risk of non-insulin-dependent diabetic mellitus are well established [2]. There is also evidence that insulin resistance may cause predisposition to diabetic nephropathy [3-5]. It is thus conceivable that the association observed

by McCance et al. [1] between parental diabetic nephropathy and risk of diabetes in offspring might be largely mediated by adiposity and consequent insulin resistance. Information on subjects' BMI and, if possible, other measures of insulin sensitivity, and the results of logistic regression analysis including these variables would facilitate the interpretation of this paper's results.

Yours sincerely,
R.J. Sigal, M.B. Freire, A.S. Krolewski

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Response from the authors

Dear Sir,
Sigal et al. ask whether the effect of parental diabetic nephropathy on the risk for non-insulin-dependent diabetes mellitus (NIDDM), observed in our recent paper [1], might be mediated by adiposity or insulin resistance. Suitable measures of in-

Table 1. Multiple logistic regression models for diabetes in offspring of [DR × D], [DR × ND], [D × D] and [D × ND] parental combinations. Dependent variable: diabetes in offspring

Variable	Odds ratio	95 % CI	p value
<i>Model without offspring's BMI</i>			
Age of offspring (per 10 years)	4.15	3.08–5.57	0.0001
DR in first parent (DR vs D)	2.47	1.41–4.32	0.0015
D in second parent (D vs ND)	1.65	0.93–2.94	0.0899
Age at onset of parental diabetes (per year)	0.95	0.92–0.98	0.0003
<i>Model including offspring's BMI</i>			
Age of offspring (per 10 years)	4.30	3.17–5.84	0.0001
DR in first parent (DR vs D)	2.42	1.38–4.24	0.0021
D in second parent (D vs ND)	1.68	0.92–3.06	0.0901
Age at onset of parental diabetes (per year)	0.94	0.92–0.97	0.0002
BMI of offspring (per 5 kg/m ²)	0.99	0.84–1.17	0.8746

95 % Confidence interval (CI)

DR, Diabetic with renal disease; D, diabetic without renal disease; ND, not diabetic. Age, at onset of diabetes in diabetic parent (or younger of two ages if both parents diabetic). The top section of the table is equivalent to Table 3 in McCance et al. [1]

ulin resistance are not available for most of our subjects but we do have data on body mass index (BMI). To shorten the manuscript, we omitted these data from our paper; we felt that BMI was not a confounder, but a potential intermediate in the causal pathway. However, as shown in Table 1, incorporation of the offspring's BMI in the logistic regression model did not substantially change the estimates of the odds ratios for parental nephropathy. In fact, the effect of BMI was not significant in this model; this may reflect the fact that individuals in this population tend to lose weight after the diagnosis of diabetes [2]. It is therefore possible that the current BMI does not represent pre-diabetic adiposity and that obesity is still intermediate between parental nephropathy and diabetes in the offspring. However, in contrast to nephropathy, obesity does not strongly cosegregate with diabetes in Pima families [3]. Moreover, among diabetic subjects, the incidence of elevated urinary albumin excretion is higher among thinner than among heavier individuals [4]. These findings, taken together, suggest that the effect of parental diabetic nephropathy on the risk of NIDDM in the offspring is not mediated by adiposity.

Yours sincerely,
D.R. McCance, R.L. Hanson, D.J. Pettitt, L.T.H. Jacobsson,
P.H. Bennett, D.T. Bishop, W.C. Knowler

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