patients. The authors reported that insulin-dependent diabetic patients, in whom left ventricular ejection fraction (EF) as assessed by radionuclide ventriculography was normal at rest, had a poor increase or even a decrease in EF during dynamic exercise. Coronary angiography and endomyocardial biopsy were performed on 8 of the 16 patients with an abnormal EF response to dynamic exercise. All these 8 patients had normal coronary arteries, but biopsy specimens showed arteriolar wall thickening and interstitial fibrosis in 5 patients and basement membrane thickening suggestive of diabetic microangiopathy in 2 patients. It is logical to consider that diabetic microangiopathy involving myocardium may be causally related to the impaired left ventricular function observed in these patients, but, as the authors emphasize, other factors may also be involved. There is both experimental and clinical evidence to suggest that metabolic abnormalities may play a role in this respect. Thus, impaired left ventricular function or diabetic cardiomyopathy in experimental diabetes is corrected with insulin therapy [2, 3]. We reported some years ago an improvement of systolic time intervals (STI) in a group of newly diagnosed Type 2 (non-insulin-dependent) diabetic patients after starting diet therapy for diabetes. The correction in STI was correlated with the decline in fasting blood glucose level. Furthermore, physical working capacity of the diabetic patients improved concomitantly with the correction of STI and hyperglycaemia [4]. The results yielded indirect evidence for reversibility of impaired left ventricular function. Recently, we evaluated left ventricular systolic function at rest and during exercise in 9 Type 2 diabetic patients with low postglucagon C-peptide, indicating partial insulin deficiency. Before starting insulin treatment these patients showed a prolonged pre-ejection period (PEP) and an elevated PEP/LVET-ratio at STI-registration. In addition, the patients had a poor increase in EF during exercise as assessed by radionuclide ventriculography. After starting insulin therapy the metabolic control improved; concomitantly the abnormalities in STI changed to the normal direction, and EF response to dynamic exercise improved significantly (J. Mustonen et al, unpublished results), confirming our previous findings on newly diagnosed Type 2 diabetes. Therefore, we emphasize that metabolic disturbances, e.g. hyperglycaemia, insulin resistance or other related metabolic abnormalities, may play an important role in the pathogenesis of left ventricular dysfunction in patients with Type 2 diabetes. This dysfunction is not necessarily a "long-term" complication of diabetes, since it may be present already at the time of diagnosis of Type 2 diabetes and, as observations show, it may be reversible by improved metabolic control.

Yours sincerely,

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More on the question of a specific heart disease in diabetes

Dear Sir,

I was interested to read the recent report by Fisher et al. [1] in which the authors conclude that abnormalities in left ventricular function in diabetic patients with normal coronary angiography are due to underlying specific diabetic heart disease.

The presence of fibrosis and basement membrane thickening in biopsy specimens from hearts of diabetic patients has been previously reported. However, the authors' histological data is based on only 8 patients; only 5 of the patients showed interstitial fibrosis and only 2 showed basement membrane thickening. The authors themselves comment that the latter observation may well be due to artefact. While they have attempted to relate these pathological features to measurements of left ventricular function, this is a very small number of patients on which to base firm conclusions. In addition, their specimens were from the *right* ventricle while they were measuring *left* ventricular function.

It has been shown [2, 3] that left ventricular function may vary over time, depending on diabetic control, and a one-off measurement of left ventricular function need not imply permanent change. The authors have carried out their measurements once only, and cannot conclude that any observed abnormalities of left ventricular function are fixed or permanent. Under these circumstances, it is invalid to relate histological conclusions to functional studies.

In contrast to the authors' conclusions, I would suggest that their evidence is not substantive enough to support the concept of a specific heart disease in diabetes, although this remains a possibility. They may well have added a further piece to the jigsaw which in time, hopefully, will become completed.

Yours sincerely,

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Prevalence of diabetes mellitus in elderly subjects in east Finland

Dear Sir,

In a recent article by Tuomilehto et al. [1] published in *Diabetologia*, very high prevalence rates for diabetes mellitus in east Finland were reported. According to their results, 30% of men aged 65 to 84 years had diabetes and 32% had impaired glucose tolerance (IGT).

These prevalence rates are of similar magnitude as those observed in Pima Indians – known to have the highest prevalence of diabetes in the world [2, 3]. Some methodological aspects related to the performance of oral glucose tolerance tests may, however, have led to an increased prevalence of abnormal glucose tolerance in the study of Tuomilehto et al. In their study the fasting period was not standardised and could be as short as 4 h. Furthermore, diurnal variation in glucose tolerance – higher 2 h blood glucose values after noon – was not taken into account, since glucose tolerance tests were carried out from 08.00 until 16.30 hours. In addition, the study population of Tuomilehto et al. was not representative of the population living in east and west Finland because the study was based on 763 survivors of the Finnish cohort of the “Seven Countries Study” of 1,711 men first examined in 1959 and followed up for 25 years [4, 5]. In such a cohort of elderly men one would rather expect a low prevalence of abnormal glucose tolerance.

We have observed very different prevalence rates for IGT and diabetes in our ongoing study of elderly subjects aged 65–74 years living in the town of Kuopio, east Finland. The main aim of our study is to determine the prevalence rate of asymptomatic hyperglycaemia and its relation to cardiovascular morbidity and cardiovascular risk factors. The study population has been randomly selected from the population register of Kuopio. All study subjects undergo a 2-h oral glucose tolerance test (75 g of glucose) at 08.00 hours. Plasma glucose is determined by glucose dehydrogenase method (Merck Diagnostica, FRG). Over 350 individuals (about one-third of the whole sample) have been studied so far. Of the 256 subjects without a history of previously diagnosed diabetes, 71.6% of men (68/95) and 66.5% of women (107/161) had normal glucose tolerance according to the WHO criteria [6], 18.9% of men (18/95) and 23.6% of women (38/161) had IGT and 9.5% of men (9/95) and 9.9% of women (16/161) had diabetes. The corresponding prevalence rates calculated on the basis of Table 2 in the article of Tuomilehto et al. were for men (women were not studied): normal glucose tolerance 45.7% (90/197), IGT 37.6% (74/197), and diabetes 16.8% (33/197). Prevalence of abnormal glucose tolerance (including IGT and diabetes) was in our study 28.4% in men but 54.3% in the study of Tuomilehto et al. The two-fold higher prevalence rate reported by Tuomilehto et al. is probably related to their study design. Our results on the prevalence of diabetes in the elderly resemble quite closely those published from the United States [7, 8] and do not support the view suggested by Tuomilehto et al. that elderly subjects living in east Finland would have an exceptionally high prevalence rate of diabetes, comparable to that observed in Pima Indians.

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Response from the authors

Dear Sir,

We thank Drs. Mühlhauser, Bruckner and Howorka for their kind interest in our papers and the review [1] on near-normoglycaemia and microvascular complications. As far as we understand, the authors state that it is not necessary to perform any further investigations into the impact of near-normoglycaemia on diabetic microangiopathy. We do not share their view. As we stated clearly in the review [1], the dose response curve between blood glucose and the magnitude of diabetic microangiopathy is not known. Furthermore, it is not known if the blood glucose needs to be normalized totally or only partially to avoid diabetic microangiopathy. Neither does the impact of poor metabolic control seem to be the same in different individuals [2]. These are important points, because it is not without hazards to try to normalize blood glucose, since hypoglycaemia and what we call “regulopathy” might be severe side effects. Regarding their comparison between glycosylated haemoglobin from different studies, this direct comparison is problematical. It has been shown [3] that the relationship between mean blood glucose and glycosylated haemoglobin is curvilinear. Thus, a decrement of glycosylated haemoglobin at a high level represents a larger reduction in mean blood glucose than at a lower level of glycosylated haemoglobin.

The “control group” in the Oslo study was intensified, and received the same care and attention as those in the intensified groups. They had lower glycosylated haemoglobin than the average diabetic patient.

We conclude that it is still necessary to perform well controlled clinical trials, taking into account that the knowledge at which we have arrived is achieved not only by “clinical experience”, but by careful long-term trials.

Yours sincerely,
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