Despite the fact that Deckert et al. quoted 113 references to support their case it is more likely that the enhanced extravasation and glomerular filtration of albumin in diabetic patients are consequences of blood viscosity-related increases in intracapillary pressure rather than to compositionally-induced increases in basement membrane permeability. The clinical significance of this conclusion is that the blood viscosity of diabetic patients is potentially correctable.

Yours sincerely,
L. O. Simpson

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Dr. L. O. Simpson
Department of Pathology
University of Otago
P.O. Box 913
Dunedin
New Zealand

Combined response from the authors

Dear Sir,

We are well aware of Dr. Simpson's fascinating contribution to the pathogenesis of diabetic complications and we appreciate his fighting spirit. However, we did not mention his ideas in our review because they do not seem to be in accordance with the natural history of diabetic complications. Increased blood viscosity might well contribute to increased glomerular permeability and impaired tubular reabsorption of macromolecules but – besides during periods of very poor

diabetes control – increased blood viscosity seems not to be present in diabetic patients before the later stages of diabetic nephropathy [1, 2]. We, therefore, do not believe that changes in blood viscosity can help us to explain why some patients develop nephropathy and why those who are affected by persistent albuminuria also seem to suffer from a much higher incidence of proliferative retinopathy, exaggerated mesangial expansion and macroangiopathy.

It seems evident that not all studies on proteinuria and diabetic patients could be mentioned in our list of references. Especially we decided to give studies with sodium dodecyl sulfate-polyacrylamide gel electrophoresis a low priority because of the well-known risk for artefacts. Furthermore, we excluded studies on non-diabetic subjects during exhaustive exercise because such conditions are less relevant in the elucidation of what happens during the peaceful life of diabetic patients.

It is evident from many studies as also mentioned in our review that blood pressure plays an important role for the degree of proteinuria in diabetic patients. However, we have many reasons to believe that increased hydrostatic pressure is not the cause of albuminuria and the complications associated with it. We will review the experimental and epidemiologic data on this topic very soon (K. Nørgaard, B. Feldt-Rasmussen, T. Deckert, unpublished observations).

Dr. Simpson argued against genetic factors in the development of nephropathy by pointing to one case of a diabetic kidney which was grafted into a non-diabetic recipient [3] but he has forgotten to mention that according to our hypothesis hyperglycaemia or hyperglycaemia-related changes are necessary but not sufficient conditions for the development of late diabetic complications.

We are thankful for the letter of Drs. Roy and Rick and we apologize for having overlooked their publication [4]. The observations of Drs. Roy and Rick would fit beautifully to our hypothesis.

Accumulated biological and epidemiological knowledge about diabetes makes it increasingly difficult to understand the problem of diabetic complications. We do hope that our hypothesis can give new spirit to sound experiments – but we must not neglect the natural history of what really is happening.

Yours sincerely,
T. Deckert, B. Feldt-Rasmussen, K. Borch-Johnsen, T. Jensen and
A. Kofoed-Enevoldsen

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Dr. T. Deckert
Steno Memorial Hospital
Niels Steenensvej 2
DK-2820 Gentofte
Denmark