Kidney International, Vol. 41 (1992), pp. 717–718

Introduction: Symposium on the Progress in Diabetic Nephropathy

In the past decade since *Kidney International* first published a collection of original research articles on diabetes mellitus and the kidney [1] the magnitude of the problem has revealed itself in the ever increasing population of diabetic patients entering end-stage renal failure treatment programs. Thus, as a contributor to end-stage renal disease, diabetes exceeds all forms of glomerulonephritis added together, and as a single cause, is rivaled only by hypertension. That these sad facts underestimate the enormity of the problem is reflected in the paper of Damsgaard et al in this issue [2], in that the concordance of serious kidney and macrovascular complications of diabetes confers a much higher risk of cardiovascular mortality in patients with microalbuminuria, before uremia ensues. In this past decade the pace of research in diabetic nephropathy has substantially quickened. Hopefully, this special edition of *Kidney International* devoted to diabetic nephropathy presents an accurate reflection of those ongoing scientific efforts which will eventually contribute to improved approaches to prevention and treatment of this growing public health problem.

Perhaps the linchpin of the understanding of diabetic nephropathy is a clear delineation of the epidemiology and natural history of the disorder. Hypothesis or experimental observations which conflict with known clinical patterns must be viewed with great skepticism. Thus, for example, it will be important to unravel the factors contributing to the familial aggregation of diabetic nephropathy risk [3], whether this is an inherited predisposition, perhaps related to hypertension (indeed an area of intense debate which is represented by papers in this issue) or due to familial clustering of noninherited risk factors remains to be determined. It should be self-evident that the clinical expressions of diabetic nephropathy would not occur unless the specific and unique constellation of structural abnormalities underlying this disease were far advanced. Although much has been learned in the last decade regarding the structural-functional relationships in diabetic nephropathy, this remains an area of fruitful study, as reflected in this issue of *Kidney International*. The universality of the effects of diabetes on the kidney is documented in the paper of Hayashi et al [4], indicating typical lesions of diabetic nephropathy in Japanese patients with non-insulin dependent diabetes mellitus. However, as Parving et al point out [5], not all patients with diabetes and proteinuria have diabetic nephropathy and, particularly among type II patients without retinopathy, a high index of suspicion for other renal diseases is warranted.

It is also clear that the aggregrate of structural abnormalities which we call diabetic nephropathy represent increased production, decreased breakdown, or both of renal extracellular matrix components, thus resulting in their accumulation over time. Papers reflecting new hypothesis as to the nature of the biochemical derangements, new technologies for the study of the regulation of matrix production in diabetes and new views regarding fundamental glomerular chemistry are presented in this collection of articles. These research directions are very likely to be important in improving our understanding of the genesis of the critical lesions of diabetic nephropathy and, thus, in our ability to interfere with the early processes.

Diabetes is clearly a highly complex disturbance of the body's internal milieu, and altered hormonal regulation could, through hemodynamic perturbations, through more direct effects on extracellular matrix kinetics or through other mechanisms, influence the rate at which the lesions of diabetic nephropathy develop. A series of papers, two of them by Jaffa et al [6] and Correa-Rotter et al [8] using newer molecular biologic techniques, address these important directions.

Early functional disturbances of the kidney in diabetes have long been recognized [1]. Several papers dealing with prognostic significance of increased glomerular filtration rate and microalbuminuria continue the ongoing focus toward evolving earlier, relatively non-invasive, markers and predictors of the later development of serious renal disease and its associated cardiovascular complications (Messent et al [7]). These studies may also be pointing in important pathogenetic directions. Further, these papers may change how we evaluate clinical parameters in diabetic patients. Thus, Hansen et al indicate that the ambulatory blood pressure measurements in microalbuminuric type I diabetic patients are more closely related to urinary albumin excretion rates than are standard clinic visit blood pressures [9].

The debate regarding the increased prevalence of abnormalities of cation transport in diabetic patients with nephropathy is well represented by the four papers dealing with this subject. The ultimate resolution of these controversies will undoubtedly accelerate our understanding of important pathogenetic factors. The possibility that there are regional or racial differences in the expression of these risk factors needs to be elucidated. Although the paper by Elving et al [10] helps to resolve some of the methodologic differences that have characterized this area, uniformity in laboratory approaches will need to be adopted in order for clarity to emerge.

Finally, there are seven papers dealing with treatment approaches in patients at risk for/or having developed diabetic nephropathy. The first five of these papers wrestle with the problem of the timing and nature of antihypertensive treatment in animals and in humans with diabetes. The paper by Dahl-Jørgensen et al [11] provides a continued hope that improvement in blood sugar control can have a salutary influence on kidney complications in diabetes. Finally, the paper by Cheung et al [12] reflects the improving technology of pancreas transplantation for the uremic diabetic, but also considers the

medical complexity of this procedure and, thus, its attendant risks.

The editors of this section on diabetic nephropathy are grateful to the authors for allowing their work to be published as a component of this special edition of *Kidney International* devoted to diabetic nephropathy. We are also most grateful to the editors of *Kidney International* for providing the impetus, space, and freedom for this project. It is hoped that these works will stimulate further research, which is mandatory if we are to develop new concepts and techniques necessary to diminish the adverse impact of diabetic renal disease. It is also hoped that the currently inadequate research funding resources directed at the solution of this problem will increase to more appropriately represent the magnitude of the impact of this disorder on the well-being of the patients that we are pledged to serve.

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Guest Editors

References

1. MOGENSEN CE: Diabetes mellitus and the kidney. *Kidney Int* 21:673–675, 1982
2. DAMSGAARD EM, FRØLAND A, JORGENSEN OD, MOGENSEN CE: Eight to nine year mortality in known non-insulin dependent diabetics and controls. *Kidney Int* (this issue)
3. BORCH-JOHNSEN K, NØRGAARD K, HOMMEL E, MATHIESEN EK, JENSEN JS, DECKERT T, PARVING H-H: Is diabetic nephropathy an inherited complication? *Kidney Int* (this issue)
4. HAYASHI H, KARASAWA R, INN H, SAITOU T, UENO M, NISHI S, SUZUKI Y, OGINO S, MARUYAMA Y, KOUDA Y, ARAKAWA M: An electron microscopic study of glomeruli in Japanese patients with non-insulin dependent diabetes mellitus. *Kidney Int* (this issue)
5. PARVING H-H, GALL M-A, SKØTT P, JØRGENSEN HE, LØKKEGAARD H, JØRGENSEN F, NIELSEN B, LARSEN S: Prevalence and causes of albuminuria in non-insulin dependent diabetic patients. *Kidney Int* (this issue)
6. JAFFA AA, CHAI KX, CHAO J, CHAO L, MAYFIELD RK: Effects of diabetes and insulin on expression of kallikrein and renin genes in the kidney. *Kidney Int* (this issue)
7. MESSENT J, ELLIOTT T, HILL R, JARRETT RJ, KEEN H, VIBERTI GC: Prognostic significance of microalbuminuria in insulin dependent diabetes mellitus: A twenty-three year follow-up. *Kidney Int* (this issue)
8. CORREA-ROTTER R, HOSTETTER TH, ROSENBERG ME: Renin and angiotensinogen gene expression in experimental diabetes mellitus. *Kidney Int* (this issue)
9. HANSEN KW, CHRISTENSEN CK, ANDERSEN PH, PEDERSEN MM, CHRISTIANSEN JS, MOGENSEN CE: Ambulatory blood pressure in microalbuminuria type I diabetic patients. *Kidney Int* (this issue)
10. ELVING LD, WETZELS JRM, DE PONT JJHHM, BERDEN JHM: Increased erythrocyte sodium-lithium countertransport: A useful marker for diabetic nephropathy? *Kidney Int* (this issue)
11. DAHL-JORGENSEN K, BJØRO T, KIERULF P, SANDVIK L, BANGSTAD HJ, HANSSEN KF: The effect of long-term strict glycemic control on kidney function in insulin-dependent diabetes mellitus. *Kidney Int* (this issue)
12. CHEUNG AHS, SUTHERLAND DER, GILLINGHAM KJ, MCHUGH LE, MOUDRY-MUNNS KC, DUNN DL, NAJARIAN JS, MATAS AJ: Simultaneous pancreas-kidney transplant versus kidney transplant alone in diabetic patients. *Kidney Int* (this issue)