A COMPARISON OF KIDNEY DISEASE IN

TYPE I AND TYPE II DIABETES

S. Michael Mauer and
Blanche M. Chavers

Department of Pediatrics
University of Minnesota Medical School
Minneapolis, Minnesota 55455

It should be self-evident that the manifestations of clinical diabetic nephropathy are dependent upon the development of serious lesions in the kidney. Thus, a comparison of nephropathy in Type I and Type II diabetes might logically focus on a comparison of the natural history of these lesions in these two disorders of glucose metabolism. Unfortunately, there is insufficient information available to provide a very precise description of either of these progressive processes let alone a comparison of the two. Herein we will attempt to summarize what, in our view, are some of the central issues in this area.

INCIDENCE

Marks reported that uremia caused 42% of the deaths in Type I diabetes. Uremia was considered the cause of death in approximately 2.5% of Type II diabetic patients aged 40 to 59 at onset of disease and 0.8% of patients beyond age 60 at the onset of disease. Among 702 patients presenting with ESRD in Brooklyn 24.6% were diabetic and approximately one-half had each type of diabetes. Thus, diabetes represents the most important cause of renal insufficiency. One-third of the diabetic patients with end-stage renal disease (ESRD) receiving hemodialysis treatment at the Regional Kidney Disease Center in Minneapolis, Minnesota, between 1966 and 1981 were Type II diabetics. Uremia, resulting from discontinuation of dialysis, caused 16% of the total deaths in this group.
IS DIABETES REQUIRED FOR THE DEVELOPMENT OF DIABETIC NEPHROPATHY?

It has been argued that the secondary microvascular complications of diabetes may represent an inherited tendency which, although genetically linked to diabetes, is separate from the diabetic dysmetabolism. However, Osterby has shown that the kidney is structurally normal at the onset of Type I diabetes and develops progressive lesions only with time. Further, we have evidence that non-diabetic individuals who have identical twins with Type I diabetes have completely normal kidney structure despite discordance for diabetes for as long as three decades (unpublished data). Although there are individual case studies reporting that the lesions of diabetic nephropathy can develop in patients with Type II diabetes prior to manifestation of glucose intolerance, a careful review of these reports failed to substantiate these claims. Thus, it appears that in both Type I and Type II diabetes glucose dysmetabolism is a necessary prerequisite for renal lesions. We feel, however, that hyperglycemia is not, per se, a sufficient cause. Patients with many years of either type of diabetes may escape the development of significant renal lesions. Thus, there appears to be a spectrum of susceptibility to renal disease in diabetes.

THE LESIONS OF DIABETIC NEPHROPATHY

The pathology of the kidney has been more thoroughly studied in Type I compared to Type II diabetes. The most sensitive indicator of diabetes is glomerular basement membrane (GBM) thickening while the most specific, widening of the glomerular mesangium, especially the Kimmelsteil-Wilson nodule, and afferent and efferent arteriolar hyalinosis, are found in uremic patients with both Types I and II diabetes. Recent studies, using quantitative electron microscopic morphometric analysis in Type I patients have indicated that the functional abnormalities of diabetic nephropathy (proteinuria, hypertension and decreased glomerular filtration rate) are correlated with mesangial expansion and not with GBM thickening. Mesangial expansion appears to adversely influence glomerular function through its effects on constricting glomerular capillary lumenal space and peripheral capillary wall filtration surface. Progressive interstitial fibrosis may also be an important component of the renal pathology. Although much less well studied, the pathology of Type II diabetic nephropathy appears to be essentially similar to that of Type I.

THE ROLE OF GLYCEMIC CONTROL IN THE TREATMENT AND PREVENTION OF CLINICAL DIABETIC NEPHROPATHY

Once clinical proteinuria is well established in Type I