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NEPHROLOGY BOARD REVIEW MANUAL

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Diabetic Nephropathy

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Diabetic Nephropathy

INTRODUCTION

Diabetes mellitus is a chronic, genetically determined metabolic disease that affects nearly every organ system. In the United States, 16 million people are diagnosed with diabetes, and approximately 5 million more remain undiagnosed.¹

Diabetes is broadly classified into 2 types. Type 1 (insulin-dependent) diabetes is characterized by an absolute deficiency of insulin, is typically diagnosed in the first to third decade of life, and accounts for approximately 10% of all cases of diabetes. Type 2 (non-insulin-dependent) diabetes is characterized by a relative lack of insulin secondary to insulin resistance, is usually diagnosed after the fourth decade of life, and accounts for roughly 90% of diabetes diagnoses. Over time, patients with either type develop numerous macrovascular complications as a result of accelerated atherosclerosis as well as microvascular complications, including retinopathy, neuropathy, and nephropathy. Only about one third of all diabetic patients will develop diabetic nephropathy. However, because of the sheer prevalence of the disease, diabetes has long remained the leading cause of end-stage renal disease (ESRD) in the United States and other industrialized nations. In the United States, diabetes accounted for 43.1% of all new cases of ESRD between 1994 and 1998.² This manual describes the natural history of nephropathy in type 1 and type 2 diabetes and presents an approach to the diagnosis and management of this common form of renal disease.

INCIPIENT NEPHROPATHY IN TYPE 1 DIABETES

INITIAL PRESENTATION AND HISTORY

A 26-year-old white woman with a long-standing history of diabetes is referred for evaluation of possible diabetic renal involvement. The patient was diagnosed with type 1 diabetes at age 14 years when she presented with polydipsia and polyuria and was found to have a random blood glucose level of 335 mg/dL. At that time, her urine was positive for ketones. She was started on 20 U of subcutaneous 70/30 insulin twice daily, but she has not been compliant with the insulin regimen. Her hemoglobin A_{1c} (HbA_{1c}) level has averaged between

9% and 10% for the past 12 years. She has no other chronic medical illnesses and currently has no symptoms from diabetes.

- **What is the natural history of nephropathy in the first 10 years of type 1 diabetes?**
- **How is microalbuminuria detected, and what is its clinical significance?**

NATURAL HISTORY

Latent Disease

This patient's disease course is consistent with the natural history of nephropathy in type 1 diabetes. All patients with type 1 diabetes progress through an initial clinically silent phase that lasts approximately 10 years. The only detectable changes in this latent phase are mild nephromegaly and an increase in the glomerular filtration rate (GFR) due to increased renal blood flow (hyperfiltration). Nephromegaly may be documented by renal ultrasonography, and hyperfiltration may be shown by methods for measuring GFR or creatinine clearance. Neither test is routinely performed, however.

Although the patient with latent type 1 diabetes is asymptomatic, the kidneys have undergone well-defined structural changes as a result of the diabetic state. Renal biopsies done as early as 2 to 3 years after diabetes onset have shown diffuse thickening of glomerular basement membrane (GBM) and tubular basement membrane (TBM).³ Glomerular and tubulopitthelial cell hypertrophy are also evident and are the histologic counterparts of nephromegaly. These functional and structural changes, while abnormal, do not necessarily imply the development of true kidney disease; nor do they portend a poorer prognosis. Only a minority of patients (roughly 30%) will progress to the next stage of diabetic renal disease—incipient nephropathy marked by the development of microalbuminuria.

Incipient Nephropathy and Microalbuminuria

Approximately 10 or more years after the onset of diabetes, patients may develop microalbuminuria, which is defined as urine albumin excretion greater than 30 mg/day but less than 300 mg/day (or 20 to 200 µg/min). Microalbuminuria is the earliest and most readily available clinical marker that heralds the onset of diabetic renal disease that is likely to progress. The classical teaching for type 1 diabetes is