

Detection and Estimation of Proteinuria

Evaluation of all patients with CKD should include testing for proteinuria.^[357] Strategies aimed at reducing proteinuria have been shown to slow the rate of decline in GFR in CKD due to hypertension, diabetes, and the glomerulonephritides.^{[348] [358] [359] [360] [361]}

Detection and quantification of microalbuminuria in patients with CKD and a negative urine protein dipstick test result should be performed on an initial visit. For the patient in whom a urine protein dipstick test result is positive, quantification of proteinuria should be performed as described below. For individuals referred for proteinuria with a negative urine protein dipstick test result but positive sulfosalicylic acid test result or a 24-hour urine sample demonstrating protein, a test for urine light chains should be performed. As discussed in [Chapter 43](#), unrelenting proteinuria has been shown to greatly increase risk for progression of CKD in diabetic and nondiabetic nephropathies including the glomerulonephritides, hypertensive nephrosclerosis, and autosomal dominant polycystic kidney disease.

Proteinuria has been extensively studied as a marker for progression of renal disease.^{[348] [358] [359] [361] [362] [363] [364] [365] [366] [367] [368] [369] [370] [371] [372] [373] [542]} Numerous clinical trials have shown that patients with impaired renal function and high-grade proteinuria (>1 g/day) progress at a faster rate than those with low-grade proteinuria (≤1 g/day).^{[275] [286] [369] [542]} For example, in both diabetic and nondiabetic patients with proteinuric renal disease, acceleration of renal disease progression correlates with the level of baseline proteinuria. Even in patients with controlled essential hypertension and no evidence of renal disease, the onset of proteinuria may be a marker of future decline of renal function.^{[374] [375] [376]} Also, the Modification of Diet in Renal Disease Study demonstrated that baseline proteinuria was an independent risk factor for progression of renal disease in nondiabetic patients and that the extent of proteinuria reduction might be a measure of the effectiveness of blood pressure control.^{[286] [377]} Normal individuals excrete less than

TABLE 23-9 -- Microalbuminuria and Macroalbuminuria

	MICROALBUMINURIA	MACROALBUMINURIA
Definition (mg albumin/mg creatinine)	>30–299	≥300
Routine dipstick test result	Negative	Positive
Renal significance	At risk for nephropathy	Marker of rapid progression
Effect on cardiovascular risk	Increased	Increased

150 mg/day of protein. Loss of protein (albumin) in the urine becomes apparent on reagent test strip tests when the urine contains 300 mg/L or more, or 300 mg or more albumin per g creatinine ([Table 23-9](#)).

The recommended method of screening for abnormal albuminuria is to first measure albumin by urine dipstick test. If the result is negative, it is preferable to obtain a freshly voided morning urine sample ("spot" or "random") and send it to the laboratory for measurement of albumin and creatinine and calculation of the albumin-to-creatinine ratio. Collection of a 24-hr urine sample to screen for albuminuria is not recommended; instead, a random specimen should be collected for determination of urine albumin or protein to urine creatinine ratio.^[277] Under normal circumstances, urinary albumin, measured as the ratio of albumin to creatinine, in a random urine sample is less than 30 mg per g creatinine.

Microalbuminuria, defined as an albumin excretion in the range between 30 and 300 mg per g creatinine, is not detected by the routine dipstick method (which, by the way, detects only albumin, not other proteins such as light chains). *Macroalbuminuria* is defined as an albumin excretion rate of more than 300 mg per g creatinine. Both are markers for risk for progression of nephropathy in patients with type 1 and type 2 diabetes and for increased risk of cardiovascular death.^{[267] [322] [378] [379] [380] [381] [382] [383] [384] [385] [386]} Moreover, more than 300 mg/g of protein is associated with higher risk of progression of kidney disease in hypertensive nephrosclerosis.

A simple algorithm for screening and evaluation of proteinuria is illustrated in [Figure 23-6](#). Monitoring proteinuria or albuminuria in CKD can be accomplished without 24-hour urine collection, but instead by repeated determinations of the urine albumin-to-creatinine or urine protein-to-creatinine ratio. As with screening samples, these determinations should be performed on freshly voided morning urine samples.

