Microalbuminuria: An Early Screening Test for Diabetic Patients at High Risk of Developing Nephropathy.

Leonardo O. Chait, M.D., FACP, FACC
Associate Clinical Professor of Medicine, UCLA
Medical Director, Executive Life Insurance Co.

It is well known that when patients with IDDM develop persistent proteinuria, their course becomes rapidly downhill and their survival time is short in spite of the progress in the control of uremia with dialysis and renal transplantation. On the other hand, the patients that survive 25 years of diabetes without developing dipstick positive proteinuria appear to be almost free of subsequent risk of diabetic nephropathy. It is obvious that a test that would allow an earlier separation of the patients that are prone to develop diabetic nephropathy would have tremendous importance for the insurance industry as well as for the affected individuals because the progression of the nephropathy might be slowed down by intensive treatment.

Modern technology has provided that kind of a test by increasing the sensitivity and specificity of the tests used to detect albuminuria and proteinuria. New normal ranges for albuminuria and proteinuria have been established. All the studies involve measurement of 24H urinary excretion because concentrations on random samples vary with the degree of hydration. In spite of this, it is still possible to obtain useful information from the random sampling of urine. I will correlate the 24H urine values with the random samples we customarily use in practice.

The early increase in proteinuria is due in large part to an increased excretion of albumin; furthermore there is a new qualitative agglutination test for the detection of albumin in the urine; it is reported to be sensitive, simple and inexpensive. It has been known for over 20 years that “dipstick negative” diabetic patients may have AER values which are several times higher than normal. The clinical relevance of this finding has not been recognized until recently when different investigators, following patients that displayed this early “microproteinuria”, saw it gradually evolve into “macroproteinuria”. They demonstrated that this microalbuminuria in diabetic patients predicts an 80% likelihood of later development of diabetic nephropathy. Viberti and Vergani developed a three drop slide agglutination assay that is specific for human albumin present in the urine, it does not cross-react with other proteins. It is an easily readable latex agglutination test with positive reaction at urinary concentrations between 25 and 170 mg/L. Higher and lower concentrations yield negative results. The negative readings at higher concentrations are explained by the nonlinearity of the antigen antibody reaction known as the pro-zone phenomenon. Using this test, Viberti et al expanded their early studies and reported that the AER was elevated in approximately 30% of diabetic patients and that the incidence reached 45% when the disease had been present for over 10 years.

The commonly used dipstick test detects proteinuria rather than albuminuria and it becomes persistently positive when the protein excretion is at least 550 mg/24H. This corresponds to an AER in excess of 250 mg/24H. These dipstick-positive levels of excretion have been defined as macroproteinuria and macroalbuminuria respectively. The range between 26 mg and 250 mg/24H has been defined as microalbuminuria. Obviously the cutoff values are somewhat arbitrary. Common sense should be applied in assigning a borderline AER value to one or the other category, especially so when we use concentrations of albumin rather than 24H excretions.

It is obvious that for insurance purposes we will not be able to use 24H collections. Our measurements will be concentrations expressed in mg per Liter, and will vary with the state of hydration. The sensitivity of the test has been adjusted to detect 25 to 170 mg/L and, therefore, a positive test should be significant unless done in a very dehydrated individual. It is important to keep in mind that we should insist on an average state of hydration, otherwise, during water diuresis, the concentrations can be 10 to 20 times lower and the purpose of the examination could be defeated.

<table>
<thead>
<tr>
<th>Albumin Excretion Rate (AER)</th>
<th>Normalalbuminuria</th>
<th>Microalbuminuria</th>
<th>Macroalbuminuria</th>
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</thead>
<tbody>
<tr>
<td>AER</td>
<td>2.5 - 26 mg/24H</td>
<td>26 - 250 mg/24H</td>
<td>Over 250 mg/24H</td>
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<tr>
<td>Geom. Mean</td>
<td>9.5 mg/24H</td>
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<tr>
<td>Mean ± 2 S.D.</td>
<td>92% have less than 18mg/24H</td>
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(The dipstick will usually be positive)
It is easy to check the state of hydration by measuring the specific gravity of the urine used for the test.

References