

Urine Albumin

Urine protein assays don't get much respect, but they should. As most people know, one of the earliest signs of diabetic nephropathy is so-called microalbuminuria, the excretion of more than 30 (but less than 300) mg of albumin per day.¹ For convenience, an alternative definition is an albumin/creatinine ratio on a random urine sample of more than 30 mg (but less than 300 mg) of albumin per gram of creatinine.^{1,2}

Simple enough perhaps, but it's what most people don't know that's important. First, urine dipstick protein methods are not sensitive enough to detect microalbuminuria (nor, for that matter, are typical spectrophotometric methods for total protein).² In other words, a negative dipstick for protein (or an undetectable urine total protein) does not rule out pathologic proteinuria. Second, in order to achieve the sensitivity needed, the methods available to measure urine albumin are immunoassays and may, as a result, be subject to "hook effects". That is, at very high antigen concentrations, one may get a falsely low result. In this case, that would be particularly unfortunate: a patient with pathologic proteinuria might get a normal result.

As a result, we have included in our urine albumin Survey at least one sample per year that seeks to address this issue. Some participants have complained about the need to dilute some samples, but this is the reason. We want to ensure that laboratories, in practice, will not miss pathologic proteinuria because of hook effects.

Finally, it should be noted that all forms of pathologic proteinuria are likely to begin with albuminuria, as albumin is, simultaneously, among the smallest and most prevalent proteins. Thus, the National Kidney Disease Education Program (NKDEP) argues that all patients at risk (patients with diabetes, hypertension, family history of kidney disease) be screened for Chronic Kidney Disease (CKD) not only with serum creatinine (and estimated GFR) but also with urine albumin.³ Indeed, the most recent National Health and Nutrition Examination Survey (NHANES) data indicated a prevalence of 16.8% of CKD among adult Americans (more than 30 million people, 2/3 of whom had estimated GFRs > 60 ml/min/1.73m², so were categorized as having CKD based only on their urine albumin excretion).⁴

So, the next time you have to do an offline dilution for a CAP urine albumin sample, be thankful that your method is capable of detecting possible antigen excess and that you are indeed reporting accurate results.

Gary L. Horowitz, MD, Chair
Chemistry Resource Committee

References

1. American Diabetes Association: Nephropathy in diabetes. *Diabetes Care* 2004;27(Supplement 1):S79-S83.
2. Keane WE, Eknoyan G. Proteinuria, albuminuria, risk, assessment, detection, elimination (PARADE): a position paper of the National Kidney Foundation. *Am J Kid Dis* 1999;33:1004-11.
- 3) National Kidney Disease Education Program, http://nkdep.nih.gov/professionals/chronic_kidney_disease.htm (last accessed February 4, 2010)

4) MMWR, http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5608a2.htm?s_cid=mm5608a2_e#tab
(last accessed February 4, 2010)