Finding New Sea Legs for Urine Proteomics

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We draw attention to a commentary published in this issue of *JASN* by Knepper[1] regarding studies undertaken in search of new biomarkers using urinary proteomics. Many of us who review or read these studies want important information to grace our journal pages. Proteomic technology today, even as it rapidly evolves, is capable of clever *measurement and presentation*, but harnessing this technology to better understand clinical or experimental disease is where true progress lies. By and large, we are not there yet. Reasonable people acknowledge this concern is more of an observation than a complaint about a discipline in its adolescence.

Identification of protein/fragment signatures in urine needs context and credible evidence of improving on what is already known. A useful experimental design should test protein signatures for relevance to pathophysiology and specificity for certain diseases. We cannot get to this level without everyone making an effort to raise the bar.

As editors of your journal, like any well-regarded journal, we are always torn between publishing new preliminary data of potential interest *versus* a more penetrating story that truly advances the ball. We hope Knepper's insightful discussion now, and what will come from new work by our community of investigators, forges greater expectations for future studies: Expectations for replication in parallel populations accompanying the initial identification of a signature, disease specificity controls where appropriate, and additional biochemical or immunologic confirmation where available. When contemplating a more advanced validation study, the design should develop along the lines of a comparative clinical trial against other markers, other diseases, or various treatments with appropriate attention to sensitivity and specificity of the results.

JASN editors going forward will expect future manuscripts using urinary proteomics to contain the above enhancements. If we all promote a rigorous scientific body of work, then we can be optimistic that urinary proteomics will provide a powerful tool by which we can identify new markers, understand their use, and better care for our patients.

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DISCLOSURES

None.

REFERENCES

1. Knepper MA: Common sense approaches to urinary biomarker study design. *J Am Soc Nephrol* 20: 1175–1178, 2009

See related Occasional Observation, "Common Sense Approaches to Urinary Biomarker Study Design," on pages 1175–1178.

Vascular Calcification: The Three-Hit Model

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Vascular calcification, primarily arterial calcification, is one of multiple forms of extraskeletal calcification that is highly prevalent in patients with chronic kidney disease (CKD), especially those on dialysis. Arterial calcification is not a new or novel phenomenon: Mummified bodies from the ice age and many older adults and patients with diabetes and without CKD have at least some arterial calcification.[1] The presence and magnitude of arterial calcification are associated with an increase in cardiovascular events or death in the general population[2] and, in some studies, in dialysis patients.[3,4] Cross-sectional and longitudinal studies in dialysis patients identify a plethora of risk factors, including advanced age, diabetes, duration of dialysis or magnitude of CKD, hyperphosphatemia, inflammation, and excess calcium-containing phosphate binders, but these associations are not consistently

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