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The Urine Sediment as a Biomarker of Kidney Disease

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The modern era of medicine has ushered in new diagnostic technologies to assist the clinician in evaluating patients with kidney disease. The birth of automated urine analysis technology and centralized laboratory testing has unfortunately made examination of urine sediment by physicians a rare event. At the same time, identifying novel urine biomarkers for kidney disease has become a research priority in nephrology, and the search for the "renal troponin" has progressed at a fast pace. Despite this, urine sediment examination remains a time-honored test that provides a wealth of information about the patient's kidney condition and performs favorably as a urinary biomarker. It alerts the clinician to the presence of kidney disease and provides diagnostic information that often identifies the compartment of kidney injury. In addition, sediment findings may guide therapy and assist in prognostication. As such, it is premature to abandon urine sediment examination. It may be more appropriate to combine urine sediment examination with new candidate biomarkers that enter clinical practice to create a "diagnostic panel" that provides clinicians with a useful battery of diagnostic tests. To accomplish this, we as nephrologists must encourage continued training and maintenance of competency in urine sediment examination.
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Urine sediment examination performed by an experienced nephrologist is a well-established and valuable adjunctive test used in the evaluation of patients with kidney disease. Microscopic examination of urine was introduced into clinical practice in 1830, generated significant interest through the mid-1900s as microscope technology evolved, and was viewed as an invaluable diagnostic test for patients suspected of having kidney disease.[1] Together with taking a history and performing a physical examination, directed serum tests, and kidney imaging, examination of urine sediment allows the clinician to construct a rational diagnosis. The technique is especially useful in assessing patients with acute kidney injury (AKI), hematuria, and proteinuria.[2]

Importantly, skillful examination of urinary sediment by a nephrologist may provide information not available by automated urinalysis or urine sediment examination by a laboratory technician. An expert can discern subtle alterations in urinary cell morphology, accurately identify cellular and noncellular casts (Fig 1), and recognize various endogenous and drug-related crystals. These observations facilitate quick diagnosis of the kidney-related process.[3] As a result, urine sediment examination has been considered as the "liquid biopsy" that provides a window into the kidney.[1-3]

Urine Sediment Examination on the Wane in Nephrology

With the birth of automated urinalysis technology and centralized laboratory testing, examination of urine sediment appears to have fallen out of favor over the past 2 decades.[4] At the same time, identifying novel urine biomarkers for kidney disease has become a research priority in nephrology.[5] This effort was born of the desire in the nephrology community for new tests that more accurately diagnose kidney injury at earlier times than possible with currently used markers such as serum urea and creatinine concentrations, use of which was believed to diminish the potential benefit of therapeutic agents. Thus, a major focus in nephrology has been to identify tests that provide earlier and more site-specific information about kidney injury.[6]

The search for the "renal troponin" began with great energy, and the birth and evolution of biomarker research in nephrology has continued at a rapid pace during the past 10 years. While nephrology scientists seek new tests that more accurately identify and diagnose kidney disease, it may be premature to move away from the reliable and time-tested examination of urine sediment. With this concept in mind, this article focuses on urine sediment as a biomarker of kidney disease. I provide

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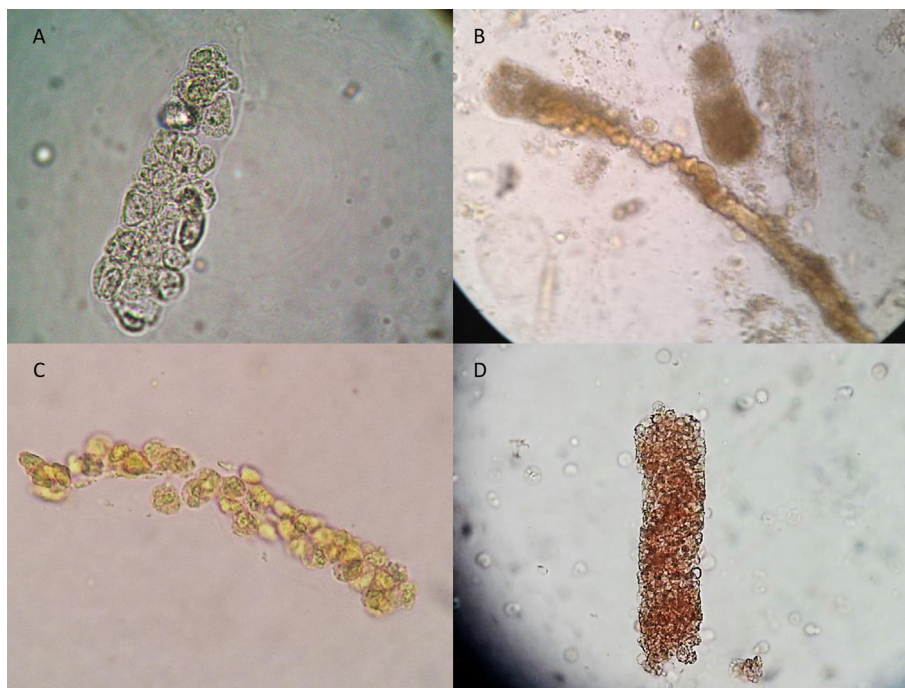
Figure 1. Urinary casts seen in the setting of kidney disease. (A) Renal tubular epithelial cell cast, often seen with acute tubular injury/necrosis; (B) muddy brown granular casts seen with severe acute tubular necrosis; (C) white blood cell cast seen with acute interstitial nephritis or acute pyelonephritis (rarely glomerulonephritis); and (D) Red blood cell cast seen with acute glomerulonephritis or small-vessel vasculitis.

data that support the important role of this test in the practice of clinical nephrology, perhaps in tandem with the newly identified candidate urinary biomarkers that are currently undergoing intense scrutiny.

Is Urine Sediment Examination a Legitimate Biomarker?

Biomarkers have undergone increased study in nephrology as the hunt for serum and/or urine tests that more quickly and more accurately diagnose AKI and also provide prognostic information has ensued. A biomarker, a measure of the underlying biological state of the organism, is defined as "a characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacological responses to a therapeutic intervention."[7(p1)] Biomarkers are the measures used to perform a clinical assessment. As such, they are used to predict and monitor the state of health or disease in an individual or population, with the ultimate goal to plan an appropriate therapeutic intervention.[6,7] Examples of biomarkers include blood pressure measurement, quantification of urine volume, electrocardiograms, diagnostic imaging tests, and serum or urine tests.

Urine sediment examination is a biomarker in the sense that it is a biological measure that is objectively measured as an indicator of a normal or pathogenic

process in the kidney. It is used for clinical assessment in individuals to predict or diagnose kidney disease and monitor the course of disease or response to therapy in those with known kidney disease. The information gleaned from urine sediment examination frequently leads to diagnosis and formulation of an appropriate therapeutic intervention. Examples include diagnosis of: (1) prerenal AKI in a volume-depleted patient with relatively bland sediment with hyaline casts, which prompts treatment with intravenous fluids; (2) glomerulonephritis in a patient with lupus with an active urine sediment and AKI, leading to initiation of therapy with steroids and performance of a kidney biopsy; and (3) acute interstitial nephritis (AIN) in a patient with AKI, sterile pyuria, and white blood cell casts following exposure to a culprit drug, ultimately leading to drug discontinuation, possible kidney biopsy, and consideration of steroid therapy.

Is Urine Sediment Examination an Ideal Biomarker of Kidney Injury?

An ideal biomarker for any biological process should have certain characteristics that make it useful in the evaluation of a particular disease condition. In clinical practice, the most important urinary biomarker characteristics include those that are safe with widespread availability, easy to measure/perform, and inexpensive (cost-efficient). It should also be stable and devoid of interference by other substances when