ARF, AKI, or ATN?

In the past, the patient whose serum creatinine level rose over a few days was diagnosed as having acute renal failure (ARF). The accepted diagnostic approach then was to query whether ARF was caused by prerenal, postrenal, or intrarenal factors. Prerenal ARF—also termed prerenal azotemia—can be caused by extracellular volume depletion (for example, gastrointestinal, third-space or renal fluid loss caused by diuretics, glycosuria, or Addison disease), or by extracellular fluid expansion accompanied by arterial underfilling secondary to either decreased cardiac output (for example, heart failure) or to systemic arterial vasodilation (for example, cirrhosis). A diagnosis of prerenal ARF assumes intact tubular function, defined as a fractional excretion of sodium (FENa) <1.0% in the absence of diuretics, glycosuria, and bicarbonaturia. The assumption is therefore that early intervention could potentially reverse prerenal ARF. Postrenal ARF or postrenal azotemia can be caused by obstruction at any site along the urinary tract.

Once prerenal and postrenal causes of ARF were excluded, the diagnosis would focus on intrarenal causes of ARF such as renal parenchymal disease, which can be classified according to the anatomic location of the injury—for example, whether it occurs in the glomerulus (acute glomerulonephritis), the vasculature (vasculitis), the interstitium (acute interstitial nephritis), or the tubule (ischemic injury and/or nephrotoxic injury). The last condition has also been termed acute tubular necrosis (ATN). The presence of red blood cell casts and proteinuria places the focus on glomerulonephritis or vasculitis rather than on ATN. Since any morphological evidence of tubular necrosis on biopsy is often either patchy or nonexistent, the term ATN is used to refer to the clinical syndrome of intrarenal ARF secondary to ischemic and/or nephrotoxicity rather than as a morphological description. Tubular dysfunction, defined as FE_{Na} >2.0% in the absence of diuretics, glucosuria, and bicarbonaturia, is a feature of ATN, and tubular epithelial cells are generally present in the urine of patients with this entity.

In the context of ARF, several important changes have recently emerged in the literature. First was the suggestion that the term 'renal' be changed to 'kidney' and the term 'failure' changed to 'injury' to encompass the entire range of renal failure based on data showing that a small change in serum creatinine influences outcome. The term acute kidney injury (AKI) is therefore now widely used in place of ARF. Second, as many definitions for ARF or AKI were used, two different groups proposed criteria to more specifically define this entity. The RIFLE classification proposes that increases in serum creatinine level over 7 days correlates with disease severity. These criteria categorize an increase in serum creatinine from baseline of 150–200% as Risk of injury (R), an increase of 200–300% as Injury (I), an increase of >300%, a serum creatinine >354 μmol/l (>4 mg/dl), or a decrease in glomerular filtration rate of >75% as Failure (F), the need for dialysis >4 weeks as Loss of kidney function (L), and the need for dialysis for >3 months as End-stage renal disease (E) (Bellomo, R. *et al. Crit. Care* **8**, R204–R212; 2004). The Acute Kidney Injury Network (AKIN) eliminated the 'loss' and 'end-stage kidney disease' categories of the RIFLE criteria and changed 'risk', 'injury' and 'failure' to stages I, II and III, respectively (Mehta, R. L. *et al. Crit. Care* **11**, R31; 2007). The most important change with the AKIN criteria, however, was to define AKI as an increase in serum creatinine over 48 h rather than 7 days. Stage I was defined as an increase in serum creatinine of 26.5 μmol/l (0.3 mg/dl) or of 150–200%, stage II as an increase in serum creatinine of 200–300%, and stage III as an increase in serum creatinine of >300% or >354 μmol/l (>4 mg/dl), or commencement of acute renal replacement therapy (irrespective of the preceding increase in serum creatinine level or urine output).

The RIFLE and AKIN definitions have been shown by several epidemiological studies to be useful in predicting mortality risk in AKI. These definitions do not, however, distinguish between prerenal, postrenal, or intrarenal causes of injury. Besides serum creatinine, both staging systems incorporate decreased urine output as a diagnostic criterion. The AKIN, however, have cautioned that adequate volume resuscitation should be ascertained and urinary tract obstruction ruled out before the urine output criteria are used. Nevertheless, decreased urine output is less helpful than serum creatinine in diagnosing AKI because >50% of patients with AKI may be nonoliguric (Anderson, R. J. *et al. N. Engl. J. Med.* **296**, 1134–1138; 1977) and the early urine output criteria for AKI (<0.5 (ml/kg)/h for 6 h) is compatible with the urine output that can occur postoperatively, despite intact kidney function. Although the frequency and severity of AKI necessitates clear terminology, confusing terms such as 'AKI/ATN' and 'prerenal ATN' have been used in the recent literature. I hope this Editorial clarifies some of these definitions.

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Competing interests
R. W. Schrier declares associations with the following companies: Astellas Pharma and Otsuka Pharmaceuticals. See the article online for full details of the relationships.