A Closer Look at the Critical Care PRN

The Critical Care PRN is made up of pharmacists practicing in a variety of settings across the world, but primarily intensive care units and emergency departments. The PRN has a rich history. Since its establishment as one of the two original PRNs in 1992, its membership has grown to include 2348 active members, including 229 residents, 8 research fellows, and 385 students. Rarely does a day go by in which there is not active discussion on the PRN e-mail list regarding the newest evidence being published on the care of critically ill patients, sharing of best practices between institutions, and weighing in of experts on the clinical controversies that members face in their practices. The Critical Care PRN is exceptionally proud of the financial support it has been able to provide its members. The PRN has funded members to participate in both of ACCP's researcher training programs, Focused Investigator Training (FIT) and Mentored Research Investigator Training (MeRIT), because of its strong belief that well-trained clinical pharmacist researchers have moved, and will continue to move, the profession forward. The PRN has also supported members with annual research grants and travel awards as well as the ACCP Research Institute (RI) by donating to the Frontiers Fund annually since 2003, and it has had many members on the RI's Board of Trustees, including the current chair, Dr. Denise Rhoney.

Opportunities and Resources for Resident and Fellow Members of the PRN

The PRN supports the registration for or travel to the ACCP Annual Meeting for two residents and two student members. Students, residents, and fellows serve on each of the six committees and have an active voice within the PRN. Complementary PRN memberships are provided to all interested PGY2 critical care and emergency medicine residents. In addition, the opportunities for networking are plentiful, both through online interactions and in person at the PRN business meeting. The PRN also provides several resident research grants, and residents receiving these awards present their findings at the Critical Care PRN Business Meeting and Networking Session held annually at the ACCP Annual Meeting.

Clinical Issue: Augmented Renal Clearance in the Critically Ill

Therapeutic drug monitoring is an integral service provided daily by pharmacists. The traditional methodology has been to monitor estimations in renal function and adjust medications in relation to decreased renal function estimations. This emphasizes the safety profile of medications when pharmacists cannot rapidly measure serum drug concentrations. Recently, however, the phenomenon of supraphysiologic renal clearance, termed *augmented renal clearance* (*ARC*), has received increased emphasis.

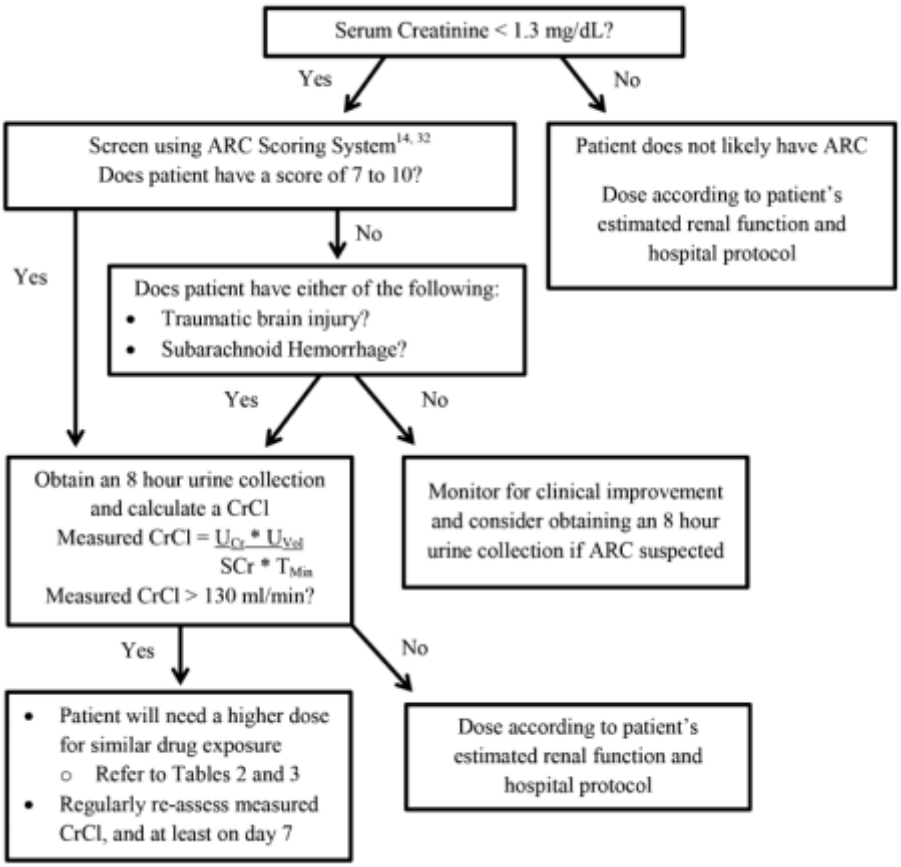
Augmented renal clearance refers to enhanced elimination of solute, including medications, and has been described in a variety of critically ill populations, primarily those with sepsis, trauma, and neurologic injury.[1-6] This phenomenon is defined by a creatinine clearance greater than normal values—120 mL/minute/1.73 m^2 for women and 130 mL/minute/1.73 m^2 for men—and has been observed in up to 65.1% of critically ill patients.[7,8] Traditional estimations of renal function, such as Cockcroft-Gault and Chronic Kidney Disease Epidemiology Collaboration estimated glomerular filtration rate, do not accurately estimate clearance. Direct calculated creatinine clearance through timed urine collections is the gold standard for determining the presence of ARC.[9,10] Augmented renal clearance in critically ill patients occurs through alterations in glomerular filtration, renal tubular secretion, and tubular reabsorption and can have a clinically significant effect on drug concentrations.[11-15]

The following validated ARC screening tool has a 75% positive predictive value and a 100% negative predictive value when using 0–6 as low probability and 7–10 as high probability.

Risk Factor	No. of Points
Age ≤ 50 yr	6
Trauma admission	3
Modified SOFA score ≤ 4	1
Probability of ARC • Low (0%): 0–3 • Intermediate (36%): 4–6 • High (82%): 7–10	

SOFA = sequential organ failure assessment.
Adapted from: Udy AA, Roberts JA, Shorr AF, et al. Augmented renal clearance in septic and traumatized patients with normal plasma creatinine concentrations: identifying at-risk patients. Crit Care 2013;17:R35.

Commonly used medications that may be of concern and that have been studied include antibiotics (e.g., β-lactams, vancomycin, daptomycin), target-specific oral anticoagulants (e.g., edoxaban), and anticonvulsants (e.g., levetiracetam). Several other medications have similar pharmacokinetic considerations and are likely affected by ARC. Hobbs and colleagues[16] have proposed a management algorithm for critically ill patients with ARC.



Augmented renal clearance has a significant impact on plasma drug concentrations in clinically significant renally eliminated medications. Decreased plasma concentrations, secondary to ARC, may have significant pharmacodynamic effects, ultimately leading to treatment failure. Critical care pharmacists are best positioned to identify patients who are experiencing, or at risk of experiencing, ARC, and to optimize their pharmacologic treatment regimens, thus improving their clinical outcomes.

1. Conil JM, Georges B, Fourcade O, et al. Assessment of renal function in clinical practice at the bedside of burn patients. Br J Clin Pharmacol 2007;63:583-94.
2. Cook AM, Arora S, Davis J, et al. Augmented renal clearance of vancomycin and levetiracetam in a traumatic brain injury patient. Neurocrit Care 2013;19:210-4.
3. May CC, Arora S, Parli SE, et al. Augmented renal clearance in patients with subarachnoid hemorrhage. Neurocrit Care 2015;23:374-9.
4. Minville V, Asehnoune K, Ruiz S, et al. Increased creatinine clearance in polytrauma patients with normal serum creatinine: a retrospective observational study. Crit Care 2011;15:R49.
5. Udy A, Boots R, Senthuran S, et al. Augmented creatinine clearance in traumatic brain injury. Anesth Analg 2010;111:1505-10.
6. Udy AA, Roberts JA, Shorr AF, et al. Augmented renal clearance in septic and traumatized patients with normal plasma creatinine concentrations: identifying at-risk patients. Crit Care 2013;17:R35.
7. Stevens LA, Coresh J, Greene T, et al. Assessing kidney function—measured and estimated glomerular filtration rate. N Engl J Med 2006;354:2473-83.
8. Udy AA, Baptista JP, Lim NL, et al. Augmented renal clearance in the ICU: results of a multicenter observational study of renal function in critically ill patients with normal plasma creatinine concentrations. Crit Care Med 2014;42:520-7.
9. Udy AA, Morton FJ, Nguyen-Pham S, et al. A comparison of CKD-EPI estimated glomerular filtration rate and measured creatinine clearance in recently admitted critically ill patients with normal plasma creatinine concentrations. BMC Nephrol 2013;14:250.
10. Baptista JP, Neves M, Rodrigues L, et al. Accuracy of the estimation of glomerular filtration rate within a population of critically ill patients. J Nephrol 2014;27:403-10.
11. Udy AA, De Waele JJ, Lipman J. Augmented renal clearance and therapeutic monitoring of beta-lactams. Int J Antimicrob Agents 2015;45:331-3.
12. Udy AA, Jarrett P, Stuart J, et al. Determining the mechanisms underlying augmented renal drug clearance in the critically ill: use of exogenous marker compounds. Crit Care 2014;18:657.
13. Udy AA, Lipman J, Jarrett P, et al. Are standard doses of piperacillin sufficient for critically ill patients with augmented creatinine clearance? Crit Care 2015;19:28.
14. Udy AA, Roberts JA, Boots RJ, et al. Augmented renal clearance: implications for antibacterial dosing in the critically ill. Clin Pharmacokinet 2010;49:1-16.
15. Udy AA, Varghese JM, Altukroni M, et al. Subtherapeutic initial beta-lactam concentrations in select critically ill patients: association between augmented renal clearance and low trough drug concentrations. Chest 2012;142:30-9.
16. Hobbs AL, Shea KM, Roberts KM, et al. Implications of augmented renal clearance on drug dosing in critically ill patients: a focus on antibiotics. Pharmacotherapy 2015;35:1063-75.