Renal Supportive Therapy for Pediatric Acute Kidney Injury in the Setting of Multiorgan Dysfunction Syndrome/Sepsis

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Summary: In the setting of sepsis and multiorgan dysfunction syndrome, the development of acute kidney injury can be an ominous event, particularly in the pediatric patient. In this setting, rapid initiation of renal supportive therapy is likely to positively impact on mortality rates. Therapeutic initiation and choice of dialytic modality are dependent on physician beliefs, as well as patient and organizational characteristics. Patient-specific factors including adequacy of nutrition provision, acuity of acute kidney injury, degree of uremia, and severity of fluid overload all must be taken into account during the decision on whether or not to initiate renal supportive therapies. In addition to the utilization of classical renal supportive modalities such as acute hemodialysis, peritoneal dialysis, and continuous renal replacement therapies, the increasing use of plasma exchange therapies and other alternatives are actively being explored for use in sepsis-associated acute kidney injury. This article reviews these concepts and current literature in the context of pediatric specific sepsis-associated acute kidney injury.

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Conceptually, the nephrologist’s consultative approach to children with multiple organ failure has been driven by acute kidney dysfunction terminology and its inherent meaning. The supplanting of the term acute renal failure with acute kidney injury (AKI) and the evolving concept of renal support therapy (RST) rather than renal replacement therapy (RRT), should force a shift in our consultative and care provision paradigms. Indeed, early consultation from our intensive care unit (ICU) colleagues is imperative if we are to make any impact on mortality rates in pediatric patients such as the one described in the case by Symons and Picca.1

The following discussion focuses on the approach to provision of RST in critically ill pediatric patients. The first component of this discussion pertains to the timing of initiation of RST, the second pertains to modality choice, the third pertains to nutritional provision, and, finally, when to consider discontinuation. Throughout the discussion the case specifics are cited. An overall review of RST approaches to pediatric AKI is beyond the scope of this article and the readers are referred to other broader resources.2,3

Fundamental questions must be addressed to provide optimal care for the critically ill child with AKI. The overall approach is to develop criteria for the timing of RST initiation. Subsequently, we must perform a uniform clinical assessment to determine the major goal of RST, which is by patient characteristics and organizational resources. Does the patient need only solute clearance? Do they need primarily ultrafiltration? What are the resources available? What limiting/extenuating factors are present in terms of the patient’s condition? All of these considerations must be taken into account if we are to deliver appropriate therapy in the right
context. With this information we then must ask ourselves, “When should we start extracorporal renal support therapies?”

TIMING OF INITIATION OF RST

Few topics in the pediatric RST realm have been as controversial as delineating the optimal timing of RST initiation. Over the past several years both pediatric and adult data have supported the implementation of RST earlier in the course of care,\textsuperscript{4-6} such a strategy is particularly relevant in pediatric care because children tend to develop their maximal organ failures and die more rapidly than the adult population.\textsuperscript{7} Classically defined indicators for RST initiation in the setting of AKI are generally extrapolations of those commonly used for end-stage renal disease (ESRD): metabolic/electrolyte imbalance, uremia with bleeding and/or encephalopathy, and hypervolemia with pulmonary edema/respiratory failure.\textsuperscript{3} Other indications include intoxications, inborn errors of metabolism, and nutritional support.\textsuperscript{3} Although these indications should prompt RST provision, they may be viewed as late indicators because they are driven by the irreversibility of ESRD in the spectrum of chronic kidney disease progression. AKI, on the other hand, is potentially reversible, and delaying RST provision until patients show severe signs and symptoms may not be appropriate in the setting of multiorgan failure. Indeed, the absence of a generally accepted, validated, and applied definition of AKI has impeded the adequate investigation of this question and there remains wide variation in clinical practice.\textsuperscript{8-11} Timing of RST initiation is affected by physician beliefs as well as patient and organizational characteristics. Patient characteristics may include body habitus, age, illness acuity, and comorbidities. Organizational characteristics may include resource availability, country, type of institution, physician and nursing staff, type of ICU, and perceived cost of therapy. Although most clinicians accept that electrolyte abnormalities such as intractable hyperkalemia are absolute indications for prompt RST initiation, up until recently, few (if any) quantifiable values for uremia, fluid overload, and AKI severity have been published to signal an appropriate time for initiation.

Acuity/Degree of AKI

Although not yet fully supported by the literature, the acuity of AKI would reasonably suggest that earlier intervention before the establishment of the indicators used for RST in ESRD is a rational approach. More than 30 definitions exist for AKI in the literature. To date, it generally has been accepted that AKI is characterized by the failure of the kidneys to adequately regulate electrolyte, acid-base, and fluid homeostasis with a concomitant reduction in glomerular filtration rate.\textsuperscript{12,13} In practical terms this may be shown in the pediatric patient by an increase in nitrogenous waste products (blood urea nitrogen [BUN]), an associated increase in serum creatinine level (>50% above baseline), and in most cases a concomitant reduction in urine output (<0.5-1 mL/kg/h).\textsuperscript{12,14}

To address fundamental questions, a commonly accepted and used AKI criterion was proposed by the Acute Dialysis Quality Initiative group (available: www.ADQI.net). The group objectively scrutinized available AKI data and classified it as to scientific merit. These criteria are known as the Risk, Injury, Failure, Loss, and End stage renal disease [RIFLE] criteria and have since been validated.\textsuperscript{15} A recent pediatric study has validated a modified form of these criteria, the pediatric-modified RIFLE criteria.\textsuperscript{16} An in-depth discussion of AKI definitions and criteria is the focus of the previous article.

Uremia

The degree of uremia, quantified by the BUN concentration, often is cited as a reason for RST initiation,\textsuperscript{17} but a wide range of standards and confounding factors exist in using BUN measurements. Although increases in the BUN concentration may reflect the kidney’s inability to process solute adequately to maintain homeostasis, levels can be affected by nonrenal factors such as bleeding, steroid use, nutritional parameters, and catabolism.

A single retrospective nonrandomized cohort study used BUN concentration as a surrogate of “timing of intervention.”\textsuperscript{18} In this study from a large trauma center, patients who were started on RRT at a mean BUN concentration of
42.6 mg/dL had a 39% survival rate compared with a 20% survival rate in those who started RRT at a mean BUN concentration of 94.5 mg/dL. However, because BUN concentration may reflect factors other than time of initiation, this study may be flawed. In an adult-based, multi-center, observational analysis of critically ill patients with AKI, RST initiation at higher BUN concentrations (≥76 mg/dL) was associated with an increased risk for death. The investigators note that the results may reflect residual confounding by severity of illness, but these results provide impetus for further randomized controlled trials. A landmark study examining dosing requirements in continuous venovenous hemofiltration (CVVH) and survival in adult patients provides indirect support for RST initiation earlier in the development of uremia. Although an increase in the BUN concentration was not a primary outcome measure, patients with lower BUN levels at RST initiation had improved survival rates compared with those with higher BUN levels, independent of CVVH dose treatment group. To date, no pediatric randomized controlled trials have specifically addressed the effect of timing of intervention based on BUN levels and outcome.

**Fluid Overload**

Disturbed fluid or metabolic balance often necessitates RST initiation in the setting of AKI. Historically, the reported mortality rates for children requiring dialysis ranged anywhere from 35% to 73%. However, more recent pediatric RST demographic data have stratified diagnoses and clarified outcome numbers, suggesting that refinement of variables, use of severity of illness scores, and subsequent earlier intervention may lead to improved outcomes. Conventional approaches to the clinical case would conclude that because the patient is voiding, aggressive diuretic use may be beneficial, rather than early initiation of RST. However, diuretics may counter the efficacy of vasopressor support and in fact in adult populations diuretic support has been associated with increased mortality rates. What does the literature identify in terms of decision making regarding RST initiation for patients in terms of fluid overload? Perhaps the most important development in the approach to RST and AKI in pediatrics comes from the Prospective Pediatric Continuous Renal Replacement Therapy (ppCRRT) registry. This group and others have published several pediatric-specific observational studies showing that the degree of fluid overload (equation 1) is an independent predictor of mortality in the pediatric group. The ppCRRT showed that survival rates in patients with multiorgan dysfunction syndrome (MODS) were significantly better for patients with less than 20% fluid overload (FO) (58% survival rate) versus greater than 20% FO (40% survival rate) at CRRT initiation ($P < .002$), even though the pediatric risk of mortality scores for patients with less than 20% FO versus greater than 20% FO were no different at pediatric ICU (PICU) admission (14.3 ± 7.6 versus 17.3 ± 10.3) or CRRT initiation (16.1 ± 8.1 versus 17.0 ± 7.5). The majority of the 116 patients analyzed in this study had sepsis (39%) as the primary disease entity requiring RST.

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\text{Equation 1: } \% \text{ FO at CRRT initiation} = \frac{\text{fluid in (L)} - \text{fluid out (L)}}{\text{ICU admit weight (kg)}} \times 100\%
\]

**Case Specifics: Indicators**

Recently, the International Surviving Sepsis Campaign Guidelines Committee put forth guidelines for the goal-directed management of sepsis and septic shock based on the current literature. Although this is an adult-based approach, many of the principles can be applied to the management of pediatric patients as well. These guidelines form a strong basis not only for therapy guidance but also for future investigations. In the case of the patient presented here, a focused consultative approach also is warranted, with attention to the following questions: which specific indicators of initiating RST should be considered in this patient? What is the AKI severity? Does the patient have electrolyte imbalance? What is the BUN level? Is the patient metabolically capable of processing the fluid and solute load to maintain their own balance? Is the provision of nutrition being sacrificed to limit excess fluid intake?
This patient is septic and has received massive fluid resuscitation and vasopressor support. Although there is no mention of specific electrolyte abnormalities other than a low CO2 level, the patient’s serum creatinine concentration is increasing (1 mg/dL up to 2.8 mg/dL), which reflects severe AKI (pediatric-modified RIFLE “F”). In addition to this, his urinary output has dwindled.

As a result of the resuscitation, the patient’s weight has increased from 52 kg to 64 kg, and his blood pressure remains labile. Despite continued urine output, his kidneys are unable to adequately process the fluid and solute required, which is compounded by vascular leak and resulting edema (third spacing), which compromises ventilation and oxygenation despite ventilator support. By using our fluid calculation as noted in equation 1, the patient’s degree of fluid overload would be 24%. Based on the previous discussion and the literature available, this patient meets the initiation requirements for RST, but which type of RST would best meet this patient’s requirements?

PATIENT AND ORGANIZATIONAL CHARACTERISTICS

Modality Choice

A number of modalities are available for RST provision in the pediatric patient with MODS/sepsis-associated AKI. Intermittent hemodialysis (HD), peritoneal dialysis (PD), and CRRTs such as continuous venovenous hemodialysis (CVVHD) (predominantly diffusive clearance), CVVH (convective clearance), or continuous venovenous hemodiafiltration (CVVHDF) (both convective and diffusive clearance), may be used to provide enhanced solute clearance and ultrafiltration.33,34 In addition to these classic modalities, plasmapheresis may be a viable supportive option in the setting of sepsis. Sepsis-associated AKI has some unique properties that separate it from other classic causes of pediatric AKI.35 These properties include the potential removal of circulating cytokines (both proinflammatory and anti-inflammatory) and restoration of immunohomeostasis.36-38

Choosing an appropriate RST modality for AKI depends not only on the dialytic indication but also the clinical characteristics of the patient. Clinically, several important patient conditions require attention. Initial patient assessment should focus on the degree of multiple organ system involvement. Patients with AKI from causes other than sepsis and associated MODS predictably have a better potential outcome than those with multisystem failure.3,28,32

The nature of the clinical insult also drives the modality choice. For example, overwhelming sepsis with fluid overload, pulmonary edema, pressor support, and multisystem involvement may necessitate initiation of CRRT with close fluid status control, whereas a postoperative cardiac patient with minimal fluid overload may be better served by PD. In addition to these clinical variables, the use of specific modalities in terms of nutritional support to aid in patient recovery from AKI or its underlying cause must be considered.

HD

Intermittent HD offers distinct advantages in terms of efficient solute and ultrafiltration clearance compared with other RST modalities. It confers the ability to accurately prescribe targeted small solute reduction with or without ultrafiltration. Rapid toxin clearance associated with hyperammonemia, tumor lysis syndrome, or ingestions also are extremely amenable to HD.42 The use of post-HD CRRT also may provide for efficient control of potential rebound of toxic substances.43

Treatment of sepsis-associated AKI with intermittent HD usually necessitates some degree of fluid restriction because many patients will not tolerate removal of large volumes of fluid over the short treatment times typically used in intermittent HD. Daily intermittent HD may help in this regard, but will not completely eliminate the need for fluid restriction, which in turn frequently will lead to limitations on the amount of nutritional support provided. Finally, the capacity of intermittent HD for ultrafiltration will be limited further if the patient is significantly hypotensive. In such patients, HD may need to be terminated early or may not be able to be provided at all, and PD or CRRT may be preferable options because of the more gradual fluid removal provided by these modalities.
Most secondary or tertiary care centers have the equipment and expertise to provide intermittent HD. Although acute HD is the most efficient modality for metabolic and volume control, it often is not tenable in the smallest and/or sickest patients who present to the PICU, who require experienced nursing personnel to deliver HD safely to patients with small blood volumes who cannot tolerate rapid fluid shifts. In this particular case, the hemodynamic instability and labile nature of the patient’s condition would not make HD the best option for RST.

PD

Many pediatric clinicians have a relatively greater experience and comfort level using PD in pediatric patients. PD historically has provided effective therapy for the management of childhood AKI23-26,44-48 and continues to provide reasonably cost-effective, efficient therapy in resource-poor, developing nations.49-51 Over the past 10 years, CRRT slowly has supplanted PD as the primary RST modality choice for pediatric care because CRRT technological advances have allowed improved delivery of care.52

PD provides gradual and continuous solute clearance and ultrafiltration. Although possible, the ability to separate these components is limited in PD. Dialysate prescriptions may be modified rapidly to suit the patient’s exact requirements in circumstances in which avoidance of lactate-based solutions is in the patient’s best interest. Commercially prepared bicarbonate-based solutions are available outside the United States. Customized bicarbonate solutions with electrolyte modification also can be prepared by hospital pharmacies,53,54 although prescription error poses a significant risk to patient care.55 The ability to provide adequate dosing of dialysis in the AKI setting also is problematic in many of the sickest patients. Retrospective pediatric data show that PD can be performed successfully in the setting of multisystem organ failure requiring vasoressor support and cardiovascular instability.48,50 However, in patients with sepsis-induced AKI the beneficial aspects of slow solute clearance and ultrafiltration provided by PD also limit its effectiveness. Patients with sepsis and severe fluid overload/lactic acidosis who are pressor-dependent require precise fluid balance and controlled ultrafiltration, yet may not have adequate blood flow to the peritoneum and to allow for efficient solute and fluid removal. Pressor agents may alter peritoneal blood flow in septic patients, further diminishing adequate solute and fluid removal.

PD is relatively contraindicated in patients with ventriculoperitoneal shunts, prune belly syndrome, recent abdominal surgeries, and is absolutely contraindicated in patients with diaphragmatic defects. Our patient has worsening respiratory parameters and this pulmonary compromise may worsen owing to increased abdominal dialysate volumes, thereby preventing full diaphragmatic excursion.56,57 Further complications associated with PD include hernias, leaks, and catheter obstruction.48,51 Hydrothorax may result if dialysate leaks into the pleural space. The process of PD itself can cause significant losses in immunoglobulins that potentially can render such patients amenable to infections such as peritonitis. Peritonitis can enhance dialysate protein loss, worsen nutritional compromise, reduce ultrafiltration capacity, and permanently damage the peritoneal membrane.58

PD is widely available in developed and developing countries. It requires less technological expertise, resource allocation, and may be more cost effective than CRRT or HD. This dialysis modality is critical in the treatment of sepsis-induced AKI in facilities where pediatric HD and CRRT are unavailable.49,51 In terms of our patient, PD offers continuous therapy in the setting of hemodynamic instability and would be preferable to HD. However, because of its unpredictable solute and ultrafiltration removal and potential limitations on nutritional delivery PD would not provide the optimal precise control that CRRT would afford.

CRRT

CRRT has emerged as the most prevalent initial RST used in critically ill children. Several defining CRRT principles have been established to guide initiation, direct therapy in specific patient populations, and to describe outcome expectations and complications. The ppCRRT
Registry consortium has described the demographics, outcomes, anticoagulation strategies used, and other variables in the treatment approach to pediatric AKI including sepsis-associated AKI. These reports appear to have positively impacted the management of the sickest septic patients with CRRT and have resulted in an improvement in stratification of mortality rates compared with past described outcomes.

CRRT possesses several distinct advantages over PD and HD in the management of patients with sepsis-associated AKI. CRRT mimics the effect of renal function with its continual ultrafiltration and solute clearance, but unlike PD, in which continuous ultrafiltration is variable and dependent on the patient’s clinical status, CRRT can deliver prescribed ultrafiltration rates. These properties make CRRT preferable for the provision of RST in hemodynamically unstable, fluid-overloaded septic patients. Adequate nutritional delivery is possible with CRRT because there is no need for fluid restriction; ultrafiltration rates can be adjusted concomitantly with increased volume infusions associated with increased nutrition delivery. Supplemental protein may be required because amino acid loss can be quite high with CRRT.

CRRT provides superior uremia control over PD or HD. However, a recent adult study comparing PD and CRRT for sepsis-induced AKI has called this cost into question. In general, CRRT allows greater flexibility than PD and HD in terms of choice of clearance modality. Newer machinery provides multiple options in one platform including CVVH, CVVHD, CVVHDF, and in some cases therapeutic plasma exchange. The indications for specifically choosing one of these intra-CRRT modalities for specific patient conditions are in the early stages of being defined.

Convection Versus Diffusion and Dose

CRRT may have an additional benefit of restoring immunohomeostasis via removal of both proinflammatory and anti-inflammatory molecules during sepsis-associated AKI. Adult studies have shown improved survival rates with higher doses of CVVH in what has now become known as “high-volume hemofiltration.” A randomized, prospective landmark study showed that a CVVH ultrafiltration dose of 35 mL/kg/h was associated with an improved mortality rate in adult patients. Further subanalysis showed that in septic patients, higher CVVH ultrafiltration dosing of 45 mL/kg/h provided superior outcomes compared with the lesser doses. A provocative, well-designed prospective trial evaluated the utility of short-term, very high volume isovolemic hemofiltration in adult patients with refractory septic shock. Twenty patients with intractable cardio-circulatory failure who had failed to respond to conventional therapy were enrolled. Patients were prescribed 35 L of ultrafiltrate with neutral balance over the first 4 hours of therapy followed by a return to conventional hemofiltration after this period (~2 L/h). Patients who responded were defined as those with: (1) a ≥50% increase in cardiac index over the first 2 hours, (2) a ≥ 25% increase in mixed venous oxygenation over the first 2 hours, (3) an increase in arterial pH to greater than 7.3 over the 4-hour therapy course, and (4) a ≥ 50% reduction in epinephrine dose over the 4-hour therapy period. Eleven of 20 patients responded and of these 9 survived. Interestingly, responders had a significantly lower median weight (66 kg; ultrafiltration dose 0.53 +/− 0.07 L/kg) than
nonresponders (81 kg; ultrafiltration dose 0.43 L/kg), and were initiated earlier than nonresponders (6.5 versus 13.8 h), which suggests that dose should be normalized to patient size. No such studies exist in pediatrics. Convective therapies (CVVH/CVVHD) provide superior middle molecule clearance compared with diffusive therapies, which has lead to speculation that the convective therapies would therefore provide superior middle molecule clearance of septic mediators and improved mortality rates in patients with sepsis-related AKI. To date, there are no good randomized data to support this conclusion. A recent ppCRRT report of stem cell transplant recipients showed patients who received convective therapies (CVVH or CVVHDF) had a better survival rate than those who received diffusive therapy (17 of 29 [59%] versus 6 of 22 [27%]; \( P < .05 \)). The investigators concluded that the improved survival seen in the stem cell transplant patients treated with convective therapies suggested that the removal of proinflammatory cytokines by convective modalities may have provided an added beneficial effect.

Plasmapheresis

Although generally not considered a treatment of AKI specifically, the utilization of plasmapheresis in specific settings such as sepsis has been the subject of recent investigation. In cases of sepsis-related AKI, restoration of the immune balance and removal of septic mediators may improve the renal injury and hence reduce overall mortality.

The data concerning efficacy of plasma therapies is somewhat mixed and appears dependent on the primary outcome measure and the patient population evaluated. Although plasma therapies reduce concentrations of septic mediators, the pattern and specific mediators removed have shown wide variations and have not necessarily been associated with improved survival. Currently, there is a multicenter study examining the effect of plasma exchange therapy on a subset of pediatric septic patients who develop thrombocytopenia-associated (platelet count <100,000/mm\(^3\)) multiple organ failure (TAMOF). Patients with TAMOF have microangiopathic disorders including thrombotic thrombocytopenic purpura, disseminated intravascular coagulation, and secondary thrombotic microangiopathy. Daily plasma exchange appears to be the therapy of choice for removing (von Willebrand factor–cleaving protease) ADAMTS 13 inhibitors and replenishing ADAMTS 13 activity, which in turn resolves platelet von Willebrand factor–mediated thrombosis. This in turn appears to result in overall stabilization of the patient. This multicenter study was stimulated in part by a small preliminary support by Nguyen et al. In the report it was noted that children with TAMOF had a reduction or absence of von Willebrand factor–mediated thrombosis. Plasma exchange therapy reversed both of these. Patients received a median of 11 days of plasma exchange to reverse their multiple organ failure. Forthcoming data from the TAMOF trial should help define the patient population that may best benefit from this potentially important therapy.

Nutrition Provision

Children with AKI and sepsis often are at risk for undernutrition. Although RST allows for optimization of nutritional support in patients with high catabolic states, it can contribute to the development of a negative nitrogen balance through loss of free amino acids and peptides. Undernutrition can be exacerbated further by the tendency to “fluid restrict” children with AKI even after RST has been initiated. Inadequate nutrition provision in adult post-surgical patients is associated with decreased patient survival rates. No pediatric-specific studies have been conducted to date. CRRT has been used as a technique to deliver at least 100% recommended daily allowance of nutrition either by enteral or total parental nutrition (TPN).

An important consideration of nutrition in AKI includes the concept of nutritional loss when using CRRT/PD for patient care. Several adult studies have shown that CRRT dose (either CVVH or CVVHD) will affect amino acid losses and may result in a negative protein balance. In a prospective pediatric study, children receiving standard administration of 1.5 g/kg/d of protein were randomized to either CVVH or
CVVHD for the first 24 hours, and then crossed over to the opposite therapy. Both prescriptions resulted in a net negative nitrogen balance with an average loss of amino acids of approximately 10 g/1.73 m² (~10% of protein intake). Similarly, the delivery of 2.5 g/kg/d in adult patients on CVVHDF resulted in a net negative nitrogen balance. Although the patients’ nitrogen balance was improved compared with standard lower protein supplementation, the overall nitrogen balance still was negative, characterized by a preferential glutamine clearance. Ongoing work in glutamine supplementation in hypermetabolic patients (ie, sepsis, acute renal failure, bone marrow transplants) continues to evaluate and elucidate the role of this nonessential but obvious key nutrient for cellular recovery.

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Vitamins and trace elements are components added to standard TPN solutions. Recently, it was shown that some of these are lost at a significant rate into the ultrafiltrate. One recent study showed clinically significant losses of amino acids, folate, and some trace metals during the provision of CVVHD in pediatric patients measured over a 5-day period. Of particular note was the significant loss of folate (from CVVHD initiation to day 5), evident by a clearance rate of 16 mL/min/1.73 m² with a concomitant reduction in serum folate levels. Other trace elements and vitamins, particularly manganese, thiamine, selenium, and copper, may require increased replacement doses greater than standard amounts found in TPN or formulas.

Current pediatric recommendations for CRRT suggest 2.5 to 3.0 g/kg/d of protein (with a target BUN of around 60 mg/dL), with a daily caloric intake 20% to 30% above normal resting energy expenditure in the form of TPN or, better yet, enteral feeds.

**Discontinuation**

The factors determining when or how RST should be discontinued (or transitioned to another modality) are less well understood than the factors determining initiation. Although step-down case reports exist for CRRT after HD in patients with inborn errors of metabolism and toxic overdose, no approach has been defined for patients with sepsis. No studies have examined timing of cessation of RST for any of the modalities discussed earlier. Logically it would seem that although the patient remains nutritionally dependent and critically ill in terms of inability to maintain fluid and solute homeostasis, RST should continue. Currently, experiential data and practice standards suggest that RST cessation or modality change is influenced by multiple factors. Once again, similar to modality choice, the largest influence is driven by patient characteristics including urine output, hemodynamic instability, nutritional and volume status, and clinical improvement/deterioration. Other considerations may include ongoing resource use, staff availability, family wishes, and long-term patient needs. For example, if a patient with multiorgan failure and sepsis-induced AKI is at the point of extubation and is hemodynamically stable it may be perfectly reasonable to change that patient from a continuous therapy to HD to facilitate patient movement from the PICU to the ward.

Currently no strategies have been published or studied that outline a clear weaning approach to RST. Unlike mechanical ventilation weaning, which has been studied rather extensively, approaches to RST weaning is an area ripe for investigation. It is very likely that determining when and how RST should be stopped or transitioned will significantly impact on the economic and clinical outcomes associated with patient care.

**Case Specifics: Patient Characteristics and Modality Choice**

The clinical case of an adolescent with meningococcal sepsis, AKI and multi-organ failure described by Symons and Picca illustrates the constellation of features that should lead physicians to consider provision of renal supportive therapy.

Based on the previous discussion it would appear that our modality choice should be hemodynamically tolerable owing to the patient’s poor blood pressure, pressor requirements, and significant fluid resuscitation. Under these circumstances, HD would be unlikely to provide adequate supportive therapy. It is likely that the patient would not tolerate the therapy initia-
tion, and if he did it might have to be cut short as a result of hemodynamic issues, resulting in less than adequate solute and fluid clearance and potentially worsening his clinical status.

The choice between PD and CRRT certainly includes the availability of equipment and other organizational characteristics. If CRRT is unavailable then PD should be initiated rapidly. The patient is experiencing increasing respiratory distress and we might exacerbate this by filling the peritoneum with fluid. PD may not suffice in this patient in terms of finite fluid control and adequate delivery of caloric requirements. Dosing disparity also may play a role if we are unable to deliver adequate peritoneal fills or if the patient’s blood pressure and pressor requirements interfere with ultrafiltration and solute clearance. This variability is clearly not in the patient’s best interests.

In this case, given the available resources, CRRT (CVVH or CVVHDF) would be the optimal RST. A Food and Drug Administration–approved filter replacement fluid would be used with an ultrafiltration rate of 45 mL/kg/h. Fluid removal would be aimed at a level tolerated and could be titrated to maintain urine output. A starting point would be to keep the patient’s fluid balance neutral for a few hours after CRRT initiation, and then increase the net fluid removal to 1% to 3% of the patient’s blood volume. Once CRRT was initiated, the patient could receive 3 to 4 g/kg/d to aim for a positive nitrogen balance.

If this adolescent began to develop thrombocytopenia (platelet count <100,000/mm³), it would be reasonable to consider implementation of a therapeutic plasma exchange daily for 5 days, based on early reports from the TAMOF trial.

CONCLUSIONS

Significant questions remain with respect to the initiation timing, modality choice duration, and frequency of these therapies in the clinical setting. The variables impacting these decisions are numerous and significant. Wider approaches to blood purification in sepsis are promising and these techniques usually are well tolerated and are effective in clearing septic mediators with subsequent improvement in physiologic parameters. Direct demonstration in improvement in mortality rates has been elusive and large multicenter trials are necessary to address these issues. With the advent of multiple hybrid therapies incorporating CRRT, adsorption cartridges, and a variety of other new technologies the future of treating sepsis-associated AKI is encouraging. At present, the most effective strategies for treating children with sepsis-associated AKI includes careful consideration of clinical status, early goal-directed intervention, and use of the appropriate RST/blood purification therapies at the right time.

REFERENCES


