Extracorporeal therapy in intensive care units: more to be learned on modalities, practice and outcomes from observational and randomized clinical trials

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Introduction
Acute kidney injury (AKI) is increasingly seen as part of multiple organ failure (MOF) in critically-ill patients.1–4 Severe sepsis and septic shock are the primary causes of MOF and develop as a result of the host response to infection of Gram-negative and Gram-positive bacteria. The incidence of severe AKI in hospital settings varies from 5.5 to 8.6 cases/100,000 adult year5,6. Infectious sepsis and non-infectious systemic inflammatory response syndrome (SIRS) is the leading cause of AKI responsible for over 25% of these cases. Isolated severe AKI is uncommon with more than 80% of patients with AKI having associated multi-organ failure (MOF).7 AKI associated with MOF is a severe co-morbidity pertaining a mortality exceeding 60%.8 The incidence of AKI, the alarmingly high mortality and health care costs have attracted great interest in research, and therapeutic modalities targeted to ameliorating this poor prognosis. New insights in the pathogenesis of AKI have shown the inflammatory nature of the systemic and renal tissue response as well as the possible existence of a cross-talk with other organs as the causation of acute lung injury (ALI)9. The large study by Metnitz et al10 has convincingly shown that the occurrence of AKI increases the risk for death, thus disproving the old perception that patients die with AKI.

Since the pioneering studies in 1977 by Kramer et al11, CRRT has evolved from an adjuvant therapy to a well-established, widely used, fully independent form of extracorporeal therapy. This evolution has taken place because of the shortcomings of standard intermittent hemodialysis in the treatment of an increasingly large population of severely-ill patients with MOF. This evolution has also taken place because of the shortcomings of standard intermittent hemodialysis in the treatment of an increasingly large population of severely-ill patients with MOF. This evolution has taken place because of the shortcomings of standard intermittent hemodialysis in the treatment of an increasingly large population of severely-ill patients with MOF. This evolution has taken place because of the shortcomings of standard intermittent hemodialysis in the treatment of an increasingly large population of severely-ill patients with MOF. This evolution has taken place because of the shortcomings of standard intermittent hemodialysis in the treatment of an increasingly large population of severely-ill patients with MOF.

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Inside...

Sorbent Technology
Past, Present & Future
of a Space-Age Innovation

By Susan K. Hansen, MBA, R.N., CN.N. Director Clinical Business Development, Renal Solutions, Inc.

Past
Simple, flexible, portable – those were the advantages of applying sorbent technology to some of the basic issues of human survival during long duration space flights. In 1966, an aerospace engineer, Allan Johnson, envisioned a more down-to-earth application. He suggested the possibility of regenerating hemodialysate using zirconium-based sorbents. This suggestion led to the development of the R E D Y (R Er-circulating DIALYsis) System, first introduced clinically in 1973.

Figure 1. First Commercial Sorbent System: The R E D Y URS, 1973

Unlike the older single pass technology systems, which mix dialyze from continuous supplies of treated water and dialysate concentrate, these new systems passed a 6 L batch of dialysate made with potable tap water through a cartridge containing specially formulated chemical sorbents. The cartridge sorbents purified the initial dialysate and then continuously regenerated that dialysate after it passed through the dialyzer throughout
Wide differences, however, exist in the practice (dose prescription, anticoagulation, timing of start and end etc) among ICUs, which are influenced by the patient case-mix and local (USA) practice. Despite the lack of clear evidence, the paper by Laurent et al clearly suggested that early initiation of high-volume RRT, such as CRRT, results in a decreased mortality rate compared with standard intermittent RRT. The study from Ronco et al demonstrated a clear relationship between dose and outcome has been established ahead of the target sample size was reached due to ethical reasons since the R enco study was in the meanwhile pub-
lished. Recently, a meta-analysis by Seibert et al suggested that early RRT would be associated with improved survival and renal recovery. These authors also warned against the possibility of RRT and the use of variable definitions of “early” RRT. The editorial by Gilsen et al summarized the main priori-
ties for future RRT trials in patients with AKI and the goal of standardizing care and improving outcome, including timing of ini-
tiation of RRT. The importance of determining timing of initiation and its influence on outcome is undisputed.

The evolution of AKI may be negatively affected by hypotension which can aggravate renal damage. Early care for AKI is largely a process of preventing rather than reversing processes. The increased awareness of hypotension in AKI patients has established two initial studies, four additional dose/out-
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the entire treatment. This simplicity meant home and travel dialysis were far more feasible. Since 40% of US maintenance HD patients were on home hemodialysis (HHD) in the early 1970s, the original sorbent system was specifically developed for that purpose.

 Ironically, 1973 was also the year the federal government initiated financial support for the treatment of ESRD. The federal program was specifically developed for that purpose. By the early 1990s, sorbent dialysis was a major force in the treatment of acute renal failure, as well as other needs of the complicated medical conditions of certain dialysis. The fact that sorbent dialysate composition can characterize that made sorbent technology ideal for the renal community.

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Continued from page 2

References


34. Acute Vision [http://www.acutevision.it]


### The 11th International Conference on Dialysis A

**CONFERENCEx**

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**WEDNESDAY, JANUARY 28, 2009**

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<td><strong>WELCOME</strong></td>
<td>Nebal Youssef, MD</td>
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<td>8:00-9:30am</td>
<td><strong>What is a biochip and what should you understand about dialysis machine?</strong></td>
<td>Lennard Yeates, PhD</td>
<td>University of Louisville, Louisville, KY, USA</td>
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<td>9:30-10:45am</td>
<td><strong>How to change the dialysate water quality and anticoagulation therapy and calculate statistical outcomes?</strong></td>
<td>Nicholas Herseh, MD</td>
<td>Temple University, Philadelphia, PA, USA</td>
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<td>10:45-11:00am</td>
<td><strong>What is expected of a renal dialysis in the new CMS Conditions of Coverage?</strong></td>
<td>Peter De Cosse, MD</td>
<td>Southern Baptist Cardiovascular Group, USA</td>
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<td>11:00-11:25am</td>
<td><strong>The evolution of vascular access in dialysis - what does the future hold?</strong></td>
<td>Jeffrey Bond, MD</td>
<td>Fresenius Medical Care, Celebration, FL, USA</td>
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<td><strong>Are we ready to use novel hemodialysis in end-stage renal disease?</strong></td>
<td>Andrae Thomas, MD</td>
<td>University of Connecticut Health Center, USA</td>
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<td>12:05-12:30pm</td>
<td><strong>The impact of medication control on the weight and meal tolerance in patients on haemodialysis</strong></td>
<td>Robert Plotz, MD</td>
<td>University of Colorado School of Medicine, USA</td>
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<td>3:00-3:15pm</td>
<td><strong>KEYNOTE ADDRESS GENITOURINARY PATHOLOGY</strong></td>
<td>E. David Thomas, MD</td>
<td>University of Oxford, Oxford, UK</td>
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<td>3:45-4:00pm</td>
<td><strong>What is the role of novel hemodialysis in the new CMS Conditions of Coverage?</strong></td>
<td>Peter De Cosse, MD</td>
<td>Southern Baptist Cardiovascular Group, USA</td>
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<td>4:00-4:15pm</td>
<td><strong>Opportunities for improvement in early ESRD patient care: strategies and outcomes</strong></td>
<td>Raymond Hesselink, MD</td>
<td>Penn State Medical Center, Hershey, PA, USA</td>
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<tr>
<td>4:30-5:00pm</td>
<td><strong>WELCOME RECEPTION FOR ALL ATTENDEES</strong></td>
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**WELCOME RECEPTION**

Wednesday, January 28, 2009 • 6:00 - 7:00 PM

Entertainment Provided by the “Kidney Stones”

Caesars Palace, 3570 Las Vegas Boulevard, South Las Vegas, Nevada, 89109, USA
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**ONLINE REGISTRATION AVAILABLE AT WWW.RENALRESEARCH.COM**

**REGISTRATION FEES**

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## DAY 2

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## TECHNICAL

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Because it requires no alteration in the body chemistry, the dialysate and the sorbent cartridges. Thus, both cartridge selection and dialysate sodium bicarbonate prescription are determined by cartridge urea nitrogen capacity compared to patient urea load, based on predialysis EUN and body fluid volume of the patient, as well as patient predialysis sodium and urea clearance levels. This relationship holds true for the recently updated cartridges, as reported by R. Osemann et al. The group used a simple prescription guide, available from the manufacturer.

In a recent article, Dr. Stephen Ash provides multivariant analysis of data, indicating the validity of these cartridges and dialysate prescription parameters with the updated cartridges as shown in Figures 5 and 6.

There are two other features unique to sorbent dialy- sils that are important to note: the patient-dialysate volume relationship and dialysate purity. In single pass dialysis the large volume of dialysate (120 L) compared to the body fluid volume of a standard adult patient (40 L) ensures that the level of dialyzable chemicals in the patient will be forced to conform to that of the dialysate. With sorbent systems, the volume of the patient is much larger than the 6 L of dialysate (about 7:1 ratio). Thus, except for those substances removed by the sorbent cartridge (mainly urea, bicarbonate or the inhaled system (potassium, calcium and phosphate levels, the patient controls the dialysate composition. This can have advantages in the areas of patient safety and comfort. For example, as the cartridge emits sodium in exchange for binding am-monia from urea degradation, dialysate sodium gradually rises throughout dialysis as shown in Figure 7. The prescription guide takes patient body size and predialysis sodium and urea levels into account, providing an initial dialysate sodium prescription that is somewhat lower than that used in single pass dialysis. The result is a small initial patient sodium loss. As the dialysate sodium level rises during dialysis, some sodium does transfer to the patient. However, due to the volume relationship, for every 7 mL of dialysate, the patient only accumulates 1 mL of sodium, since he has a much larger volume of distribution. Thus, if the dialysate sodium starts low and the patient donates 2 mL of sodium at the start of treatment, he can afford to gain 3 mL of sodium during treatment without issue. Thus, this sodium shift into the patient towards the latter part of treatment helps reduce symptoms such as hypertension and muscle cramps and is imitated by some of the “programmable” sodium patients in single pass programs. The result is desired fluid loss with minimal patient discomfort.

Finally, the sorbent cartridge produces a much higher purity dialysate than standard single pass or in-center dialysis systems. This is a natural function which occurs when the dialysate is passed through a large carbon layer of the cartridge; it requires no additional equipment or disposables. Dr. Derrick L. Labos of Wheeling Renal Care has demonstrated that the current sorbent cartridges produce dialysate that is very near the international standard for pure dialysate and easily exceeds the AAPCC and European quality standards for dialysis bacteria and endotoxin levels.

Currently, there are many concerns regarding the provision of maintenance HD in outpatient facilities. Dialysis centers are challenged to meet the needs of an ever-expanding pool of dialysis patients with a decreasing number of healthcare workers, as baby-boomer M.D.’s & R.N’s retire. Dialysis facilities continue to be challenged by the increasing costs of in-center dialysis, in the face of expanding patient numbers and increasing national debt/limited financial resources. Additionally, as dialysis patients become more internet savvy, the pros and cons of all possible treatment options – including the benefits of home dialysis and the right to have input into treatment decision-making – are discussed with increased frequency. These pressures are encouraging the industry to again look at home dialysis as an alternative treatment option. It is clear that sorbent technology has much to offer in these situations, where portability and lack of complicated water treatment systems are highly valuable (and perhaps essential) dialysis system characteristics.

There is ample historical data on the equivalence of sorbent technology in home dialysis, including stable aluminum and other metals levels in long term sorbent HHD patients compared to long term single pass HHD patients12. A data has been collected on short duration sorbent dialysis with continuous antihypertensives and dialysis, where it was found to be comparable in adequacy – although treatment duration may need to be prolonged by 15-20 minutes for larger patients to compensate for the lower DFR (400 ml/min) required by sorbent cartridges. Data collection on long duration sorbent dialysis (up to 8 hours) is currently in progress.

Future Options
Various industry trends towards reducing total cost of care and offering more flexible treatment options, in combination with sorbent chemistry innovations, suggest an expanded future for this technology. Some examples include:

Home HD
Because it requires no alteration in the water or electrical supply to the home, sorbent technology has significant potential for allowing HHD to be performed in a wide array of living situations, including rental properties, high rise buildings and older walk-up apartments, as well as homes in remote locations, thus expanding the availability of HHD to a broader segment of the patient population. The small equipment size attainable with sorbent technology is also a major advantage in this application. Furthermore, there is no significant increase in household water and electrical bills, a fact greatly appreciated by patients.

Alternate care dialysis sites
One such alternative is the Extended Day Dialysis system. A large number of HHD sites, as opposed to subjecting patients to the stress and strain of twice weekly travel and waiting at a conventional dialysis center, results in improved quality of life for each dialysis patient and may improve rehabilitation therapy for those patients with rehabilitation potential. Sorbent dialysis systems require less space in the nursing home, not to mention no need for initial and ongoing water treatment systems. Patients can be dialyzed at their bedside or in a communal dialysis room, depending on their condition and preference.

Acute dialysis
Acute dialysis, its small size, freedom from water treatment equipment and ease of customization of dialysate composition should continue to ensure the utility of sorbent technology in standard acute hemodialysis applications. Now that longer duration cartridges are available, long slow extended duration dialysis (EEDD) procedures can also be offered. Treatment can be set up and initiated by the nephrology nurse and the patient subsequently monitored by the ICU nurses, who then disconnect the patient once the treatment is completed. The machine can be pushed out of the way until the nephrology nurse comes to remove it. Since the EEDD treatments can be done overnight, the patient (and staff) is available for other procedures during busy daytime hospital hours.

Disaster dialysis
Sorbent dialysis systems have been successfully operated for prolonged periods on gas-powered electric generators. This characteristic plus their requirement of only 11 gallons of water for an entire treatment makes sorbent systems ideal for civilian disaster as well as military field hospital applications. It is easy to develop a system that requires even less energy.

Sorbent application to membrane technology is another area of investigation. Suggestions include placing sorbents on the dialyzer membranes to effect endotoxin and endotxin product removal from dialysate before they can cross the membrane, or depositing a sorbent as an initial layer inside the membrane for direct removal of larger molecular weight solutes from the bloodstream.

Weearable sorbent HD and PD systems are currently under development. They could make maintenance dialysis available to a far wider population of patients, as the therapy could be managed even in very limited home settings. In the case of sorbent PD, no need for a small cartridge continuously regenerates the dialysate and is charged 2-3 times a day; a battery is recharged (perhaps at night) and a UF bag emptied periodically. A wearable HD system is somewhat more complicated. In addition to the above, periodic (perhaps weekly) dialyzer replace- ment, some form of anticoagulation - and most problematic of the moment – continuous connec- tion to a vascular access. However, the current technological obstacles are not insurmountable and both options hold great promise.

Renal replacement therapy is evolving. Sorbent technology – simple, flexible, portable - has the potential to lead that evolution.

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