

# Technology Insight: treatment of renal failure in the intensive care unit with extended dialysis

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## SUMMARY

Sustained low-efficiency dialysis (SLED) is an increasingly popular extracorporeal renal replacement therapy for patients with renal failure in the intensive care unit (ICU). Several centers across the world employ this 'hybrid' technique, which has advantages of both intermittent and continuous methods. The goal of these centers is to provide an easy-to-perform treatment with reduced solute clearances for prolonged periods. Many centers use standard, sophisticated dialysis equipment for SLED. An increasing number of hospitals in Europe and South America employ a single-pass batch dialysis system, the procedural simplicity of which makes it an ideal modality for SLED in the ICU. All systems offer the advantages of flexible timing of treatment and reduced costs; their ease of handling means that SLED is readily accepted by ICU staff. Prospective controlled studies have shown that SLED clears small solutes with an efficacy comparable to that of intermittent hemodialysis and continuous venovenous hemofiltration (even when the latter employs high rates of fluid substitution). Cardiovascular tolerability associated with SLED is similar to that associated with continuous renal replacement therapy, even in severely ill patients. Nocturnal dialysis—a special form of SLED—has all the advantages outlined above, with the added benefit of unrestricted physician access to the patient during the day, minimizing the interference of renal replacement therapy with other ICU activities.

**KEYWORDS** acute renal failure, continuous renal replacement therapy, intensive care unit, night-time dialysis, sustained low-efficiency dialysis

## REVIEW CRITERIA

We searched PubMed, MEDLINE (Silverplatter) and the Cochrane Library using the following terms: "acute renal failure", "sustained low efficiency dialysis", "slow flow dialysis", "extended dialysis" and "acute dialysis". We selected all publications relevant to the field, including reports in supplements. We searched the reference lists of articles identified by this strategy and selected those we deemed relevant. We also included relevant review articles. No limits were imposed on the basis of language of publication. Finally, we used relevant data from providers of dialysis technology.

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## INTRODUCTION

There is renewed interest in prolonged or extended dialysis modalities for critically ill patients with renal failure in the intensive care unit (ICU). One should remember, however, that the first extracorporeal treatments for patients with acute renal failure (ARF) were in fact lengthy dialysis sessions. The first successful renal replacement therapy for a patient with ARF was described as follows.

"A 67-year-old woman is admitted to the surgical service with a high fever, a painful and distended abdomen, jaundice, and almost complete anuria. A urinalysis revealed dark red-brown urine notable for albuminuria, erythrocytes, leukocytes, and casts. The patient was treated with antibiotics, but continued to have oligoanuria. On the eighth day of hospitalization, the following laboratory tests were obtained: serum potassium 13.7 mEq/l and BUN 396 mg/dl. At this time the patient was noted to be encephalopathic with deteriorating clinical condition. Renal replacement therapy was initiated using a rotating drum. The initial dialysis treatment lasted 690 minutes (i.e. 11.5 hours), blood flow was 116 ml/min and urea reduction rate 69% (i.e. pre- and post-treatment urea serum concentrations were 396 and 121 mg/dl). The calculated urea clearance was 87 ml/min and Kt/V 1.40. After the initial dialysis treatment, the patient went on to become nonoliguric, followed by gradual recovery of urea clearance. She survived her acute illness, left the hospital, and at 7 months posthospitalization was doing quite well."

The physician that performed this first successful extracorporeal treatment for ARF in Kampen, Holland, on 11 September 1945, was WJ Kolff.<sup>1</sup> Kolff described a renal replacement therapy that has only recently become established as a treatment for severely ill patients with renal failure in the ICU—prolonged dialysis with low blood and dialysate flow rates.

## EXTRACORPOREAL TREATMENT OF ACUTE RENAL FAILURE

Many aspects of treating patients with ARF have changed since the time of Kolff. Today,

ARF is generally one feature of a multiple organ dysfunction syndrome in critically ill patients, which develops in response to major surgery, cardiogenic shock or a systemic inflammatory response syndrome. In a recent multicenter, multinational study of 30,000 patients, ARF was associated with septic shock in almost 50% of cases.<sup>2</sup> Mortality rates for these patients are high, despite modern intensive care medicine and extracorporeal renal replacement therapy.<sup>2-5</sup> Patients are usually hemodynamically unstable and hypercatabolic. They therefore require treatment with large doses of catecholamine and volume expanders, and parenteral nutrition, which inevitably causes hyperhydration, especially in the presence of oliguria/anuria. In light of these unfavorable clinical characteristics of critically ill patients, physicians have increasingly used continuous renal replacement therapies (CRRTs) in the ICU, particularly continuous venovenous hemofiltration (CVVH).

CVVH seems to offer better cardiovascular stability in the critically ill patient than conventional intermittent hemodialysis (IHD). To date, however, controlled studies have not detected a definitive advantage of CRRTs over IHD in terms of patient survival.<sup>3,4,6,7</sup> The efficacy of CVVH with respect to urea clearance is limited by the exchange volume and the need for frequent interruptions for other interventions.<sup>6,8</sup> CVVH requires continuous anticoagulation therapy and makes mobilization of patients difficult. The need for sterile hemofiltration fluid makes treatment costs considerable,<sup>9</sup> particularly if higher rates of fluid substitution are employed. On the other hand, conventional IHD is technically demanding, requiring trained (dialysis) personnel, a fresh water supply and hygienic removal of spent dialysate. Furthermore, the relatively short treatment time increases the likelihood of cardiovascular instability in patients who need larger ultrafiltration volumes. The relative advantages and disadvantages of intermittent versus CRRTs are summarized in Box 1.

As a survival benefit associated with use of continuous therapies in ARF patients in the ICU has yet to be proven, selection of the best method for a given patient should be based on the clinical situation, physician proficiency with the available techniques, and logistical capacity of the ICU and dialysis personnel. More important than the choice of renal replacement modality in the ICU is delivery of a sufficient treatment

**Box 1** Comparison of intermittent and continuous renal replacement therapy.

#### Intermittent hemodialysis

##### Advantages

- Short duration makes more time available for (out-of-unit) diagnostic and therapeutic procedures
- Lower risk of (systemic) bleeding as a result of less heparin use
- More suitable for severe hyperkalemia
- Optional online bicarbonate dialysate production
- Less labor-intensive and therefore less expensive

##### Disadvantages

- Technically sophisticated requiring specific infrastructure (e.g. water supply)
- Qualified (dialysis) staff required to supervise the procedure
- Periodic solute control with subsequent disequilibrium
- Dialysis dose and nutritional support might be inadequate at low treatment frequencies
- Frequent hypotensive episodes with aggressive ultrafiltration

#### Continuous renal replacement therapy

##### Advantages

- Machines are generally easy to operate and do not require specific infrastructure
- Intensive care unit staff can operate machines and perform monitoring (but increases workload)
- Prolonged gradual solute and volume removal achieves superior solute and fluid control
- Ultrafiltration over a longer period provides better hemodynamic stability
- Adequate nutritional support possible

##### Disadvantages

- Higher requirement for heparin and higher risk of (systemic) bleeding
- Impairs mobilization of patients
- Treatment frequently interrupted due to filter problems, and diagnostic and therapeutic procedures
- Expensive sterile substitution solutions substantially increase treatment costs

dose to critically ill patients.<sup>4,10,11</sup> Large clinical trials have shown that survival of patients with ARF can be improved by increasing the dose of renal replacement therapy.<sup>12,13</sup> As such, current treatment strategies for patients with ARF in the ICU focus on highly efficacious elimination of uremic toxins and concomitant gentle volume removal. This can be achieved with

**GLOSSARY**  
**ACUTE PHYSIOLOGY**  
**AND CHRONIC HEALTH**  
**EVALUATION SCORE**  
**(APACHE II)**

Scoring system used to quantify the severity of disease of intensive care patients, based on physiologic and laboratory measurements, age and previous health status

**Table 1** Studies of sustained low-efficiency dialysis and extended nocturnal dialysis for treatment of patients with renal failure in the intensive care unit.

Author	Dialysis machine	Blood/dialysate flow (ml/min)	Prescribed treatment time (h)	Nocturnal treatment
Fiaccadori <i>et al.</i> <sup>24</sup>	AK200® Ultra	200/100	8–9	No
Kielstein <i>et al.</i> <sup>21</sup>	Genius®	200/100	12	Yes
Kielstein <i>et al.</i> <sup>43</sup>	Genius®	150–200/150–200	8	Yes
Kumar <i>et al.</i> <sup>18</sup>	2008H® <sup>a</sup>	200/300	6–8	No
Lonnemann <i>et al.</i> <sup>19</sup>	Genius®	70/70	18	Not reported
Marshall <i>et al.</i> <sup>20</sup>	2008H® <sup>a</sup>	200/100	12	Yes
Marshall <i>et al.</i> <sup>22</sup>	2008H® <sup>a</sup>	200/100	12	Not reported
Marshall <i>et al.</i> <sup>22</sup>	4008S ArRT-Plus	250–350/200	8	No
Morgera <i>et al.</i> <sup>33</sup>	Genius®	180–200/180–200	4–6	No
Naka <i>et al.</i> <sup>51</sup>	Not reported	100/200	6–8	Not reported
Ratanarat <i>et al.</i> <sup>25</sup>	Not reported	200–250/67–150	6–12	Not reported
Schlaeper <i>et al.</i> <sup>17</sup>	2008H® <sup>a</sup>	100–200/100–300	8–24	Yes

<sup>a</sup>Modified for SLED treatment mode.

either daily IHD or high volumes of substitution fluid during CVVH.<sup>4,6</sup> Unfortunately, the costs (e.g. equipment, disposals and staff) associated with these labor-intensive techniques are increasingly important obstacles to their implementation. Alternative strategies have therefore been developed, with the aim of providing an easy-to-perform and less-expensive treatment with reduced solute clearances that can be maintained for prolonged periods.

**‘HYBRID’ RENAL REPLACEMENT THERAPIES**

The theoretical basis and clinical implications of the new modality of extracorporeal renal replacement therapy, called ‘slow continuous hemodialysis’,<sup>14,15</sup> dates back to 1988.<sup>16</sup> This technique utilizes equipment originally developed for treatment of patients with chronic renal failure and does not require industrially produced substitution fluid.<sup>14,17</sup> The term ‘sustained low-efficiency dialysis’ (SLED) is the most widely used, but alternatives used in the literature include ‘extended daily dialysis’ (EDD) and ‘slow continuous dialysis’ (SCD). This means of renal replacement combines several advantages of both intermittent and CRRTs,<sup>18–20</sup> most notably excellent detoxification and cardiovascular tolerability akin to that associated with CVVH.

**Clinical studies of sustained low-efficiency dialysis**

Several controlled studies<sup>18,20–22</sup> and accounts of long-term experience<sup>23</sup> have been published by groups that use SLED to treat ICU patients with renal failure (Table 1). Marshall *et al.*<sup>20,22</sup> used a standard IHD machine (2008H®, Fresenius Medical Care Holdings Inc., Lexington, MA) at a reduced dialysate flow rate of 100 ml/min. They have used this approach to treat critically ill patients in whom IHD had repeatedly failed because of intradialytic hypotension, patients in whom hemodynamic intolerance was likely to occur, and patients in whom the prescribed solute control goals were not achieved despite daily IHD. In these settings, the authors achieved ultrafiltration goals and adequate solute removal in most of their 37 patients with 145 SLED procedures. Dialysis quantification in nine oliguric patients revealed a mean delivered double-pool Kt/V of 1.36 ± 0.38 per treatment. Hospital mortality was 62% (not significantly different from expected mortality determined from the ACUTE PHYSIOLOGY AND CHRONIC HEALTH EVALUATION [APACHE II] illness severity score). Moreover, ICU staff were very accepting of SLED.<sup>20</sup>

Kumar and colleagues<sup>18</sup> compared SLED with standard CVVH in a prospective study. They also used the 2008H® machine to treat

25 critically ill patients with SLED (367 total treatment days). An additional 17 patients were treated with CVVH for a total of 113 days. Median daily treatment time was 7.5 h for SLED and 19.5 h for CVVH. No differences in mean arterial blood pressure or use of catecholamines were observed between the treatment groups, despite similar median net daily ultrafiltration rates (3,000 ml/day vs 3,028 ml/day). By contrast, requirement for anticoagulation was significantly less in patients treated with SLED (median heparin dose 4,000 U/day vs 21,100 U/day with CVVH). Kumar *et al.*<sup>23</sup> have also published an account of their 2-year experience with SLED. They concluded that this technique is well tolerated and offers many of the benefits of continuous techniques, but is technically much simpler to perform and therefore well accepted by the ICU team.

The devices used in these<sup>18,20,22,23</sup> and other<sup>14,24,25</sup> studies of SLED are sophisticated dialysis machines, usually employed for IHD (the 2008H<sup>®</sup><sup>14,18,20,22,23</sup> and the AK200 Ultra<sup>®</sup> [Gambro Lundia AB, Lund, Sweden]).<sup>24</sup> The next important step in developing a straightforward SLED treatment for the ICU setting is simplification of apparatus. We have used the Genius<sup>®</sup> single-pass dialysis system (Fresenius Medical Care Germany, Bad Homburg, Germany) to treat patients with ARF in the ICU.<sup>19,21</sup> This dialysis system is currently available in Europe and South America. The technical principle underlying Genius<sup>®</sup> is based on the very first dialysis systems, the 'tank' or 'batch' devices. Briefly (technical features are described in detail elsewhere<sup>21,26,27</sup>), the dialysis machine does not require the usual infrastructure (e.g. multilocal water supply or waste removal). The sterile dialysis fluid is prepared and loaded into the dialysis machine. Following treatment, used dialysate is drained at a central 'filling station'. Other advantages are reduced thrombogenicity (tubing is completely fluid-filled [i.e. air-free]), simple and reliable control of volumetric ultrafiltration, 100% bicarbonate ultrapure dialysis fluid (with attendant beneficial effects on patient survival<sup>28</sup>) and the option of individualized treatment duration without changing software or hardware.

Different combinations of dry and liquid concentrates can be mixed to theoretically generate up to 240 dialysate compositions, allowing treatments to be tailored to the needs of individual patients. This extremely flexible, yet highly efficient, treatment modality fulfills

all ICU requirements: it offers immediate, highly effective dialysis therapy for acute hyperkalemia, whereas for less-urgent indications, treatment durations can be extended up to 18 h.<sup>19</sup> So, dialysis can be performed overnight, facilitating mobilization of the patient during the day. At our institution, the dialysis machine is completely supervised by ICU nursing staff provided that blood flow does not exceed 200 ml/min, but there is no scientific evidence governing this practice.

In a prospective, randomized controlled study, we treated ventilated critically ill patients suffering from oliguric ARF with either CVVH ( $n=19$ ) or SLED ( $n=20$ ). The urea reduction rate achieved with  $11.7 \pm 0.1$  h of SLED was comparable to that achieved after  $23.3 \pm 0.2$  h of CVVH, even though a substitution fluid exchange rate of at least 3 l/h was used.<sup>21</sup> These data support kinetic models indicating that both CVVH and SLED provide very effective control of azotemia in hypercatabolic ARF patients.<sup>29</sup> Moreover, cardiovascular parameters assessed online via invasive monitoring were not significantly different during CVVH and SLED despite comparable ultrafiltration volumes (although there was a trend towards higher systemic vascular resistance values during SLED).<sup>21</sup> These results confirm that SLED, at absolutely equivalent hemodynamic stability, is at least as efficacious as classical CVVH. The significantly reduced need for heparin associated with SLED can be a decisive advantage, especially in patients at high risk of bleeding.<sup>18,21</sup> Preliminary data indicate that the survival outcome of patients treated with SLED does not differ from that of those treated with state-of-the-art CVVH; more definitive information will become available through impending multicenter prospective randomized trials (The Acute Renal Failure Network Trial [lead investigator, P Palevsky]; and the CRRT vs SLEDD—Substudy of the Stuienberg Hospital Acute Renal Failure Trial [lead investigator, R Lins]).

#### **Night-time sustained low-efficiency dialysis**

Nocturnal SLED allows unrestricted physician access to patients for daytime procedures, thereby minimizing disruption of ICU activities by renal replacement therapy. Several centers have reported their experience with overnight SLED (Table 1). As described above, Marshall and co-workers<sup>20,22</sup> used standard IHD

equipment, and reduced blood (200 ml/min) and dialysate (100 ml/min) flow rates, so that treatment could be supervised by ICU staff (following appropriate training from dialysis personnel). Importantly, their primary intention was to perform 12-hour treatments overnight.<sup>20</sup> Although the nephrology team assumed medical responsibility, the overnight SLED treatments were largely in the hands of the ICU staff.

We have used the Genius® system for night-time SLED.<sup>21</sup> In general, there are no practical differences with respect to performing daytime and night-time SLED. Machines are supervised solely by ICU personnel during the overnight shift; a dialysis nurse is available on-call for advice and troubleshooting. Currently, about 90% of all extracorporeal renal replacement treatments in the Hannover Medical School ICUs are SLED sessions (approximately 3,000 per year). Almost half are performed overnight.

#### **Other sustained low-efficiency dialysis variants and indications**

Some important modifications of the SLED technique have been recently developed. Sustained low-efficiency daily diafiltration (SLEDD-f) combines diffusive and convective solute transport.<sup>30</sup> SLEDD-f is primarily used to improve clearance of putative middle-molecule inflammatory mediators, which are thought to have a role in the pathophysiology of systemic inflammatory response syndrome in critically ill patients. Considerably efficient removal of larger molecules has been reported even for 'standard' SLED with high-flux dialyzers.<sup>21</sup> As mentioned previously, controlled studies have failed to detect a patient survival advantage for CRRT over IHD, despite the fact that convective transport more efficiently eliminates middle molecules.

Another SLED variant is regional citrate anticoagulation.<sup>31–33</sup> Morgera *et al.*<sup>33</sup> have used the Genius® system together with a low calcium dialysate concentration (1 mM) to test the safety and feasibility of a regional citrate anticoagulation protocol with respect to acid–base and electrolyte changes in 27 critically ill patients with ARF. These investigators infused a 4% sodium citrate solution into the arterial line of the extracorporeal circuit, and adjusted the citrate dose according to the post-filter ionized calcium concentration (target values 0.5–0.7 mM) without routine calcium substitution. They observed no significant untoward effects on blood levels of calcium and sodium, and

acid–base values remained equilibrated during citrate anticoagulation. Excellent filter patency and cardiovascular stability of patients were maintained.<sup>33</sup> This was confirmed in a smaller study by Finkel and Foringer,<sup>31</sup> who reported that no clotting occurred during 1,500 h of SLED treatment with citrate infusion.

Encouraged by its efficient elimination of uremic toxins, physicians increasingly use SLED to counteract intoxications.<sup>34–37</sup> For this indication, the advantages of SLED include fewer complications (especially in comparison to charcoal perfusion) and use of regular dialysis machines (minimizing staff load). Many reports of short standard dialysis followed by SLED to prevent rebound of the offending toxin have been published.<sup>35,37,38</sup> Experience is, however, limited to case reports; hence, the optimum role for SLED in management of intoxications merits further study.

#### **Patient monitoring during sustained low-efficiency dialysis**

As SLED efficiently removes small solute molecules, attention must be paid to vital electrolytes such as phosphate. Ten years ago, highly efficient renal replacement therapy was not thought to regularly cause hypophosphatemia in ICU patients;<sup>39</sup> however, SLED in combination with high-flux dialyzers can decrease serum phosphate levels considerably (i.e. from  $2.1 \pm 0.1$  mM to  $1.2 \pm 0.1$  mM within 12 h).<sup>21</sup> As such, in institutions that perform SLED on a daily basis, phosphate supplementation is part of the treatment protocol (approximately 0.1–0.2 mmol/kg daily).<sup>20</sup> A protocol for enriching dialysate with phosphate was reported by Kumar and colleagues.<sup>23</sup> Regular laboratory evaluation allows parenteral or enteral nutrition, including supplementation of electrolytes and trace elements, to be tailored.<sup>20,21</sup>

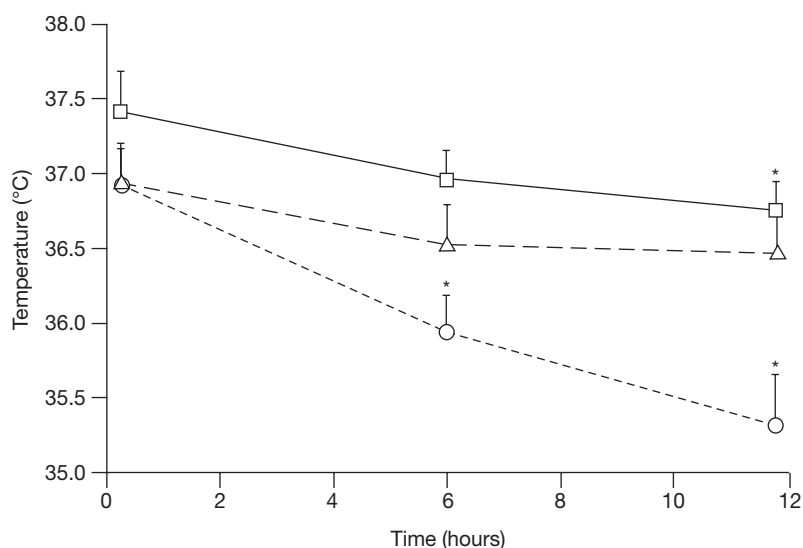
High-efficiency renal replacement therapy has profound effects on the pharmacokinetic and pharmacodynamic properties of all drugs administered to critically ill patients. Despite this, few studies have evaluated the problem, even for high-volume CRRTs.<sup>40</sup> The extent to which SLED eliminates drugs differs greatly from standard thrice-weekly IHD or CRRT. Moreover, dosing and pharmacokinetic data obtained from patients receiving either IHD or CRRT might not be applicable to patients treated with SLED because duration of treatment, the filters used and rates of blood flow are quite different. It is

somewhat surprising that there have been only four pharmacokinetic studies in patients undergoing SLED.<sup>24,41–43</sup> These studies confirmed that there are significant differences in rates of drug removal by SLED compared with IHD and CRRT. Aiming for high-dose renal replacement therapy while adhering to outdated drug-dosing recommendations could therefore lead to underdosing of important drugs, such as antibiotics, in turn having a detrimental effect on critically ill patients suffering from life-threatening infections. Therapeutic drug monitoring should be performed whenever possible. Dosing recommendations for patients with renal failure in the ICU treated with SLED must be developed if excessive mortality due to underdosing of life-saving medications is to be avoided.

Prolonged SLED using the Genius® single-pass system causes slight, but significant, cooling of the patient. The entire volume of dialysis fluid is loaded at once, such that the 90-liter glass container is completely filled and, therefore, air-free. Excessive cooling of the pre-warmed dialysis fluid is prevented by the thermal insulation of the transparent container, but the lack of a separate heater leads to some cooling. Lonnemann *et al.*,<sup>19</sup> using the 75-liter tank of a previous model over 18 h, measured a temperature drop in the venous blood line of the extracorporeal circuit from  $35.3 \pm 0.7^\circ\text{C}$  to  $30.2 \pm 0.8^\circ\text{C}$ , which is equal to an average temperature loss of  $0.28^\circ\text{C}/\text{h}$ . When we performed SLED over a period of 12 h in mainly septic patients, at a blood flow rate of 200 ml/min and a dialysate flow rate of 100 ml/min,<sup>20,21</sup> the core temperature (measured by a thermistor in the femoral artery) decreased slightly, but significantly, from  $37.4 \pm 0.3^\circ\text{C}$  to  $36.7 \pm 0.2^\circ\text{C}$  (Figure 1). The decrease in dialysate temperature, and consequently the patient's core temperature, could actually be advantageous as it increases peripheral resistance and improves cardiovascular stability (as observed in patients on chronic hemodialysis).<sup>44</sup>

#### Microbiological advantages of sustained low-efficiency dialysis

Bicarbonate-based buffers are susceptible to bacterial contamination, especially when the system used for CRRT is opened frequently to connect a bag of replacement fluid and discard the used filtrate.<sup>45</sup> This can occur as often as 40 times per day at a substitution rate of 37.5 ml/kg/h in a 100 kg patient. SLED of any kind does not involve this risk. Moreover, the Genius® system



**Figure 1** Variation in patient temperature during sustained low-efficiency dialysis. Mean core body temperature (square symbols) assessed invasively with a thermistor in the femoral artery, and mean blood temperature in the arterial (triangular symbols) and venous (circular symbols) lines of 18 patients with sepsis and acute renal failure treated with extended dialysis using the Genius® single-pass batch dialysis system. Patients were treated continuously for 12 h. \* $P < 0.05$  versus baseline.

need not be opened once filled. Its smooth, crack-free, straight glass surfaces, ultraviolet-radiator and requirement for ultrapure water make colonization by microorganisms difficult, and facilitate effective cleansing and sterilization. In one analysis, no bacterial growth was found in spent SLED dialysate, even after 18 h.<sup>19,21</sup> So, the spent SLED dialysate almost meets the threshold of sterility ( $<10^{-6}$  colony-forming units/ml).<sup>19</sup> As backfiltration of pyrogens from contaminated dialysate into the blood can induce a drop in blood pressure during high-flux hemodialysis, the high bacteriological quality of the Genius® dialysate might contribute to cardiovascular stability during SLED. The Genius® apparatus also permits easy access to the entire complement of substances removed during a dialysis session. This feature generates exciting opportunities for clinical research in the fields of uremic toxins,<sup>21,46</sup> pharmacokinetics<sup>43,47,48</sup> and intoxications.<sup>34–36</sup>

#### Economic considerations

Substantial cost reduction can be achieved if the equipment used for SLED is also employed for chronic renal replacement therapy in the same hospital. In fact, all centers offering SLED use various standard IHD machines, such as the

2008H® or the Genius® single-pass dialysis system, without adding or altering software or hardware. In some hospitals, flexible treatment modalities allow the same machine to be used for two IHD sessions and one overnight SLED treatment during a 24-hour period. This dual usage has been recognized by major manufacturers of dialysis equipment. Newer machines, like the Fresenius 4008 series (4008K in the US, 4008S ArRT-Plus in Australia [Fresenius Medical Care-Asia Pacific Ltd, New South Wales] and 4008S elsewhere), have a built-in option for SLED, which is selected from the startup screen without any delay or requirement for further adjustment. Several economic evaluations have shown SLED to be less expensive than CRRT, both within the setting of the US healthcare reimbursement scheme and within a more widely applicable nationalized healthcare system.<sup>49,50</sup> The main sources of cost savings are reduced staff load and reduced need for industrially produced sterile substitution fluid.

### CONCLUSIONS

Indications for SLED have the potential to expand to include prolonged high-volume treatment of severely ill patients, such as highly catabolic patients with systemic inflammatory response syndrome. SLED permits normalization of indicators of uremic intoxication (e.g. blood urea concentration) in a short time, as well as hemodynamic stabilization.<sup>10,27</sup> High-volume CVVH is currently too expensive to be widely used in critically ill patients. Moreover, SLED offers an alternative to conventional IHD in treatment of acute intoxications with a variety of drugs, including carbamazepine and salicylate.<sup>34–37</sup> We reported that SLED can be a safer and less-costly alternative to hemoperfusion of substances that are believed to be poorly responsive to dialysis (e.g. life-threatening intoxication with valproic acid in a thrombopenic patient).<sup>35</sup>

In summary, SLED is an increasingly utilized renal replacement therapy that facilitates efficient detoxification and has a favorable cardiovascular tolerability profile, even in critically ill patients with ARF in the ICU. The technically simple single-pass batch dialysis systems are easy for ICU staff to operate and offer a high degree of flexibility with regard to the timing of treatment. As an alternative to classical intermittent or CRRTs, SLED will have an important role in renal replacement therapy for critically ill patients in the future. This potential

is currently being explored in comparative studies of treatment outcomes with SLED, IHD and CRRT.

### KEY POINTS

- Renal failure in the intensive care unit is increasingly being managed with prolonged dialysis at low blood and dialysate flow rates ('sustained low-efficiency dialysis' or SLED)
- Advantages of SLED are efficient clearance of small solutes, good cardiovascular tolerability, low risk of microbiological contamination, flexible treatment schedules and reduced costs
- Standard dialysis equipment or single-pass batch systems can be used for SLED
- Studies comparing outcomes of SLED with those of standard intermittent and continuous modalities are being performed

### References

- 1 Himmelfarb J and Ikizler TA (2000) Quantitating urea removal in patients with acute renal failure: lost art or forgotten science? *Semin Dial* **13**: 147–149
- 2 Uchino S *et al.* (2005) Acute renal failure in critically ill patients: a multinational, multicenter study. *JAMA* **294**: 813–818
- 3 Augustine JJ *et al.* (2004) A randomized controlled trial comparing intermittent with continuous dialysis in patients with ARF. *Am J Kidney Dis* **44**: 1000–1007
- 4 Lameire N *et al.* (2005) Acute renal failure. *Lancet* **365**: 417–430
- 5 Metnitz PG *et al.* (2002) Effect of acute renal failure requiring renal replacement therapy on outcome in critically ill patients. *Crit Care Med* **30**: 2051–2058
- 6 Kellum JA *et al.* (2002) The first international consensus conference on continuous renal replacement therapy. *Kidney Int* **62**: 1855–1863
- 7 Uehlinger DE *et al.* (2005) Comparison of continuous and intermittent renal replacement therapy for acute renal failure. *Nephrol Dial Transplant* **20**: 1630–1637
- 8 Venkataraman R *et al.* (2002) Dosing patterns for continuous renal replacement therapy at a large academic medical center in the United States. *J Crit Care* **17**: 246–250
- 9 Manns B *et al.* (2003) Cost of acute renal failure requiring dialysis in the intensive care unit: clinical and resource implications of renal recovery. *Crit Care Med* **31**: 449–455
- 10 Cole L *et al.* (2001) High-volume haemofiltration in human septic shock. *Intensive Care Med* **27**: 978–986
- 11 Schrier RW *et al.* (2004) Acute renal failure: definitions, diagnosis, pathogenesis, and therapy. *J Clin Invest* **114**: 5–14
- 12 Ronco C *et al.* (2000) Effects of different doses in continuous veno-venous haemofiltration on outcomes of acute renal failure: a prospective randomised trial. *Lancet* **356**: 26–30
- 13 Schiffi H *et al.* (2002) Daily hemodialysis and the outcome of acute renal failure. *N Engl J Med* **346**: 305–310
- 14 Kudoh Y *et al.* (1988) Slow continuous hemodialysis—new therapy for acute renal failure in critically ill patients—Part 2. Animal experiments and clinical implication. *Jpn Circ J* **52**: 1183–1190
- 15 Kudoh Y and Iimura O (1988) Slow continuous hemodialysis—new therapy for acute renal failure in critically ill patients—Part 1. Theoretical consideration and new technique. *Jpn Circ J* **52**: 1171–1182

- 16 Tam PY *et al.* (1988) Slow continuous hemodialysis for the management of complicated acute renal failure in an intensive care unit. *Clin Nephrol* **30**: 79–85
- 17 Schlaefer C *et al.* (1999) High clearance continuous renal replacement therapy with a modified dialysis machine. *Kidney Int Suppl* **72**: S20–S23
- 18 Kumar VA *et al.* Extended daily dialysis: a new approach to renal replacement for acute renal failure in the intensive care unit. *Am J Kidney Dis* **36**: 294–300
- 19 Lonnemann G *et al.* (2000) Extended daily veno-venous high-flux haemodialysis in patients with acute renal failure and multiple organ dysfunction syndrome using a single path batch dialysis system. *Nephrol Dial Transplant* **15**: 1189–1193
- 20 Marshall MR *et al.* (2001) Sustained low-efficiency dialysis for critically ill patients requiring renal replacement therapy. *Kidney Int* **60**: 777–785
- 21 Kielstein JT *et al.* (2004) Efficacy and cardiovascular tolerability of extended dialysis in critically ill patients: a randomized controlled study. *Am J Kidney Dis* **43**: 342–349
- 22 Marshall MR *et al.* (2002) Urea kinetics during sustained low-efficiency dialysis in critically ill patients requiring renal replacement therapy. *Am J Kidney Dis* **39**: 556–570
- 23 Kumar VA *et al.* (2004) Extended daily dialysis vs continuous hemodialysis for ICU patients with acute renal failure: a two-year single center report. *Int J Artif Organs* **27**: 371–379
- 24 Fiaccadori E *et al.* (2004) Removal of linezolid by conventional intermittent hemodialysis, sustained low-efficiency dialysis, or continuous venovenous hemofiltration in patients with acute renal failure. *Crit Care Med* **32**: 2437–2442
- 25 Ratanarat R *et al.* (2005) Phosphate kinetics during different dialysis modalities. *Blood Purif* **23**: 83–90
- 26 Dhondt AW *et al.* (2003) Studies on dialysate mixing in the Genius® single-pass batch system for hemodialysis therapy. *Kidney Int* **63**: 1540–1547
- 27 Fliser D and Kielstein JT (2004) A single-pass batch dialysis system: an ideal dialysis method for the patient in intensive care with acute renal failure. *Curr Opin Crit Care* **10**: 483–488
- 28 Barenbrock M *et al.* (2000) Effects of bicarbonate- and lactate-buffered replacement fluids on cardiovascular outcome in CVVH patients. *Kidney Int* **58**: 1751–1757
- 29 Liao Z *et al.* (2003) Kinetic comparison of different acute dialysis therapies. *Artif Organs* **27**: 802–807
- 30 Marshall MR *et al.* (2004) Sustained low-efficiency daily dialysis (SLEDD-f) for critically ill patients requiring renal replacement therapy: towards an adequate therapy. *Nephrol Dial Transplant* **19**: 877–884
- 31 Finkel KW and Foringer JR (2005) Safety of regional citrate anticoagulation for continuous sustained low efficiency dialysis (C-SLED) in critically ill patients. *Ren Fail* **27**: 541–545
- 32 Marshall MR *et al.* (2003) Regional citrate anticoagulation during simulated treatments of sustained low efficiency dialysis. *Nephrology* **8**: 302–310
- 33 Morgera S *et al.* (2004) A simple, safe and effective citrate anticoagulation protocol for the genius dialysis system in acute renal failure. *Nephron Clin Pract* **98**: c35–c40
- 34 Kielstein JT *et al.* (2002) High-flux hemodialysis—an effective alternative to hemoperfusion in the treatment of carbamazepine intoxication. *Clin Nephrol* **57**: 484–486
- 35 Kielstein JT *et al.* (2003) Efficiency of high-flux hemodialysis in the treatment of valproic acid intoxication. *J Toxicol Clin Toxicol* **41**: 873–876
- 36 Kielstein JT *et al.* (2004) One for all—a multi-use dialysis system for effective treatment of severe thallium intoxication. *Kidney Blood Press Res* **27**: 197–199
- 37 Lund B *et al.* (2005) Efficacy of sustained low-efficiency dialysis in the treatment of salicylate toxicity. *Nephrol Dial Transplant* **20**: 1483–1484
- 38 Hicks LK and McFarlane PA (2001) Valproic acid overdose and haemodialysis. *Nephrol Dial Transplant* **16**: 1483–1486
- 39 Zazzo JF *et al.* (1995) High incidence of hypophosphatemia in surgical intensive care patients: efficacy of phosphorus therapy on myocardial function. *Intensive Care Med* **21**: 826–831
- 40 Mueller BA *et al.* (2003) Higher renal replacement therapy dose delivery influences on drug therapy. *Artif Organs* **27**: 808–814
- 41 Ahern JW *et al.* (2004) Experience with vancomycin in patients receiving slow low-efficiency dialysis. *Hospital Pharmacy* **39**: 138–143
- 42 Fish DN and Chow AT (1997) The clinical pharmacokinetics of levofloxacin. *Clin Pharmacokinet* **32**: 101–119
- 43 Kielstein JT *et al.* (2005) Pharmacokinetics and total elimination of meropenem and vancomycin in intensive care unit patients undergoing extended daily dialysis. *Crit Care Med* **33** (online ahead of print) [doi:10.1097/01.ccm.0000190243.88133.3f]
- 44 van der Sande FM *et al.* (2001) Thermal effects and blood pressure response during postdilution hemodiafiltration and hemodialysis: the effect of amount of replacement fluid and dialysate temperature. *J Am Soc Nephrol* **12**: 1916–1920
- 45 Kanagasundaram NS *et al.* (2003) A preliminary survey of bacterial contamination of the dialysate circuit in continuous veno-venous hemodialysis. *Clin Nephrol* **59**: 47–55
- 46 Kielstein JT *et al.* (2004) Low dialysance of asymmetric dimethylarginine (ADMA)—*in vivo* and *in vitro* evidence of significant protein binding. *Clin Nephrol* **62**: 295–300
- 47 Kielstein JT *et al.* (2005) Dialysate concentration and pharmacokinetics of 2F-Ara-A in a patient with acute renal failure. *Eur J Haematol* **74**: 533–534
- 48 Liefeldt L *et al.* (2004) Treatment of secondary pulmonary hypertension with bosentan and its pharmacokinetic monitoring in ESRD. *Am J Kidney Dis* **43**: 923–926
- 49 Alam M *et al.* (2000) Cost comparison between sustained low efficiency hemodialysis (SLED) and continuous venovenous hemofiltration (CVVH) for ICU patients with ARF. *Am J Kidney Dis* **35**: A9
- 50 Ma T *et al.* (2002) Cost comparison between sustained low efficiency daily dialysis/diafiltration (SLEDD) and continuous renal replacement therapy for ICU patients with ARF. *Nephrology* **7**: A54
- 51 Naka T *et al.* (2004) Prolonged daily intermittent renal replacement therapy in ICU patients by ICU nurses and ICU physicians. *Int J Artif Organs* **27**: 380–387

**Competing interests**

The authors declared competing interests; go to the article online for details.