

Machines for Continuous Renal Replacement Therapy

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ABSTRACT

A significant number of advancements have taken place since the beginning of continuous renal replacement therapy (CRRT). In particular, high volume hemofiltration and high permeability hemofiltration have been successful extensions of the technique. The additional and combined use of sorbent has also been tested successfully. Specific machines have now been designed to permit safe and reliable performance of the therapy. These new devices are equipped with a friendly user interface that allows for easy performance and monitoring. The apparent complexity of the circuit is made simple by a self-loading circuit or a cartridge which includes the filter and the blood and dialysate lines. Priming is performed automatically by the machine and pre- or postdilution (reinfusion of substitution fluid before or after the filter) can easily be performed by

changing the position of the reinfusion line. These new machines permit all CRRT methodologies to be performed by programming the flows and the total amounts of fluid to be exchanged or circulated as a countercurrent dialysate at the beginning of the session. Progress has been made not only in technology in this area but also on our understanding of the pathophysiology of acute renal failure. New biomaterials and new devices are now available with new frontiers are on the horizon. We might, however, speculate that although improvements have been made, a lot remains to be done. There is no doubt that technology has progressed enormously in critical care nephrology and that more progress will come in the near future. The goal, and likely outcome, is an improvement in the morbidity and mortality of the most severely ill patients.

In 1977, Peter Kramer introduced a simple therapy called continuous arteriovenous hemofiltration (CAVH) (1). In the following years, CAVH represented an important alternative to hemodialysis (HD) or peritoneal dialysis especially in those patients where severe clinical conditions precluded the traditional forms of renal replacement (2). CAVH enabled small centers not equipped with HD facilities to perform acute renal replacement therapy (RRT). The technique, however, rapidly displayed its limitations and despite good fluid control, urea clearance could not exceed 15 l/24 hours. Since most critically ill patients are severely catabolic, the amount of urea removed frequently resulted in an insufficient control of blood urea levels and inadequate blood purification.

For this reason, Geronemus et al. in 1984 introduced the use of continuous arteriovenous hemodialysis (CAVHD) (3). The treatment was similar to CAVH but a low permeability membrane could be employed and countercurrent dialysate flow was provided to increase urea removal by the addition of diffusion. A daily urea clearance in the range of 24–26 l could be achieved with

CAVHD. During that time, we applied the same concept to a highly permeable hollow fiber hemodiafilter, and we first described the treatment called continuous arteriovenous hemodiafiltration (CAVHDF) (4). In this treatment, the high convection rates combined with the countercurrent dialysate flow allowed increased removal of small and large molecules.

One of the major limitations imposed by the arteriovenous approach was the unstable performance of the circuit because of reductions of extracorporeal blood flow from patient hypotension, or line kinking and filter clotting. This frequently resulted in treatment interruptions, reduced daily clearance, and treatment failure (5). On the other hand, the perception of continuous renal replacement therapy (CRRT) had changed over time and, by the late eighties, CRRT had become more and more accepted in the intensive care units (ICUs) as a standard form of therapy (6). Therefore, thanks to the development of reliable double lumen venous catheters and a new generation of blood pump modules for continuous therapies, the use of CAVH started to decline and the more efficient continuous veno-venous hemofiltration (CVVH), continuous veno-venous hemodialysis (CVVHD), or continuous veno-venous hemodiafiltration (CVVHDF) became the golden standard (7,8). CVVH can be performed in postdilution mode reaching daily clearances for urea in the range of 36–48 l. When predilution is performed, the requirement of heparin may be remarkably reduced and ultrafiltration (UF) can be increased up to 48–70 l/24 hours. Since predilution

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decreases the effective concentration of the solute in the filtered blood, the amount of solute removal is not proportional to the amount of UF and it must be scaled down by a factor depending on the percent of predilution versus blood flow.

The increased amount of fluid exchanged per day in CVVH led to the utilization of automated blood modules equipped with blood leak detectors, pressure alarms, and pressure drop measurement in the dialyzer (9). However, despite the achievement of higher efficiency, safety and reliability were still questionable in these machines that were basically derived from HD blood modules and were never designed as self-standing units for CRRT. In most cases, volumetric pumps were added to a blood module to achieve UF and replacement fluid volume control. This approach is still in use in several units and it is defined as adaptive technology. Adaptive technology may be very effective but it presents the risk of operating with components that are not interconnected and therefore they are not completely safe according to the standards of an integrated machine (9). For this reason, a full spectrum of CRRT machines has been developed over the years (Fig. 1).

Machines for CRRT

The modern history of CRRT is characterized by the development of CRRT machines designed specifically for acute renal replacement in intensive care patients (Fig. 2). These machines are all equipped with integrated safety alarms, fluid balancing controls, and connected blood modules with the possibility to perform CVVH, CVVHD, and CVVHDF. Such machines can now achieve a smooth conduction of RRT in the ICU, and they can perform continuous as well as intermittent RRTs with increased levels of efficiency. Blood flows up to 500 ml/minutes and dialysate/replacement fluid flow rates in the same ranges lead to urea clearances that reach levels close to standard HD machines. At the same time, the highly permeable membranes utilized in CRRT systems achieve improved clearances of the larger molecular weight solutes. Because of the higher blood and dialysate flow rates achievable, higher surface areas can now be utilized and more efficient treatments can be carried out. The fluid control is achieved via gravimetric

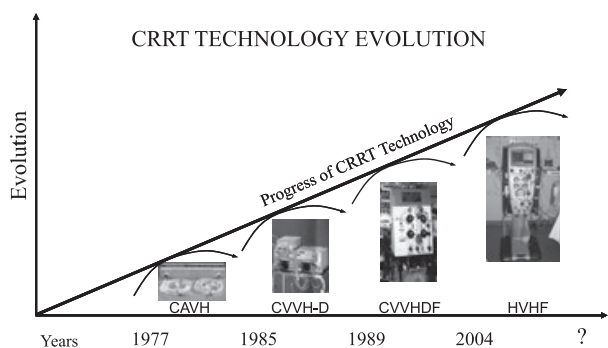


FIG. 1. Evolution of CRRT machines from CAVH to the latest generation of equipment.

or volumetric control systems which drive peristaltic pumps both for UF and reinfusion. The priming procedures are simplified because of the step-by-step on-line help and the self-loading of preassembled tubing sets.

The new machines are also equipped with a friendly user interface, leading to an increased confidence of the personnel with the therapy while constant levels of efficiency can be obtained without major problems or complications (10). In Table 1, we compare different features of each machine. Although blood and dialysate flow ranges vary from one to another, they have overall dramatically increased in comparison to the first generation of machines. Some of the new machines present operational conditions similar to those utilized for chronic HD, allowing for the use of the machine for different treatments and purposes. Most machines work either in pure convection or in diffusion, or in combined mode. They have the capability to perform treatments with high exchange volumes such as high volume hemofiltration (HVHF). In these circumstances, the presence of an adequate warmer for the replacement fluid is very important to maintain thermal balance. Separate on-line monitors for thermal balance and for blood volume determination are available on the market but are integrated in the machines only in isolated cases (11,12). New machines are equipped with preset disposable circuits or with easy instructions for the rinsing/priming phase of the therapy.

The friendly user interface plays an important role in the selection of the therapy mode and the smooth conduction of the entire session. This makes these machines well suited for the use in ICUs where the experience of the personnel may not be as wide as in the dialysis setting. The presence of an increased number of pressure sensors in the machines renders the monitoring of the treatment easier and accurate. In particular, the measurement of the end-to-end pressure drop in the dialyzer allows for the monitoring of the patency of the blood compartment and permits early identification of signs of clotting or dialyzer malfunction. In some machines, the pressure transducers are designed to prevent the contact of blood with air and the lines are constructed with special membrane buttons that transmit the pressure values to the sensor without air-to-blood interface. The measurement of net filtration and the balance between UF and reinfusion is performed with one or two scales in different machines. Most of these systems also operate in continuous HD to achieve the desired balance between the dialysate inlet and the dialysate outlet. A remarkable accuracy is observed in most cases.

The metabolic control of acute kidney injury (AKI) generally requires at least 30 l of urea clearance per day and several studies have considered an adequate dose above 35 ml/kg/hours, although recent evidence suggests that doses between 20 and 35 ml/kg/hours can be equally effective. The combination of diffusion and convection has shown that satisfactory clearances of small and medium large molecules can generally be achieved. In septic patients with increased levels of substances in the middle molecular weight range (500–5000 Dalton) such as chemical mediators of the humoral response to endotoxin, treatment should control not only urea and

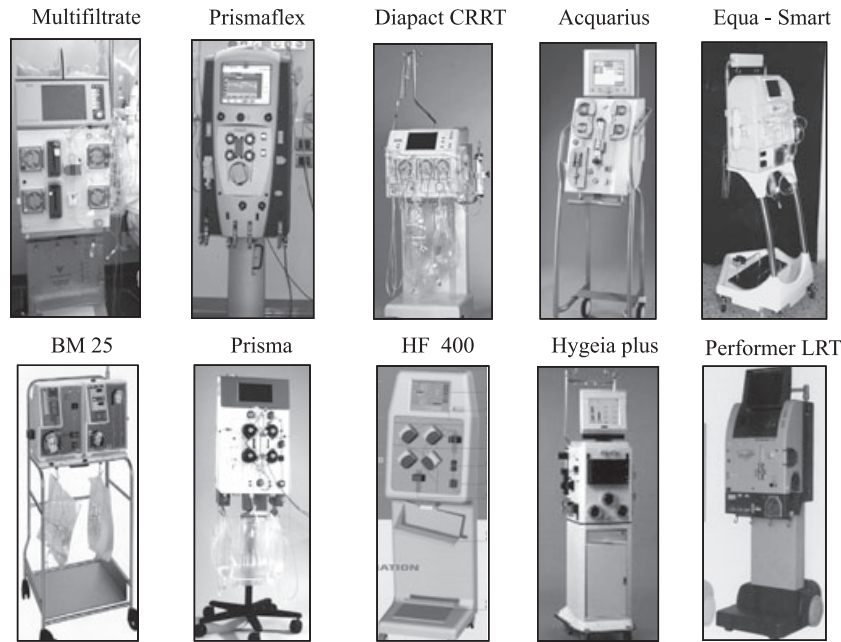


FIG. 2. Examples of CRRT machines available in the market. Details are reported in Table 1.

other waste products, but also the circulating levels of these proinflammatory substances (13).

To achieve such a complex task, high convective rates may be required (14). In these conditions, the necessary rate of convection can be obtained in continuous hemofiltration (HF), in continuous hemodiafiltration (HDF) (in this case, four pumps are required) or in continuous high flux HD with continuous dialysate volume control (three pumps are required and a reliable UF control system). In HDF, dialysate outlet flow exceeds the volume of inlet dialysate volume and the required UF, and for this reason, a replacement fluid is required. In high flux dialysis, replacement fluid is not required and the balance is obtained by a mechanism of internal backfiltration. Warmed dialysate is delivered at a programmed flow rate and the second pump regulates the dialysate outlet flow rate and net UF with a continuous volume control. In some machines, this treatment has been performed in recirculation mode and has been defined as continuous high flux dialysis because of the filtration-backfiltration mechanism similar to that of high flux dialysis in chronic HD (15). Once the patient's dry weight has been achieved, the circuit may operate at zero net filtration using sterile dialysate at various flows (50–200 ml/minutes). With relatively high volume HF (2–3 l/hours), HDF or high flux dialysis, the clearance of small and large molecules is improved. If performed continuously, the treatments can provide weekly Kt/V in the range of 7–10, thus resulting in treatment efficiency much higher than that achieved with other intermittent HD therapies (16). At the same time, significant amounts of proinflammatory mediators can be removed leading to an improved hemodynamic stability (17).

Besides the number of the pumps, an important feature of CRRT machines is the operator interface. The wide color screen of some machines allows an easy access to the required information and on-line help for

most of the functions (Fig. 2). The issue of collecting the treatment data is an important one and almost all the machines are now equipped with a RS232 computer port that allows a complete extraction of data and the ability to export the data to a spreadsheet or a database. Some machines are even equipped with built in printers with automatic printing of the data at the end of the session.

The transportability of the machine is an important aspect to be considered since these treatments may be performed in different sites of the same hospital or even outside, especially in peripheral units or disaster areas. The structure of the machines includes, in most cases, a practical trolley with easy movement of the equipment.

Technical Characteristics of Common CRRT Machines

The Prisma

The Prisma Machine (Gambro-Sweden) was the first integrated equipment specifically designed for CRRT. The machine features a preassembled cartridge including lines and the dialyzer. Tubing loading is automatic as well as the priming procedure. The presence of four pumps and three independent scales allows performing all the CRRT techniques. Blood flow can vary from 0 to 180 ml/minutes while dialysate flow ranges between 0 and 40 ml/minutes. The fluid handling capacity is 5 l. Pre, post, and simultaneous pre-post dilution modes are available (Fig. 3).

The Prismaflex Machine

The new "Prismaflex machine" (Gambro-Sweden), like all new generation platforms for CRRT, presents new features specifically designed to perform therapies with high fluid volume exchange (HVHF), supposedly

TABLE 1. Characteristics of recent CRRT machines

	Company	Pumps	Qb (ml/min)	Qd (ml/min)	Fluid manag (liters)	Heater	Heparin pump	Reinfus sites	Pressure sensors	Printer/ RS-332 P	Scales	Possible techniques
Acquarius	Ew L S Baxter	4	0-450	0-165	10.1	Y	Y	Pre Post	4	No Y	2	(IHD-IHFD)-IHF, PEX-PAP SCUF-CVWH-CVVHD- CVVHFD Pediatric Tx
BM 25	Ew L S Baxter	3	30-500	0-150	16.1	No	No	Pre-post Post	2	No Y	2	SCUF-CVWH-CVVHD-PEX Pediatric Tx (Qb = 5-150 ml/minutes)
Diapact	B. Braun	3	10-500	5-400	25.1	Y	No	Pre Post	4	No Y	1	IHD-IHFD-IHF, PEX-PAP SCUF-CVWH-CVVHD- CVVHFD
Equa-Smart	Medica	2*	5-400	0-150	10.1	Y	Y	Pre Post	3	Y Y	3	SCUF-CVWH-CVVHD- CVVHDF-PEX-Pediatric Tx
2008H 2008K	FMC-NA	1+3**	0-500	0-300	Open	Y	Y	No	3	No	Volumetric	IHD-IHFD, SLED-SCUF- CVVHD Pediatric Tx
Multimat B	Bellco	2***	0-400	0-75	25.1	No	Y	Pre Post	3	No No	1	SCUF-CVWH-CVVHD-CPFA
HF 400	Infomed	4	0-450	0-200	12.1	Y	Y	Pre Post	4	No Y	2	IHD-IHFD-IHF, PEX, SCUF- CVWH-CVVHD-CVVHFD- CVVHDF-Pediatric Tx
Hygeia plus	Kimal	4	0-500	0-65	4.1	Y	Y	Pre-Post Pre Post	4	Y Y	Volumetric	SCUF-CVWH-CVVHD CVVHDF-PEX
Performer	Rand	4****	5-500	0-500	20.1	Y	Y	Pre-Post Pre Post	4	Y Y	1	IHD-IHFD-IHF, PEX-PAP- SCUF-CVWH-CVVHD- CVVHFD-CVVHDF
Prisma	Gambro	4	0-180	0-40	5.1	Blood warmer	Y	Pre Post	4	No Y	3	SCUF-CVWH-CVVHD- CVVHFD-CVVHDF-PEX
Multifiltrate	FMC	4	0-500	0-70	24.1	Y in-line	Y	Pre-Post Pre Post	4	No Y	4	SCUF-CVWH-HV-HF CVVHD CVVHFD-CVVHDF-PEX
Prismaflex	Gambro	5	0-450	0-133	15.1	Y in-line	Y	Pre-Post Pre Post Pre-BP	5	No Y	4	SCUF-CVWH-HV-HF CVVHD CVVHFD-CVVHDF-PEX

*2 Pumps + 2 intelligent clamps; **the 3 pumps for dialysate and fluid replacement are positioned inside the hydraulic circuit of the monitor; ***every pump runs two tubing segments; ****the machine is equipped with thermal sensors.

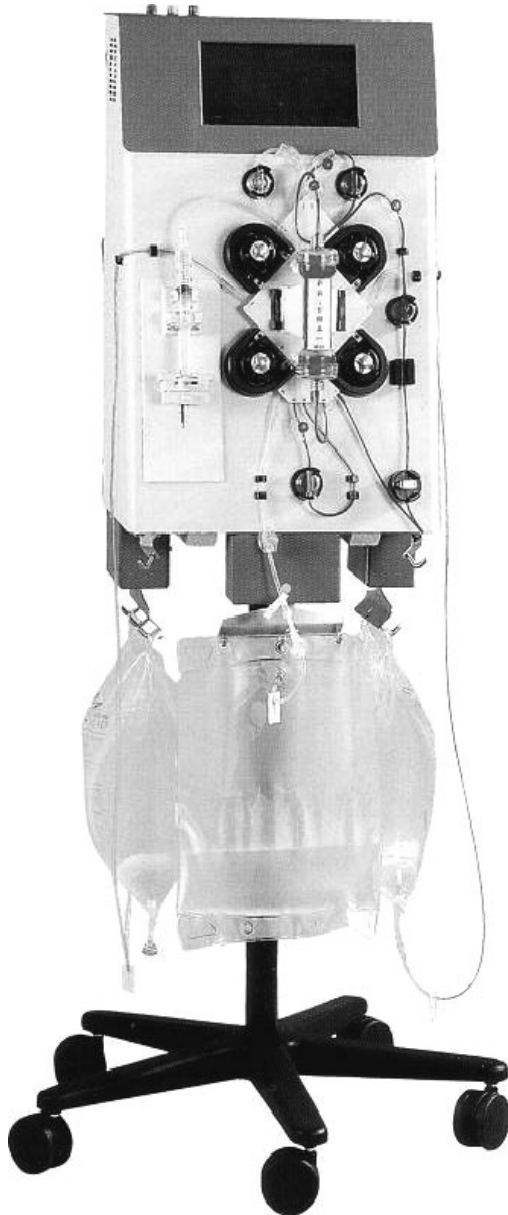


FIG. 3. The Prisma machine.

effective in AKI, sepsis, and multiple organ dysfunction syndrome. The machine features five pumps [blood, dialysate, preblood-pump replacement solution (PBP), postblood-pump replacement solution, and effluent], four scales (effluent, dialysate, and two for replacement solutions), and a disposable set with preconnected high flow dialyzers and fluid circuitry. The machine performs a complete spectrum of therapies [slow continuous ultrafiltration (SCUF), CVVH, CVVHD, CVVHDF, therapeutic plasma exchange (TPE/PE_x), and hemoperfusion (HP)]. Three different preconnected kits with different surface area dialyzers for adult treatments are available: the M100 (the same as the Prisma set with AN69 membrane), the HF 1000, and the HF 1400 (Fig. 4), which have a larger surface (0.60, 1.00, and 1.40 meters square respectively) that are useful in high-volume therapies. The last two have also different membranes [polyaryl-

thersulphone (PAES)]. Contrary to the previous configuration in the classic Prisma machine, the blood inlet is at the bottom of the dialyzer, facilitating the priming procedure and eliminating air bubbles from the blood compartment. The innovative technique of two pinch valves provides the ability to vary the ratio between pre- and postdilution with different simultaneous infusion rates. This ratio can also be changed during therapy. Pre- or postdilution mode can also be selected for CVVHDF modality. A heparin syringe pump has been designed to accommodate different types and sizes of syringes.

Another innovative feature is now present in the Prismaflex machine: the fifth pump. This pump delivers pre-blood-pump (PBP) fluid infusion, permitting the use of citrate for circuit anticoagulation. This feature, in fact, allows citrate infusion just after the connection between the arterial access and the blood line.

The blood pump is bigger than in the earlier version and allows blood flows within a range of 10–450 ml/minutes (depending on the filter in use). Fluid flow rate allows a maximum fluid handling of 8000 ml/hours: both in HF and in HDF. If PBP replacement solution is used, fluxes can be further increased; in this case, the blood pump is able to automatically adjust its rotational speed in order to maintain the prescribed blood flow, which otherwise would be relatively decreased by the scaling down factor induced by PBP infusion. Total effluent delivery is from 0 to 10,000 ml/hours, allowing a maximum UF of 2000 ml/hours combined with the maximum dialysate/reinfusate flow rate. All these schemes are clearly designed to facilitate HVHF.

Prismaflex software controls fluid flow by an accurate pump-scales feedback: 30 g per hour is the accepted error for each pump and an alarm warns the operator if this limit is exceeded. The accuracy warranty is further ensured by an end-of-treatment set up, in case of scales damage or need for calibration. When the therapy is interrupted by a pressure alarm, it automatically restarts if the pressure level normalizes within a few seconds (i.e., during coughs or inadvertent line kinking because of patients movements). Scales have become four parallel sliding “drawers” positioned below the monitor, and are able to shift-out and allow easy collection of fluid bags.

One of the most frequent concerns, the development of clots in the deaerating chamber, has been removed by an innovative design. The chamber is connected by a line to a pressure sensor which is able to adjust chamber blood level through a pump. A reversed cone inside the chamber makes the blood run into the return line with a whirling movement, which reduces stagnant flows; furthermore, when replacement solution is reinfused postfilter, it is poured directly on top of this cone in order to create a fluid layer between air and blood.

Sets are completed with 9 l effluent collection bags (Fig. 5), allowing for the application of high volume therapies without generating an excessive workload of ICU nurses. The colored monitor displays pressures and flows in the first page and complete full graphs and events lists in other history pages. A PCMCIA card allows for the download of these data into laptop

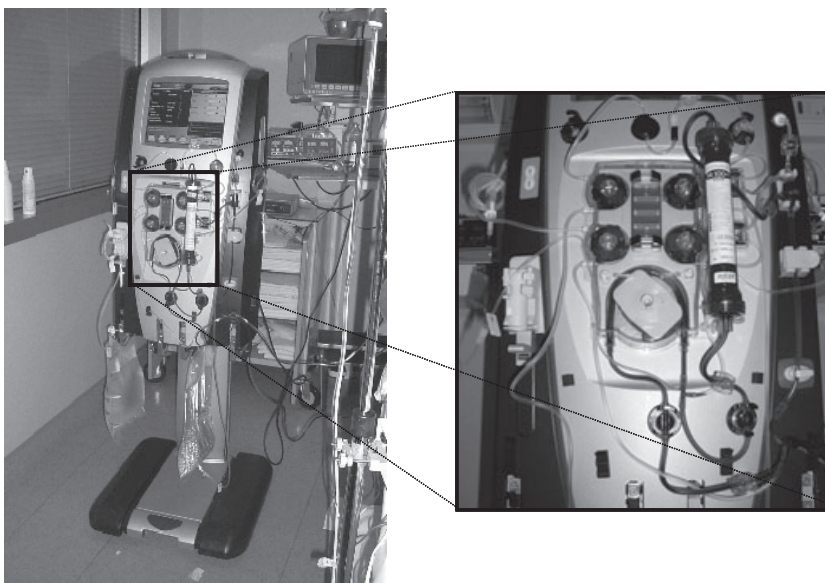


FIG. 4. The Prismaflex machine and the detail of the extracorporeal circuit.

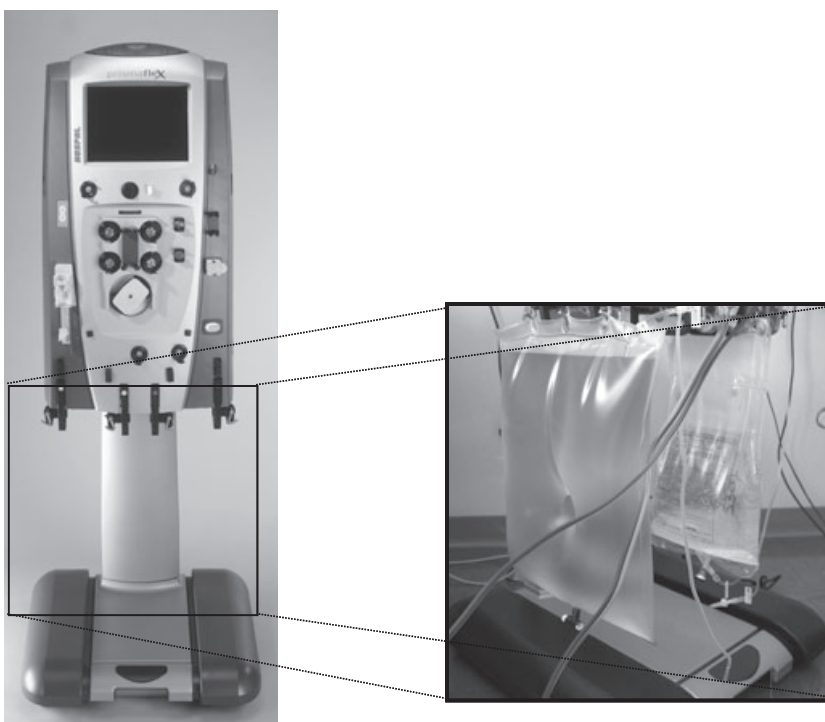


FIG. 5. Scales of the Prismaflex machine with fluid bags for replacement and dialysate.

computers. Among the new features, filters with modified and treated surfaces (ST 60, ST 100, ST 150) are available with various surface areas in different kits.

The Diapact CRRT

The Diapact machine (B.Braun, Melsungen) is derived from a series of prototypes called ECU (Emergency case units). The system contains three pumps with a wide range of blood flows (10–500 ml/minutes) and dialysate flows (5–400 ml/minutes) (Fig. 6). Fluid handling and UF control is gravimetric with one scale

(Fig. 7). Dialysate is warmed and the heparin pump is included. Reinfusion can be performed either in pre- or in postdilution mode during HF. The machine is particularly suited for continuous high flux dialysis and can be operated either in single pass or in recirculation mode.

The Acquarius/Accura

The Acquarius/Accura machine (Edwards Life Sciences, Irvine, CA, USA) is a modern machine for CRRT (Fig. 8). The system includes four pumps and two scales with a possibility of performing all the CRRT



FIG. 6. The Diapact machine.

techniques (Fig. 9). The blood flow can be varied from 0 to 450 ml/minutes while the dialysate flow rate ranges between 0 and 165 ml/minutes. The system includes a preassembled tubing set and a wide color screen with a friendly user interface. The priming procedure is automatic. A fluid heater and the heparin pump are included in the machine. Two independent scales allow for an accurate and continuous fluid balancing while four pressure sensors help to monitor the extracorporeal circuit function. Pre-, post, and simultaneous pre-post dilution modes are available. A remarkable flexibility and versatility characterize the machine.

The 2008H/K

The 2008H/K machine (Fresenius Medical Care, Walnut Creek, CA, USA) is basically a standard HD

machine which has been adapted to CRRT and mostly sustained low efficiency dialysis (SLED) by modifying the software and the operational parameters (Fig. 10). The machine is equipped with a blood pump plus three pumps for dialysate which are internal. Blood flow can vary from 0 to 500 ml/minutes while the dialysate flow in CRRT mode can be set at three fixed values of 100, 200, and 300 ml/minutes. Dialysate is warmed and the heparin pump is built-in. The system does not include a reinfusion pump and HF techniques cannot be performed. The UF control is open-volumetric.

Other machines as depicted in Fig. 2 are available in the world but not in the United States. The evolution of machines is continuous and changes may occur every day. We did not intend to be complete in the description of all available machines but rather to describe some models as an example of CRRT technology. Therefore, the fact that our list may be incomplete does not mean that we suggest or prefer one model against another. For a more detailed description of the machines, set up and troubleshooting, purchase, and maintenance, we suggest to contact the nearest agent of the chosen company.

High Volume Hemofiltration

Recent experimental findings (18) have demonstrated the beneficial impact of increasing the volume of UF during continuous HF therapy. Hemodynamic improvement has been observed in the experimental animal injected with endotoxin. Although the possibility of preventing the septic shock syndrome in humans by this technique has not been proven yet, in a controlled-randomized trial we could demonstrate a clear reduction of the required dose of norepinephrine in septic patients treated with UF rate 6 l/hours. The treatment seems to be promising and further investigation should include the use of larger surface areas as well as the use of more open membranes.

To perform HVHF, a clear definition of the operational ranges of the technique and a precise description of the technical requirements imposed by this form of therapy are definitely needed. According to present clinical practice, CVVH is generally performed with an average UF rate between 1 and 2 l/hour. Above the value of 50 l/day, the amount of UF begins to be considered "high" and the treatment can be defined as HVHF.

There are two ways to perform HVHF. In treatment schedule 1, the standard CVVH treatment schedule is maintained and the rate of UF is maintained at 3–4 l/hours; in treatment schedule 2, the standard CVVH therapy is maintained overnight, but during few hours of the day, a large amount of UF is produced at rates above 6 l/hours. In both cases, the amount of UF exchanged per day may exceed 60 l. To perform this treatment, several requirements must be fulfilled and above all, a deep knowledge of the mechanism of transmembrane UF in the hemofilters is required.

HVHF requires large hemofilters to accomplish the task of achieving a daily fluid exchange in the range of 60–100 l. In treatment schedule 1, hemofilters of 1.0 square meters can be utilized; for schedule 2, hemofilters

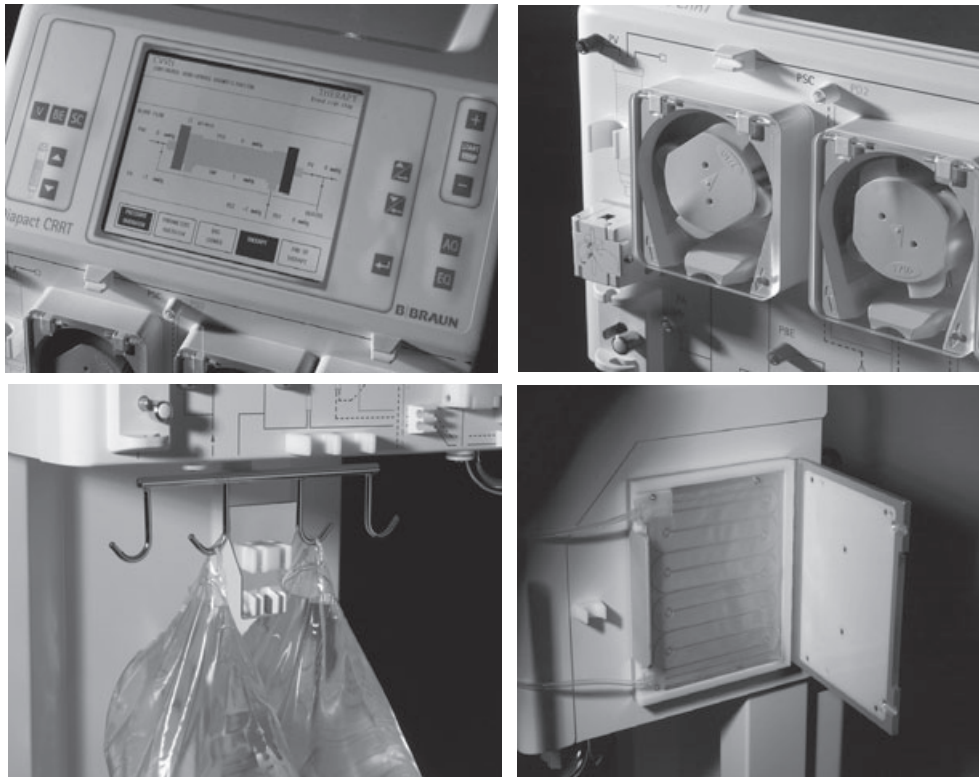


FIG. 7. Details of the Diapact machine: Screen with pressure profiles, pumps, scales, and fluid warmer.



FIG. 8. The Acquarius machine.

in the range of 1.6–2 m² are needed. For all filters, high flux membranes are utilized. AN69, Polysulfone, or Polyamide membranes are generally employed with a permeability coefficient between 30 and 40 ml/hour/mmHg × m². These membranes have solute sieving coefficients close to 1 in a wide spectrum of molecular weights. Therefore, in most cases, clearance equals the amount of UF achieved. There may be some

exception to this rule. One case is when the sieving coefficient is < 1 for a given solute. In other cases, there may be a reduction in permeability of the membrane due to concentration polarization and secondary layer formation by the proteins. This is most likely to occur in the presence of high filtration fractions or in the case of long-term utilization of the hemofilter (over 24 hours). Finally, clearance may be reduced by the presence of

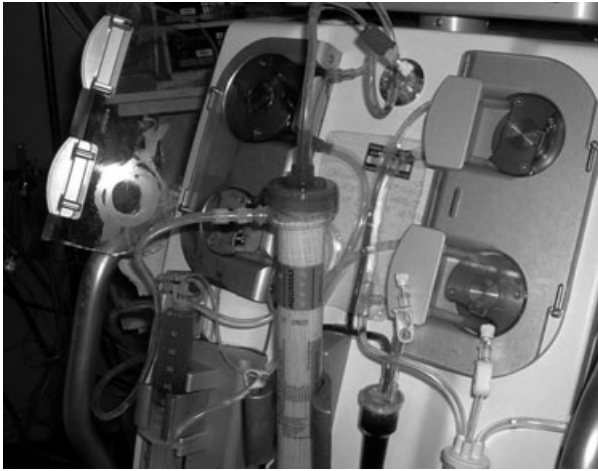


FIG. 9. Blood and dialysate circuit in the Acquarius machine.



FIG. 10. The Fresenius 2008H for SLED.

predilution, i.e., in the case of administration of the replacement fluid into the arterial line to replace UF. This reduces the oncotic pressure of plasma proteins and increases UF, but the efficiency of the system may be reduced by the parallel reduction in the concentration of

the solutes in the incoming blood. Furthermore, since the availability of large quantities of replacement fluid may be limited, new trends suggest the use of on-line production of replacement solutions by machines with built-in step filtration techniques. These are already utilized in the chronic setting and may become a practical approach for the patient undergoing HVHF.

Special Treatments and Plasma Therapies

Based on the assumption that higher clearances may be required to remove proinflammatory mediators from the circulating blood, the other possible approach other than HVHF is that of utilizing a largely porous membrane. For this purpose, we have recently employed a system which includes continuous plasma filtration and a subsequent reinfusion of the filtered plasma into the venous line, after passage through a cartridge of uncoated carbon or specific resins (19,20). The system has offered interesting results *in vitro* and it is now utilized in a prospective randomized study in septic patients to evaluate the capacity of removing proinflammatory mediators and to reduce the pharmacologic requirement of amines in the patient.

More therapies emerging today are utilizing the principles of CRRT for plasma exchange, plasma adsorption techniques, immunoadsorption techniques, therapy of support in liver failure conditions, and regional therapy for cancer. All these therapies will require further refinement and studies, but they may well become part of the family of CRRT, especially in those cases when continuous and prolonged extracorporeal treatment is indicated. In these cases, the modern machines are able to accomplish the difficult tasks of performing complex and combination therapies. This is mostly done by built-in specific software that assigns a specific role to each pump and each component in the circuit.

Future Trends

The evolution in technology of CRRT has only partially followed the more sophisticated evolution that took place in the equipment for chronic HD patients (21–32). In such patients, the increased morbidity and the progressively increased age require a gentle and carefully monitored HD therapy (26–34). To achieve such results, on-line monitoring techniques have been developed including urea sensors, temperature sensors, blood volume sensors, and teledialysis or biofeedback systems with minimal errors in the delivery of therapy (32–40).

All these systems are not completely implemented in the current CRRT machines or in some cases, they are just partially utilized. The on-line monitoring techniques and the applications of information technology are, however, under scrutiny as to the possible benefits in critically ill patients, and future trends may indeed include the development of machines equipped with these technologies.

References

1. Kramer P, Wigger W, Rieger J, Matthaei D, Scheler F: Arteriovenous hemofiltration: a new and simple method for treatment of over hydrated patients resistant to diuretics. *Klin Wochenschrift* 55:1121–1122, 1997
2. Ronco C, Burchardi H: Management of acute renal failure in the critically ill patient. In: Pinsky MR, Dhaunaut JFA (eds). *Pathophysiologic Foundations of Critical Care*. Baltimore: Williams and Wilkins, 1993:630–676
3. Geronemus R, Schneider N: Continuous arterio-venous hemodialysis: a new modality for treatment of acute renal failure. *Trans ASAIO* 30:610–613, 1984
4. Ronco C: Arterio-venous hemodiafiltration (AVHDF): a possible way to increase urea removal during CAVH. *Int J of Artif Organs* 8:61–62, 1985
5. Ronco C, Bellomo R: Complications with continuous renal replacement therapies. *Am J Kidney Dis* 28/5(Suppl. 3):100–104, 1996
6. Ronco C: Continuous renal replacement therapies for the treatment of acute renal failure in intensive care patients. *Clin Nephrol* 4:187–198, 1993
7. Ronco C, Bellomo R: Continuous renal replacement therapy: evolution in technology and current nomenclature. *Kidney Int* 53(Suppl. 66):S160–S164, 1998
8. Ronco C, Bellomo R: *Critical Care Nephrology*. Dordrecht, Netherlands: Kluwer Academic Publishers, 1998
9. Ronco C, Brendolan A, Bellomo R: Current technology for continuous renal replacement therapies. In: Ronco C, Bellomo R (eds). *Critical Care Nephrology*. Kluwer Academic Publishers, 1998:1269–1308
10. Ronco C, Bellomo R, Homel P, Brendolan A, Dan M, Piccinni P, La Greca G: Effects of different doses in continuous veno-venous hemofiltration on outcomes of acute renal failure. A prospective randomized trial. *The Lancet* 356:26–30, 2000
11. Ronco C, Brendolan A, Bellomo R: On-Line monitoring in continuous renal replacement therapies. *Kidney Int* 56(Suppl 72):S8–S14, 1999
12. Rahmati S, Ronco F, Spittle M, Morris AT, Schlaefer C, Rosales L, Kaufman A, Amerling R, Ronco C, Levin NW: Validation of the blood temperature monitor for extracorporeal thermal energy balance during in vitro continuous hemodialysis. *Blood Purif* 19:245–250, 2001
13. Ronco C, Ghezzi P, Bellomo R: New perspective in the treatment of acute renal failure. *Blood Purif* 17:166–172, 1999
14. Clark WR, Ronco C: Renal replacement therapy in acute renal failure: solute removal mechanism and dose quantification. *Kidney Int* 53(Suppl. 66):S133–S137, 1998
15. Ronco C: Continuous renal replacement therapies in the treatment of acute renal failure in intensive care patients. Part 1: Theoretical aspects and techniques. *Nephrol Dial Transplant* 9(Suppl. 4):191–200, 1994
16. Bellomo R, Ronco C: Continuous versus intermittent renal replacement therapy in the intensive care unit. *Kidney Int* 53(Suppl. 66):S125–S128, 1998
17. Tetta C, Mariano F, Ronco C, Bellomo R: Removal and generation of inflammatory mediators during continuous renal replacement therapies. In: Ronco C, Bellomo R (eds). *Critical Care Nephrology*. Kluwer Academic Publishers, 1998:1239–1248
18. Bellomo R, Baldwin I, Cole L, Ronco C: Preliminary experience with high volume hemofiltration in human septic shock. *Kidney Int* 53(Suppl. 66):S182–S185, 1998
19. Tetta C, Cavaillon JM, Schulze M, Ronco C, Ghezzi PM, Camussi G, Serra AM, Curti F, Lonnemann G: Removal of cytokines and activated complement components in an experimental model of continuous plasma filtration coupled with sorbent adsorption. *Nephrol Dial Transplant* 13:1458–1464, 1998
20. Tetta C, Bellomo R, Brendolan A, Piccinni P, Digo A, Dan M, Irone M, Lonnemann G, Moscato D, Buades J, La Greca G, Ronco C: Use of adsorptive mechanisms in continuous renal replacement therapies in the critically ill. *Kidney Int* 56(S72):S15–S19, 1999
21. Kellum J, Bellomo R, Ronco C: The concept of acute kidney injury and the RIFLE criteria. In: Ronco C, Bellomo R, Kellum JA (eds). *Acute Kidney Injury*, Vol. 156. Basel, Karger: Contrib Nephrol, 2007:10–16
22. Arroyo V: The liver and the kidney: mutual clearance or mixed intoxication. In: Ronco C, Bellomo R, Kellum JA (eds). *Acute Kidney Injury*, Vol. 156. Basel, Karger: Contrib Nephrol, 2007:17–23
23. Vincent J: Critical care nephrology: a multidisciplinary approach. In: Ronco C, Bellomo R, Kellum JA (eds). *Acute Kidney Injury*, Vol. 156. Basel, Karger: Contrib Nephrol, 2007:24–31
24. Hoste E, Kellum J: Incidence, classification, and outcomes of acute kidney injury. In: Ronco C, Bellomo R, Kellum JA (eds). *Acute Kidney Injury*, Vol. 156. Basel, Karger: Contrib Nephrol, 2007:32–38
25. Bonventre J: Pathophysiology of acute kidney injury: roles of potential inhibitors of inflammation. In: Ronco C, Bellomo R, Kellum JA (eds). *Acute Kidney Injury*, Vol. 156. Basel, Karger: Contrib Nephrol, 2007:39–46
26. Pinsky M: Sepsis and multiple organ failure. In: Ronco C, Bellomo R, Kellum JA (eds). *Acute Kidney Injury*, Vol. 156. Basel, Karger: Contrib Nephrol, 2007:47–63
27. Vincent J, Taccone F, Schmit X: Classification, incidence, and outcomes of sepsis and multiple organ failure. In: Ronco C, Bellomo R, Kellum JA (eds). *Acute Kidney Injury*, Vol. 156. Basel, Karger: Contrib Nephrol, 2007:64–74
28. Baldwin I: Factors affecting circuit patency and filter 'Life'. In: Ronco C, Bellomo R, Kellum JA (eds). *Acute Kidney Injury*, Vol. 156. Basel, Karger: Contrib Nephrol, 2007:178–184
29. Becker W: Starting up a continuous renal replacement therapy program on ICU. In: Ronco C, Bellomo R, Kellum JA (eds). *Acute Kidney Injury*, Vol. 156. Basel, Karger: Contrib Nephrol, 2007:185–190
30. Baldwin I: Is there a need for a nurse emergency team for continuous renal replacement therapy? In: Ronco C, Bellomo R, Kellum JA (eds). *Acute Kidney Injury*, Vol. 156. Basel, Karger: Contrib Nephrol, 2007:191–196
31. Ricci Z, Ronco C: Information technology for CRRT and dose delivery calculator. In: Ronco C, Bellomo R, Kellum JA (eds). *Acute Kidney Injury*, Vol. 156. Basel, Karger: Contrib Nephrol, 2007:197–202
32. Schetz M: Vascular access for HD and CRRT. In: Ronco C, Bellomo R, Kellum JA (eds). *Acute Kidney Injury*, Vol. 156. Basel, Karger: Contrib Nephrol, 2007:275–286
33. Aucella F, Di Paolo S, Gesualdo L: Dialysate and replacement fluid composition for CRRT. In: Ronco C, Bellomo R, Kellum JA (eds). *Acute Kidney Injury*, Vol. 156. Basel, Karger: Contrib Nephrol, 2007:287–296
34. Ricci Z, Picardo S, Ronco C: Results from International Questionnaires. In: Ronco C, Bellomo R, Kellum JA (eds). *Acute Kidney Injury*, Vol. 156. Basel, Karger: Contrib Nephrol, 2007:297–303
35. Ronco C, Cruz D, Bellomo R: Continuous renal replacement in critical illness. In: Ronco C, Bellomo R, Kellum JA (eds). *Acute Kidney Injury*, Vol. 156. Basel, Karger: Contrib Nephrol, 2007:309–319
36. Tolwani A, Wheeler T, Wille K: Sustained low-efficiency dialysis. In: Ronco C, Bellomo R, Kellum JA (eds). *Acute Kidney Injury*, Vol. 156. Basel, Karger: Contrib Nephrol, 2007:320–324
37. Virani SA: Management of acute decompensated heart failure: renal implications. *Blood Purif* 26:18–22, 2008
38. House AA, Ronco C: Extracorporeal blood purification in sepsis and sepsis-related acute kidney injury. *Blood Purif* 26:30–35, 2008
39. Ronco C, Ricci Z, Bellomo R, Baldwin I, Kellum J: Management of fluid balance in CRRT: a technical approach. *Int J Artif Organs* Aug 28:765–776, 2005
40. Gibney N, Cerda J, Davenport A, Ramirez J, Singbartl K, Leblanc M, Ronco C: Volume management by renal replacement therapy in acute kidney injury. *Int J Artif Organs* Feb 31:145–155, 2008