

## MAIN TOPIC

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# Technology in nephrology

## Technology has improved since the first successful dialysis – it is now possible to treat all patients with acute renal failure.

The clinical specialty of nephrology spans from the basic clinical skills through to highly technological aspects of medicine. The areas of technology reviewed in this article pertain to dialysis therapies for both acute and chronic renal failure. Pre-dialysis care and prevention or delay of progression are not covered.

In the 19th century Graham described the physicochemical process of dialysis. In the early part of the 20th century laboratory attempts at dialysis were made, but successful dialysis was delayed by the difficulties in obtaining a useable anticoagulant and sterile tubing to carry the blood to the dialyser. In 1945 the first successful human dialysis was performed by W Kolff in Holland — his 16th attempted dialysis in a patient with acute renal failure. His previous 15 patients had all died, but the 16th patient was successfully treated by dialysis and went on to long-term survival. Thereafter dialysis spread across the world and ushered in a new era in the treatment of both acute and chronic renal disease. A major early problem was circulatory access for repeated dialysis treatments. The Scribner shunt and subsequently the Brescia Cimino fistula as well as the variations on this have made long-term repeated circulatory access possible. Vascular access remains a problem for

many patients requiring long-term dialysis for chronic renal failure.

### DIALYSIS MEMBRANES

Contact of the patient's blood with a bio-incompatible membrane such as the cellulose membrane results in an inflammatory response. The adhesion of platelets and white cells to the membrane, complement activation, activation of white cells and release of a number of inflammatory cytokines characterise this response. The synthetic and semisynthetic membranes minimise this problem. The patients therefore do not experience the inflammatory response, resulting in a less symptomatic dialysis. The reduction in leucocyte and complement activation which lead to retarded renal recovery as well as to adverse effects on other organs such as the lung is important in the critically ill patient with acute renal failure where pulmonary function may be compromised further. High-flux membranes are required for continuous renal replacement therapies. These biocompatible membranes are polysulphones, or acrylonitrile membranes with high permeability and high clearances in addition to the other advantages of increased biocompatibility (Table I).

*Table I. Dialysis membranes*

	<b>Bio-incompatible</b>	<b>Bio-compatible</b>
<b>Types</b>	Cellulose	Acrylonitrile, polysulphone
<b>Cost</b>	Cheaper	More expensive
<b>Clinical disadvantages</b>	Inflammatory response, lower efficiency Platelet adhesion	High permeability needs volumetric equipment
<b>Clinical advantages</b>	Adequate for many	High efficiency, no inflammatory response

## DIALYSIS FLUIDS

In the early days of haemodialysis bicarbonate was routinely used as the anion in dialysis fluid. The fluid was prepared from powdered chemicals, which were mixed for each treatment. A bicarbonate solution containing the necessary calcium and magnesium cannot be stored, as calcium and magnesium carbonate are insoluble and precipitate. These technical problems have largely been overcome by the development of two component systems which separate the bicarbonate solution from an 'acid' solution containing calcium, magnesium and a small amount of acetic or lactic acid. The modern dialysis machine blends these two components with purified water just before delivery, avoiding the problems of precipitation. The acid component reacts with bicarbonate to produce carbon dioxide. This in turn forms carbonic acid that lowers the pH of the final bicarbonate-containing solution, allowing calcium and magnesium to remain in solution. Acute renal failure is often associated with a more severe degree of acidosis than occurs with chronic renal failure; therefore bicarbonate dialysis should be used for dialysis in acute renal failure wherever possible.

In the absence of renal function, the excess non-volatile acid generated by metabolic processes cannot be excreted and must be buffered. Dialysis assists this process by transferring buffers such as bicarbonate, acetate or lactate from the dialysis solution to the patient's circulation. Although acetate-containing dialysate has been the mainstay of treatment, its use is associated with nausea and vomiting, as well as haemodynamic instability and hypotension. Acetate and lactate must be converted to bicarbonate by the liver, resulting in a delay in correction of acidosis. These problems do not

Table II. Dialysis fluids

	<b>Acetate</b>	<b>Bicarbonate</b>
Relative cost	Cheaper	More costly
Equipment	Simple/basic	More complex
Clinical side-effects	Nausea Vomiting Cramps Hypotension Haemodynamic instability	Nil

occur with bicarbonate dialysis. Correction of acidosis is rapid and patients do not have cardiovascular instability. Bicarbonate dialysis has become the standard form of treatment, particularly in the critically ill patient where severe acidosis and haemodynamic instability are common. (Table II).

Peritoneal dialysis fluids containing lactate as a buffer have been used widely for continuous haemodialysis. This can be a problem when the patient has liver dysfunction. Bicarbonate-containing fluids for continuous therapy are now commercially available.

### Glucose

Although glucose is required in dialysate fluids in order to compensate for extracorporeal losses, supraphysiological concentrations result in hyperglycaemia and should be avoided, particularly in the critically ill patient where hyperglycaemia has been linked to increased mortality.

## DIALYSIS FOR CHRONIC RENAL FAILURE

The choice of dialysis modality for patients with chronic renal failure depends on many factors, including availability and logistics, medical factors, and patient preferences. Patients who develop chronic, end-stage renal failure and who receive haemodialysis therapy usually require dialysis three times each week. Most patients will become anuric or severely oliguric

a variable time after commencing dialysis treatment. Therefore dialysis must substitute for all the excretory functions of the kidneys, such as removal of water, electrolytes and metabolic waste products. In this regard dialysis is very effective, but it is unable to replace any of the endocrine functions of the kidney.

**Patients who develop chronic end-stage renal failure and who receive haemodialysis therapy usually require dialysis three times each week.**

The standard dialysis circuit is illustrated in Fig. 1. The notable features are two circuits — a blood circuit and a fluid circuit — each guarded by a variety of monitors and alarms. These include, on the blood side, monitoring of the pressures in the dialyser and, most critically, a monitor to detect air in the circuit. The circuit is fitted with stop mechanisms to clamp it off in the event of an air leak. The dialysate circuit is monitored for temperature, pressure and conductivity as well as for the presence of blood that would indicate a blood leak. The dialysis treatment is monitored for safety throughout the course of treatment, in addition

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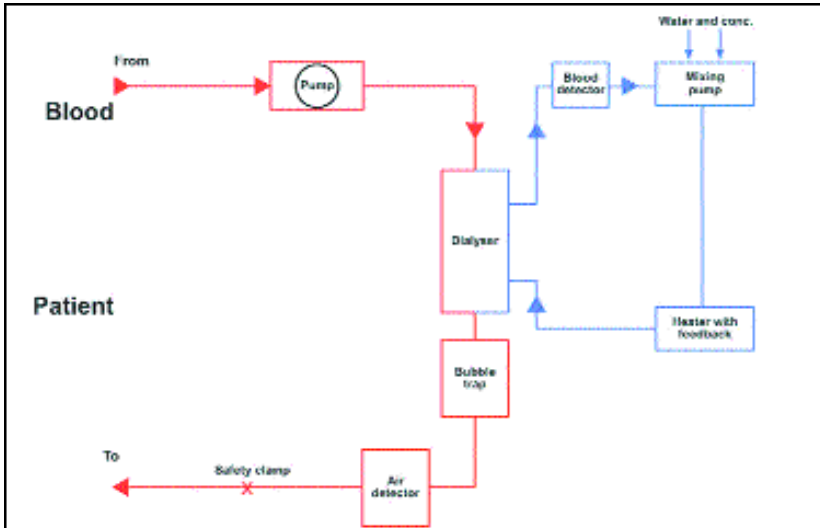


Fig. 1. Layout of basic standard dialysis circuit.

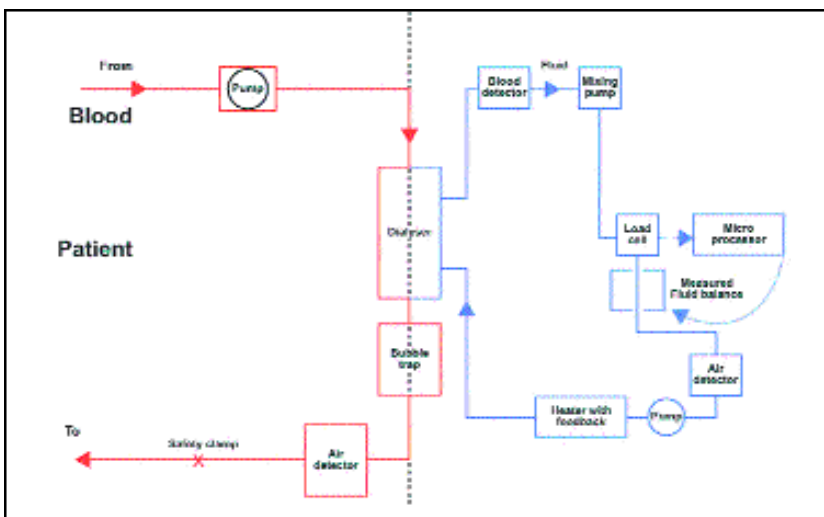


Fig. 2. Layout of dialysis circuit for high-flux dialysis.

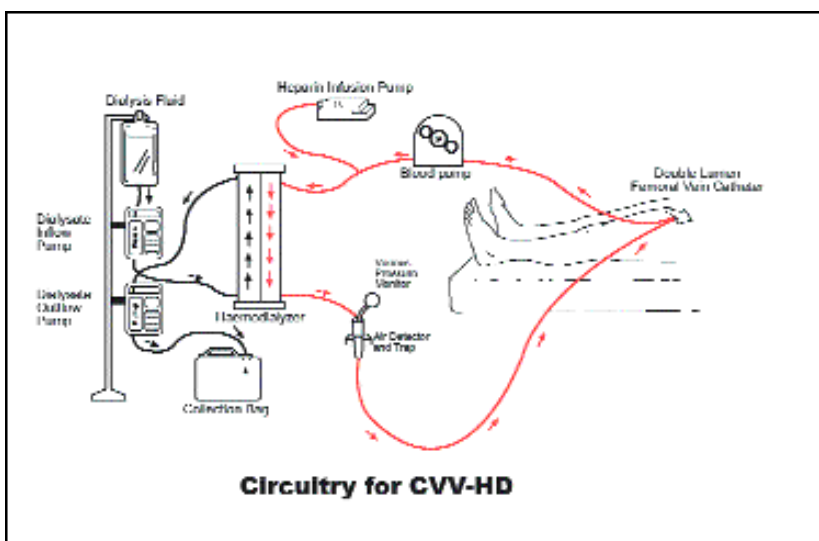


Fig. 3. Layout of CVVHD circuit

to the usual monitoring of the patient's vital signs.

Dialysis technologies have advanced rapidly over the last years with the development of biocompatible dialysis membranes, volumetric dialysis machines, increasing availability of bicarbonate dialysis fluids and improved understanding of the assessment of dialysis adequacy. New drugs such as the vitamin D analogues and recombinant human erythropoietin have been major advances in the management of these patients.

## VOLUMETRIC DIALYSIS

A critical factor in the oliguric patient is fluid management. Fluid removal must be controlled in such a manner that sufficient fluid is removed to allow for oral intake over the next 2 - 3 days, but at the same time this has to be done in such a way as to avoid symptoms such as cramps and hypotension, associated with acute volume depletion. The volumetric dialysis machine monitors the volume of dialysate entering the machine and compares this with the effluent dialysate volume (Fig. 2). A simple calculation done in the microprocessor controlling the equipment then allows the machine to display the volume removed. It is a small step from this point to allow the machine to be set at the beginning of the treatment to remove an appropriate volume of fluid. In the absence of such a facility the calculations have to be done by the staff, based on the published performance data of the dialyzer, which is imprecise and difficult (Fig. 3).

The combination of volumetric dialysis and high-flux biocompatible membranes has allowed the normal diffusive dialysis to be augmented by convective dialysis. Convective dialysis using these membranes allows for more effi-

cient dialysis with better removal of water and electrolytes as well as much improved clearance of middle and large molecular weight substances. There is a major study (HEMO study)<sup>1,2</sup> for which only preliminary data have been published, investigating the value of high-flux convective dialysis and different doses of dialysis on the outcome for the patients. It is difficult to separate the effects of biocompatibility and high-flux dialysis. It has yet to be shown that these new technologies truly will improve patient survival and quality of life. It is, however, highly probable that these techniques will have that effect.

The higher performance of these membranes in terms of larger molecular weight clearances contributes to a reduction in  $\beta_2$  microglobulin, which is important in reducing the incidence of dialysis-associated amyloidosis — an important complication of long-term dialysis.

### DIALYSIS FOR ACUTE RENAL FAILURE

The role of dialysis in acute renal failure is to provide support for the patient until renal recovery occurs and to prevent life-threatening complications such as hyperkalaemia and fluid overload.

The evolution of new dialysis techniques as well as developments in the areas of vascular access catheters, dialysis membranes, fluids and machines have all contributed to improved management of patients with acute renal failure.

#### Dialysis modality

The modality of dialysis selected is determined by the patient's clinical profile and by logistic factors. In the right circumstances, peritoneal dialysis can be an effective treatment modality and has the advan-

*Table III. Types of continuous dialysis*

SCU	Slow continuous ultra-filtration
CAVU	Continuous arteriovenous ultra-filtration
CAVHD	Continuous arteriovenous haemodialysis
CVVHD	Continuous venovenous haemodialysis
CVVHF	Continuous venovenous haemofiltration
CVVHDF	Continuous venovenous haemodiafiltration

tage of not requiring sophisticated equipment. However, the majority of patients with acute renal failure will not be treated adequately with peritoneal dialysis and will require haemodialysis. Intermittent haemodialysis remains the most widely used form of treatment for acute renal failure worldwide. A major limitation of this type of renal replacement is its unsuitability for certain categories of patients, notably critically ill patients in intensive care units, some patients after cardiac surgery and patients with raised intracranial pressure. These patients, particularly those with severe sepsis and multi-organ dysfunction, are difficult to treat with conventional intermittent haemodialysis because of haemodynamic instability and hypotension. The development of continuous renal replacement techniques has been a major development in the management of these patients. In 1977 Peter Kramer<sup>3</sup> from Göttingen, Germany, developed the technique of continuous arteriovenous haemofiltration to dialyse such patients. Varying forms of continuous therapy were subsequently devised (Table III).<sup>4</sup> The slow and continuous nature of this form of renal replacement therapy allows gradual and gentle removal of fluid, electrolytes, and uraemic toxins without exacerbating haemodynamic instability. Other specific advantages include improved metabolic control, ability to provide nutritional support, and ease with which fluid removal can be manipulated.

Initially these techniques used simple arteriovenous blood circuits, but vascular complications related to catheterisation of large arteries led to the development of venovenous circuits that required the inclusion of a blood pump in the circuit. In South Africa, continuous venovenous haemodialysis (CVVHD) (Figs 4,5) is the most widely used form of continuous therapy.



*Fig. 4. Outpatient on standard intermittent haemodialysis.*



*Fig. 5. Modern CVVHD equipment*

### **Continuous haemofiltration**

Haemofiltration is a convective technique using a transmembrane pressure gradient to filter plasma water across a highly permeable membrane. Small and large molecules are convected across the membrane with the water (solute drag effect), thus effecting blood purification. About 10 - 15 litres of ultrafiltrate are produced per day, which must be replaced by a balanced electrolyte solution infused into the inflow or outflow line of the haemofilter.

### **Continuous haemodialysis**

Continuous haemodialysis utilises the principle of diffusion of solutes across the dialyser membrane, driven by a concentration gradient between the blood and dialysate fluid compartments. Therefore fluid transport across the membrane is not a prerequisite for treatment, but is adjusted according to the need for fluid removal. This can vary from 0 to about 6 liters per day. Of all the slow therapies, continuous haemodialysis provides the highest daily urea clearances.

**Vascular access in acute renal failure is achieved by percutaneous insertion of specially designed dialysis catheters into large veins such as the internal jugular, femoral or subclavian veins.**

### **Vascular access**

Vascular access in acute renal failure is achieved by percutaneous insertion of specially designed dialysis catheters into large veins such

as the internal jugular, femoral or subclavian veins (Fig. 6). The ideal catheter is easily inserted, atraumatic to the vessel, haemocompatible to minimise thrombosis, and able to provide adequate blood flow rates. Modern dialysis catheters are designed with specific curves and lengths to suit the site of insertion. Polyurethane and silicone are regarded as the best materials for catheters. Silicone catheters are flexible and soft, characteristics that decrease the risk of vascular injury. Some catheters are designed to soften once inserted and at body temperature. Semi-rigid catheters should not be used for protracted periods.

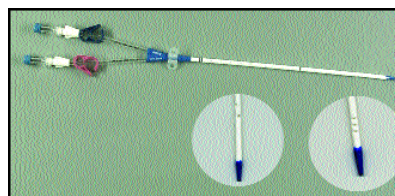


Fig. 6. Dialysis catheters.

Single- and double-lumen catheters are available. Single-lumen catheters require the use of a single blood path adapter device to split the blood flow distal to the catheter using Y tubing. This system relies on timers and valves to push and pull blood from the blood compartment of the dialyser. Double-lumen catheters permit the use of a standard blood circuit and also minimise recirculation of dialysed blood back into the dialyser, as occurs with single blood path devices.

### **Anticoagulation**

Prevention of thrombosis in the extracorporeal circuit is an important aspect of management, particularly with the continuous forms of therapy. The new heparins do not have significant advantages over the standard unfractionated form, and in some cases may have disadvantages such as prolonged action.

Blood should be drawn proximal to the heparin infusion port in order to reflect the clotting profile of the patient, rather than the extracorporeal circuit. Activated clotting time (ACT) and partial thromboplastin time (PTT) are monitored. For intermittent haemodialysis bolus doses of heparin are used, and it is possible to perform heparin-free dialysis provided blood flow rates are adequate and the dialyser is frequently flushed with saline.

Prevention of clotting in the dialysis circuit is the main technical challenge with all forms of slow continuous dialysis. The requirement for prolonged anticoagulation increases the risk of bleeding. This has to be balanced against premature circuit clotting leading to ineffective treatment. An initial bolus of heparin into the 'arterial' bloodline is followed by a constant infusion of heparin. Heparin-free continuous dialysis is possible, but difficult, as the dialyser usually clots within eight hours. Frequent changes of dialyser and circuit tubing decrease the efficacy of treatment, and add considerably to the costs.

### **Hardware**

In continuous therapy, the use of a roller blood pump ensures a constant blood flow rate through the dialyser. However, as with other pumped circuits, there is always a risk of disconnection or air in the circuit, necessitating the use of air detectors, venous pressure monitors, alarms and fail-safe devices to minimise the risk of air embolism or haemorrhage.

Modern machines for continuous therapy control fluid removal very accurately and have decreased the burden on nursing staff. However, the technique can still be performed using a basic blood pump system with two infusion pumps to control dialysate inflow and outflow from the dialyser.

**CONCLUSION**

Dialysis technology for both acute and chronic renal failure has evolved significantly since the first patient was successfully treated in 1945. It is now possible to treat all patients with acute renal failure, even those who are haemodynamically unstable. The availability of treatment for chronic renal failure is limited by financial factors to carefully selected patients in the public sector and those in the private sector with adequate funding. The improvements in technology have added to the costs of therapy and, regrettably, there are many areas that do not have access to even the most basic equipment. The challenges include making the technology affordable and improving patient outcome for acute renal failure, which has an unacceptably high mortality, as well as for chronic renal failure.

References available on request.

**FURTHER READING**

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**IN A NUTSHELL**

Early nephrological referral allows for uncomplicated transition to dialysis and improves long-term survival.

Peripheral veins require careful preservation for future vascular access in patients with renal disease.

Improved biocompatibility of modern polysulphone and other membranes reduces the inflammatory response to dialysis.

The increased permeability of these modern membranes improves the clearance of solutes but does require volumetrically controlled machines.

Volumetric dialysis equipment allows the patient's fluid balance to be very precisely controlled.

Continuous dialysis therapies for acute renal failure allow for dialysis for acutely ill patients who would not tolerate standard intermittent haemodialysis.

Continuous dialysis for acute renal failure allows for intensive nutritional support and improved and more stable metabolic and volume control than standard dialysis.

Continuous dialysis is the treatment of choice for patients with raised intracranial pressure.

Bicarbonate-buffered dialysis fluid provides better acid-base control than standard acetate dialysis.

Advances in technology are expensive and cost control is of increasing importance.

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