# Theory and practical application of blood-based renal replacement therapy

## Introduction

The term renal replacement therapy incorporates three modalities that control or correct biochemical and fluid disturbances of renal failure. Peritoneal dialysis and renal transplantation are two forms of renal replacement therapy that are outside the remit of this article. This review focuses upon the third group which are blood-based and involve direct treatment of a patient's blood in a closed, extracorporeal circuit. They provide renal replacement for end-stage renal failure and during periods of severe acute kidney injury, and also for non-renal indications such as the management of drug overdoses. Blood-based renal replacement therapies are often loosely referred to as 'haemodialysis', although this is only one of a range of treatments. This article outlines the theory and practical applications of these treatments.

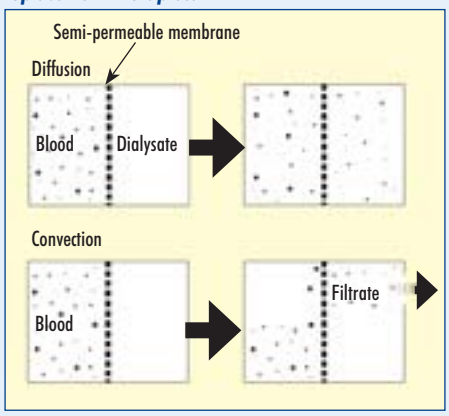
## Theory of blood-based renal replacement therapy

The goals of blood-based renal replacement therapy are to remove excess fluid and accumulated toxic solutes and to replenish deficient solutes (*Figure 1*). The two main physical forces used are convection and diffusion. Both require a semi-permeable membrane (*Figure 2*). Solute removal can occur by either process, but fluid removal can only occur through convection, which must therefore be at least a component of all modalities. The blood-based renal replacement therapies differ in the way that these two forces are used.

### Convection

Convection (also termed ultrafiltration) involves the removal of plasma water by applying a hydrostatic pressure (usually pump-driven) across a semi-permeable membrane. Within the physical limits of membrane pore size, solutes follow by a process termed 'solvent drag' (*Figure 1*). Practically, this is achieved by using a hollow-fibre device (*Figure 2*). The removal of small solutes (e.g. urea, potassium) is relatively inefficient so high ultrafiltration volumes are needed to produce sufficient toxin clearance. Simultaneous replacement of a physiological substitution fluid is needed to avoid the volume loss that would otherwise ensue. This high volume ultrafiltration and fluid replacement is termed haemofiltration (*Figure 3*). By altering the relative rates of ultrafiltration and replacement, net fluid balance can be manipulated to achieve a euvolaemic state. Isolated ultrafiltration, without simultaneous volume replacement, can be used to facilitate net fluid removal, although solute removal is minimal (*Figure 3*).

**Figure 1. Graphic illustration of the two main physical processes used in blood-based renal replacement therapies.**

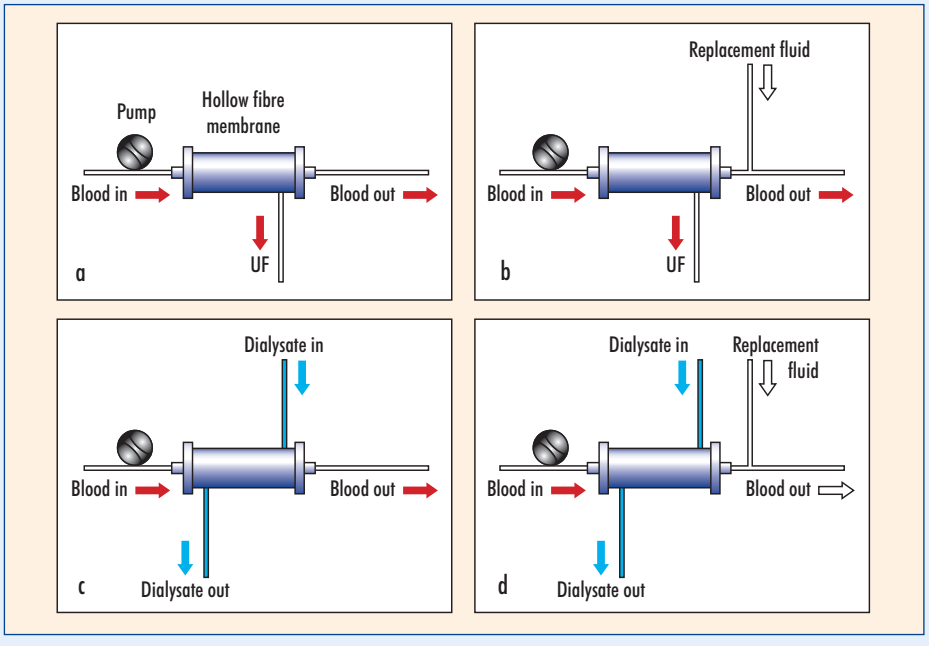



### Diffusion

Diffusion involves the net movement of solute down a concentration gradient (*Figure 1*). A semi-permeable membrane

**Figure 2. Hollow-fibre device shown in cross-section.**

**Figure 3. Commonly used extracorporeal renal replacement techniques. a. Ultrafiltration (UF). b. Haemofiltration (replacement fluid infusion may be pre-dilutional – before the blood inlet – or, as in this figure, post-dilutional – after the blood outlet). c. Haemodialysis. d. Haemodiafiltration.**

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separates blood from dialysate – a premixed solution whose chemical composition produces concentration gradients in favour of the removal of toxins (e.g. a low dialysate potassium encourages its net loss) and addition of beneficial solutes (e.g. bicarbonate). Blood and dialysate flow rates, and membrane pore size, thickness and surface area determine the efficiency of solute removal. The concentration gradient is also enhanced by blood and dialysate flows in a counter-current, rather than the same, direction. This is achieved by using a hollow-fibre device.

Diffusion is much more effective at removing small solutes, but is less efficient at removing larger solutes (e.g. beta-2 microglobulin) than convection, which drags these across the membrane en bloc. Haemodialysis relies predominantly on diffusion. As diffusion does not result in net fluid removal, ultrafiltration must be added to achieve this, although its contribution to total solute removal is minimal (*Figure 3*).

Effective small and large solute removal can be achieved by combining diffusion and (significant) convection in haemodiafiltration (*Figure 3*). The importance of large solute removal has not been defined in acute kidney injury but it may have benefits for long-term end-stage renal failure patients.

### Techniques and nomenclature

The mechanics of the different processes are illustrated in *Figure 3*. *Table 1* describes the nomenclature of the blood-based renal replacement therapies in more detail.

## Technical considerations

### Apparatus

In its simplest terms, the hardware needed for renal replacement therapy consists of a two or more pumped circuits and a hollow-fibre device. Technical elaborations in standard apparatus include safety features such as volumetric control of ultrafiltration, air detectors and bubble traps, blood leak detectors and circuit pressure monitors. A variety of 'optional extras' enhance functionality and include monitors of dialysis adequacy and of plasma volume.

### Hollow-fibre devices

Hollow-fibre devices (*Figure 2*) contain thousands of hollow fibres which comprise a wall of a semi-permeable material and a lumen through which blood flows – collectively, the 'blood compartment'. In diffusive modalities, dialysate flows (usually in an opposite direction to blood flow) around the outside of the hollow fibres in the dialysate compartment. In purely convective modalities there is no dialysate flow. The dialysate compartment is where filtrate initially accumulates after being drawn across the membrane, before it is drained away.

A wide variety of semi-permeable membranes materials and structural configurations are available. Modern practice favours more biocompatible materials (with a lower tendency to activate the coagulation cascade, complement and leucocytes on contact with blood). The intended use determines the choice of membrane structural configuration – materials with a large pore size and high hydraulic permeability are needed for large solute clearance and high ultrafiltration volumes (e.g. haemofiltration) respectively.

### Vascular access

Good vascular access is the patient's life line. The ideal access should provide adequate extracorporeal blood flows (especially important for the intermittent techniques, which require flows ≥300 ml/min) and should be free of complications (in particular infection). That the ideal is often unmet explains why vascular access is also referred to as the 'Achilles' heel' of renal medicine.

Temporary dialysis catheters, placed in the internal jugular or femoral veins, allow immediate access for blood-based renal replacement therapy. These are used when renal replacement therapy is needed only temporarily, e.g. during a period of acute kidney injury or while tiding over a chronic patient until more permanent access is ready. Subclavian access should be avoided because of the risk of venous stenosis – this may be the draining vein of future, permanent access, which would be compromised by a downstream stenosis. Temporary dialysis catheters carry the highest risk of infection. They must be changed regularly to try to limit this risk; at least weekly for femoral catheters and at least every 2–3 weeks for internal jugular access.

Tunnelled dialysis catheters are usually placed in the internal jugular vein but are passed under the skin to appear on the anterior chest wall. A cuff anchors the line within the subcutaneous tunnel. Although a longer term option than temporary dialysis lines, their insertion is not without hazard and they still carry a high risk of infection.

The arteriovenous fistula is formed by anastomosing a vein (typically the cephalic) and an artery (usually the radial or brachial). This is the best form of access because of its minimal infection risk, good flows and longevity. Two needles are inserted at

**Table 1. Extracorporeal renal replacement therapy: nomenclature and use**

| Therapy | Definition | Use | Access | Abbreviation |
|---|---|---|---|---|
| Ultrafiltration | Plasma water removal<br>Usually < 5 litres/day | Fluid overload<br>Congestive cardiac failure | AV/VV continuous<br>VV continuous<br>AV/VV intermittent | SCUF<br>CVVUF<br>IUF |
| Haemodialysis | Diffusion-based process using dialysate and semi-permeable membrane | Azotaemia<br>Acid–base disturbance<br>Electrolyte balance<br>Volume control | AV continuous<br>VV continuous<br>AV/VV intermittent | CAVHD<br>CVVHD<br>IHD |
| Haemofiltration | Convective-based process using plasma water exchange methods across semi-permeable membrane | Azotaemia<br>Acid–base disturbance<br>Electrolyte balance<br>Volume control | AV continuous<br>VV continuous<br>AV/VV intermittent | CAVH<br>CVVH<br>IH |
| Haemodiafiltration | Combining diffusion and convection for both small and middle molecular loss | Azotaemia<br>Volume control | AV continuous<br>VV continuous<br>AV/VV intermittent | CAVHDF<br>CVVHDF<br>IHDF |

Modalities are described according to frequency, technique and, for continuous techniques, vascular access. Continuous renal replacement therapy is an umbrella term for continuous techniques. I = intermittent; C = continuous (= S = slow); H = haemofiltration; HD = haemodialysis; HDF = haemodiafiltration; UF = ultrafiltration; VV = veno-venous modality (via central venous catheter; requires blood pump); AV = arterio-venous modality (via arterial + venous cannulae; usually pumpless, systemic arterial pressure providing the driving force; potentially hazardous because of the need for arterial cannulation, it is now rarely performed except in mass casualty settings when bulky hardware may not be immediately available). This descriptive system has recently been complicated by the development of hybrids of intermittent and continuous techniques, referred to as 'sustained low efficiency dialysis', 'extended daily dialysis' and 'slow continuous dialysis'. Adapted from Teo et al (2007).

each dialysis session to provide continuous circulation of blood through the dialysis circuit. If a patient's blood vessels are unsuitable for arteriovenous fistula formation, then a graft is used for the anastomosis. Arteriovenous grafts use synthetic materials (such as Goretex), autologous vessels (typically the saphenous vein) or other biological materials (such as bovine ureter). Synthetic materials pose a greater infection risk and carry an increased risk of thrombosis. Other complications of arteriovenous accesses include steal syndrome (owing to diversion of blood from the peripheries), extravasation of blood into soft tissues after needling, and aneurysm or pseudoaneurysm formation. Hinchcliffe et al (2009) covers more acute problems.

### Anticoagulation

Clotting of the extracorporeal circuit is a significant source of under-delivery of a prescribed dose of blood-based renal replacement therapy. However, the risks of this must be balanced against those of anticoagulation. Most end-stage renal failure patients undergoing intermittent haemodialysis are routinely managed with either intra-dialytic infusions of unfractionated heparin or boluses of low molecular weight heparin. Critically ill patients with acute kidney injury requiring continuous renal replacement therapy usually need unfractionated heparin infusions but lower risk alternatives (for this population at high risk of bleeding) include prostacyclin and regional citrate anticoagulation. Intermittent haemodialysis for acute kidney injury can often be performed with minimal heparin or simply with regular saline flushes of the circuit alone.

### Fluids

Sterile fluids of an appropriate chemical composition are required for both haemodialysis and haemofiltration.

In intermittent haemodialysis, the water used to make up the final dialysate solution is derived from the mains supply but first undergoes microbiological purification and removal of potentially deleterious substances, such as aluminium and chloramines. This is achieved in the static water plant of a chronic haemodialysis facility or through individual, portable purification systems when treatment must be given away from the main centre. The haemodialysis machine mixes the purified water with a chemical concentrate to yield the final dialysate solution. The chemical composition (e.g. potassium, calcium, sodium) of the dialysate can be tailored to the individual patient. All steps of fluid production happen in real time.

In continuous renal replacement therapies, replacement or dialysate fluid is premanufactured and supplied in sealed bags. This comes at a significant cost but the volumes needed are considerably lower for these slower, intensive care unit renal replacement therapies.

## Application of blood-based extracorporeal therapies

### End-stage renal failure

Intermittent haemodialysis is the primary blood-based renal replacement therapy for end-stage renal failure. Its prescription is individually tailored to provide adequate clearance of uraemic toxins, correction of electrolyte abnormalities and appropriate fluid removal. Generally, this requires at least a 4-hour treatment, thrice weekly. Key determinants of the haemodialysis prescription include a range of biochemical variables as well as clinical inputs such as blood pressure and fluid status.

Although most intermittent haemodialysis is provided on the main unit or in one of its satellite centres, increasing numbers of patients are performing home therapy – a choice that enhances lifestyle, flexibility and ownership of treatment.

Another evolving trend in end-stage renal failure is the increasing use of intermittent haemodiafiltration to enhance larger solute clearances in patients who are likely to remain on long-term dialysis (without the prospect of imminent transplantation) or who have inadequate metabolic control on standard intermittent haemodialysis.

### Acute kidney injury

There are a range of options for renal support in acute kidney injury, but the most commonly used are intermittent haemodialysis or one of the continuous renal replacement therapies. Generally, the former is reserved for the more stable acute kidney injury patient with the latter's attributes of a slower, gentler treatment being used for the haemodynamically unstable or for those with large fluid removal requirements. Despite the theoretical benefits of continuous renal replacement therapy in the critically ill, no actual advantage has been adequately demonstrated. It is beyond the scope of this article to discuss details of when and how to institute renal support in acute kidney injury, but further details are available via Davenport et al (2008).

## Conclusions

The non-renal doctor is likely to come into contact with patients requiring blood-based, extracorporeal renal replacement therapy, either on their GP list, in the accident and emergency department, on their own, non-renal ward or on the intensive care unit. Awareness of the basics of theory, technique and application form a sound basis for the non-specialist management of these challenging patients receiving this complex therapy (Hinchcliffe et al, 2009). **BJHM**

Table 1 *is adapted from Teo et al (2007) by kind permission of Mosby Inc.*

*Conflict of interest: none.*

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## KEY POINTS

- Blood-based renal replacement therapy aims to remove excess fluid and accumulated toxic solutes, and to replenish deficient solutes. It can be used to support end-stage renal failure patients and tide others over periods of acute kidney injury.
- The two main physical forces that may be used are convection and diffusion, with the former used in haemofiltration and the latter in haemodialysis.
- The nomenclature of the different modalities is usually defined by 'intermittency', technique and (for continuous renal replacement therapies) by access.
- Preservation of vascular access should remain a high priority to the non-renal clinician as this is the patient's lifeline.