

# Renal replacement

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## Summary

There are few, if any, technological advancements in the field of medicine that have been able to transform a life-threatening condition, in this case, end-stage renal failure, from a certain and horrible death, just some 100 years ago, to a condition manageable within the confines of one's home.

This refresher course, by no means a comprehensive text on peritoneal or haemodialysis, aims to provide the reader (a pre-part one FCA candidate) with the following brief overview:

1. A short history of dialysis
2. The basic physiology of fluid and solute exchange employed in renal replacement therapy (RRT)
3. The physical principals of RRT
4. Modality

**Keywords:** primer RRT, renal replacement therapy basics, introduction to RRT, dialysis, mechanisms of RRT

## A brief history of renal replacement therapy (RRT)

During the 19th century the concepts of solute and fluid movement were elucidated, and scientists were able to begin the journey toward discovering this phenomenon in the human body as well as develop technologies that could use this phenomenon.

However, it was not until 1912 when John Abel and his team from Johns Hopkins University started experimenting with what was called the "vividiffusion" device that real progress was made. The device, painstakingly made from numerous semipermeable collodion tubes, received anticoagulated blood from the femoral artery of the animal and returned it via the femoral vein. Abel and his colleagues, however, never developed the technology for human usage.<sup>1,2</sup>

During the 1940s numerous simultaneous attempts were being made around the world to create a machine capable of performing dialysis for patients. Willem Kolff's rotating drum dialyser eventually won out and his 1942 prototype began what can now be thought of as the modern age of dialysis.<sup>2</sup>

Since that time, there have been innumerable improvements to the technology used for dialysis and the development of numerous modalities have occurred. The technological advancement has dealt with many of the complications associated with both the disease of renal failure itself and also those associated with the problems caused by dialysis. In 2020 we have numerous modalities of dialysis, many of which can be employed safely in the outpatient setting and many patients now live long and prosperous lives because of this pioneering advancement.

In 1977 Kramer et al. described the first type of continuous arteriovenous haemofiltration, and this life-saving technology has progressed to become a commonplace tool in the treatment of multi-organ failure in the intensive care units of the modern world.<sup>2</sup>

## The basic physiology of fluid and solute exchange employed in RRT

The kidney performs many important functions, but the management of solute and water are perhaps its most paramount. To this end, some important concepts need to be discussed.

Extracellular tonicity is generally speaking, although not always, reflected by the plasma sodium concentration ( $Na_{pl}$ ). This  $Na_{pl}$  is proportional to the total body exchangeable sodium ( $NA_e$ ) and potassium ( $K_e$ ) concentrations divided by the amount of total body water.

*Equation 1: The relationship between plasma sodium and total body water*

$$NA_e + K_e / \text{Total body water} \propto Na_{pl}$$

As the kidney regulates water intake and excretion very tightly, changes in serum sodium usually reflect changes in water balance, not changes in serum sodium. Obviously the more complex a patient's pathology, the more likely there can be exceptions to this rule.

A basic understanding of membrane physiology is required in order to grasp the concepts found in RRT.

## Diffusion

Diffusion describes the net flux of particles from an area of higher concentration to one of lower concentration. Diffusion of molecules through a membrane is sub-divided into two entities:

1. Simple diffusion occurs down a concentration gradient and is not facilitated by protein binding and interaction with a carrier molecule.
2. Facilitated diffusion occurs when the molecule acts with a carrier protein/molecule and may act against a concentration gradient.

## Osmosis

Osmosis is the movement of water across a semipermeable membrane due to differences in solute concentrations on either side of the membrane. The osmotic pressure is the amount of pressure needed to stop osmosis.

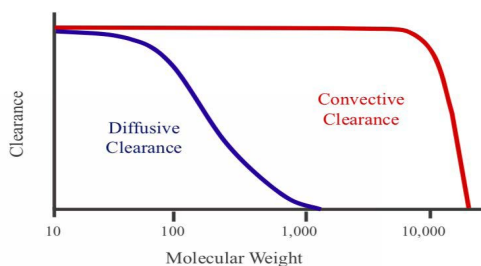
Two methods are employed in dialysis to effect solute and water clearance, namely:

1. Diffusion (dialysis)
2. Convection (haemofiltration or ultrafiltration)

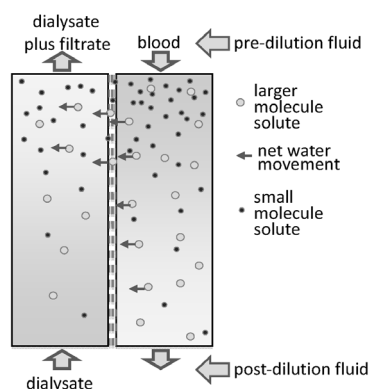
Both types require the presence of a semipermeable membrane.

Diffusive clearance occurs as solute moves down its concentration gradient from high to low across a semipermeable membrane. Water moves along with the solute as it is "dragged" through the membrane. This type of clearance is most efficient for smaller molecules such as urea and ions.<sup>2,4</sup>

### Convection versus Diffusion



**Figure 1:** The difference between diffusive and convective clearance in terms of solute size



**Figure 2:** The movement of solute and water

Convective clearance results from the creation of the transmembrane pressure which forces primarily water across the semipermeable membrane down a pressure gradient and which pushes solutes across also. This type of clearance is responsible for bigger solute molecule movement.<sup>2,4</sup>

Peritoneal dialysis (PD) relies on four simultaneously occurring processes, namely:

1. Diffusion (the most important mechanism for fluid and solute shift in PD)
2. Convection
3. Osmosis
4. Fluid absorption

In diffusive clearance the same principals as above apply. In addition to the concentration gradient mentioned above, membrane resistance, peritoneal surface area and the molecular size of the molecules to be transported are the factors that determine the effectivity of PD.

Ultrafiltration is the process that occurs as a result of the osmotic gradient (i.e. osmotic pressure) created between the relatively hypertonic dialysis solution and the relatively hypotonic peritoneal capillary blood.

The hydraulic conductance of the peritoneal membrane, the osmotic pressure gradient dependent on the type of fluid used, dwell time, peritoneal surface area and hydrostatic pressure gradient all affect PD efficiency.

Sodium sieving, whereby water moves across the peritoneal membrane and excludes sodium is due to aquaporin water transport. These aquaporins play a minor role in ultrafiltration. For any solute, a sieving coefficient of one denotes a solute that passes through the membrane completely unhindered. A sieving coefficient of zero means the molecule is completely rejected from transport across the membrane.

Fluid absorption occurs directly and indirectly via the lymphatics.<sup>4-7</sup>

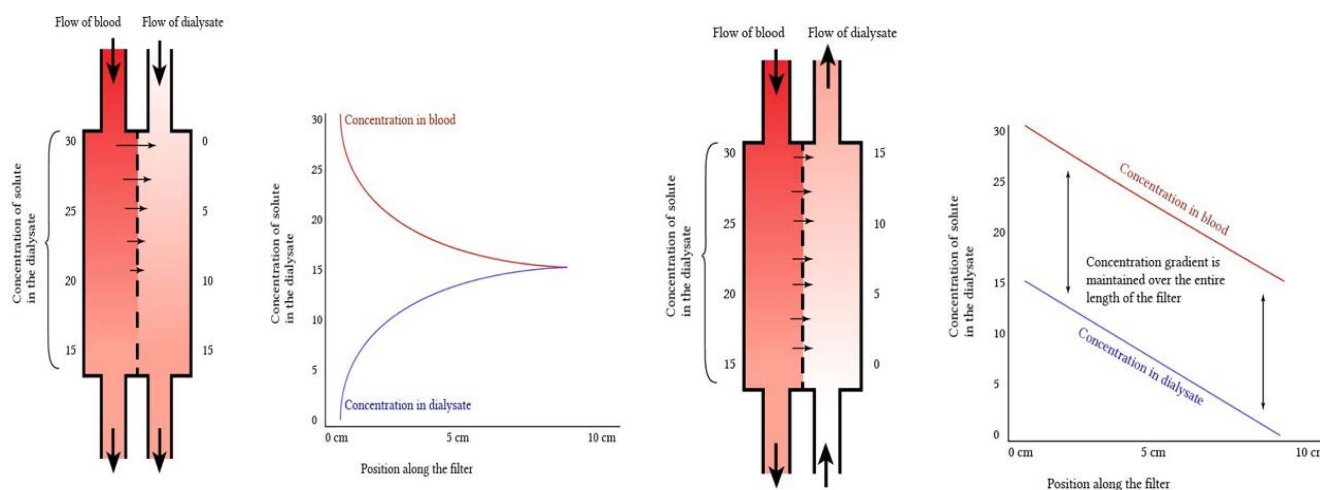
### An overview of the physics involved in RRT

There are numerous principles especially with respect to haemodialysis (HD) that I believe are important to grasp so that the non-renal clinician can understand what to expect in terms of solute and fluid clearance, and to have some knowledge of the apparatus so that basic troubleshooting can be achieved.

In the modern era most dialysers are hollow fibre dialysers. These dialysers are composed of thousands of hollow tubes which collectively serve as the dialysis membrane. Parallel plate dialysers are no longer in use in most modern centres.

### Countercurrent flow

Blood and dialysate flowing in opposite directions is key to maintaining the efficiency of the solute and water clearance. Dialysate flow rates are usually set between 1.5–2 times the blood



**Figures 3 and 4:** The importance of the countercurrent mechanism for the maintenance of the diffusive gradient

flow rate. This countercurrent flow is critical in maintaining the diffusive concentration gradient for effective solute clearance.<sup>8</sup> Concurrent flow is not efficient.

### Dialysers

Dialysers are also described in terms of:

- Type of membrane
- Surface area
- Ultrafiltration coefficient
- Dialysis solution used and others, but we will concentrate on these four.

#### Type of membrane

There are many types of membrane available, such as cellulose membranes, cellulose synthetic and non-cellulose synthetic. Biocompatibility with blood, an important quality of the membrane, thought to prevent complications, is best among synthetic non-cellulose membranes.<sup>2</sup>

Although studies such as the HEMO study did not find any benefit with biocompatible vs non-bio-compatible membranes, subsequent work has shown that the non-cellulose synthetic membranes, such as those made from polymethylmethacrylate, were associated with a lower long term mortality rate.<sup>9</sup>

#### Surface area

Clearly dialysers with a larger surface area have more efficient solute clearances.

The mass transfer coefficient (KoA) is the major quantitative measure of a given dialyser's clearance efficiency. The KoA should always be reported at a blood flow rate of between 300–400 ml/min. The KoA therefore represents the maximum clearance of any given solute, given in ml/min. The KoA is made apparent by the membranes porosity, thickness, flow rates of the blood and dialysate and the size of the solute to be cleared.<sup>5</sup>

Clearance rates are often reported for small (urea and ions) and large (Vit B12) solute clearances.

**Table 1**

Sodium	135–140 mmol/l
Chloride	87–120 mmol/l
Potassium	0–4 mmol/l
Magnesium	0–1.5 mmol/l
Calcium	1.25–2.5 mmol/l
Bicarbonate	25–40 mmol/l
Citrate (if citrate dialysate)	2.4 meq/l

#### The ultrafiltration coefficient (K<sub>uf</sub>)

This relates the volume of fluid that is transferred across the membrane per mmHg of pressure gradient. In short, the K<sub>uf</sub> is a measure of the dialyser's permeability to water. The trans-membrane pressure needed to create the gradient is created from the inherently positive pressure of blood flow in the system as well as the machine generated negative pressure in the dialysate. The lower the K<sub>uf</sub>, the lower the permeability to water and the higher the trans-membrane pressure needed to attain adequate ultrafiltration.

#### Dialysis solutions

These solutions contain water combined with other components as seen in Table 1.

Bicarbonate has largely replaced acetate as the dialysate buffer because of haemodynamic instability associated with the latter.

Water purification is necessary to remove certain dangerous components that have been associated with severe complications of RRT:

- Aluminum-dementia
- Chloramine and copper-haemolytic anaemia (I have actually seen this in the modern era as a consequence of poor water purification)
- Endotoxin and bacteria-sepsis<sup>7,10</sup>

#### Indications for urgent RRT

- Anuria or oliguria (< 200 ml urine in 12 hours)
- Severe metabolic acidosis

- Urea above 40 mmol/l or creatinine > 350 mmol/l
- Hyperkalaemia > 6.5 mmol/l
- Clinical uraemic syndromes such as encephalopathy and/or pericarditis
- Hyperammonaemia with signs of raised ICP
- Severe dysnatremia (< 115 mmol/l or > 160 mmol/l)
- Severe fluid overload
- Severe hyperthermia
- Multi-organ failure

### Modality

The decision regarding the modality of RRT is clearly influenced by numerous factors such as availability, socioeconomic concerns as well as what is deemed appropriate for any given patient.

Decisions regarding PD vs HD, home-based or dialysis centre-based care, ambulatory or not and many others need to be made and personalised for every patient and their respective circumstances.

There are large and controversial studies, beyond the scope of the lecture, which look at PD vs HD, high flux vs low flux dialysis and many other issues.

RRT has been plagued with a confusing array of nomenclature in the literature, but includes PD, intermittent haemodialysis (IHD), sustained low-efficiency dialysis (SLED), extended daily dialysis (EDD) and continuous renal replacement therapy (CRRT). CRRT is comprised of slow continuous ultrafiltration (SCUF), continuous veno-venous haemofiltration (CVVH), continuous veno-venous haemodialysis (CVVHD) or a combination of convective and diffusive therapies, continuous veno-venous haemodiafiltration (CVVHDF).

Dosing, timing and a more in-depth discussion of modality go beyond the mandate of this introductory lecture but I have included some interesting articles in the reference for your perusal, which I am hopeful you will find helpful in your studies.<sup>7-9,11-14</sup>

### Conclusion

RRT has transformed the survival and quality of life for sufferers of end stage acute and chronic renal failure. A basic understanding

of membrane physiology and the techniques employed in RRT is necessary for anaesthesiologists, intensivists and hospitalists.

### Conflict of interest

The author declares no conflict of interest.

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