

RENAL DISEASE

(3) RENAL REPLACEMENT THERAPIES

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The third in the series of articles on renal disease looks at the different types of dialysis available to patients with chronic renal failure

In renal failure, the normal function of the kidney deteriorates with time and can be lost completely. In the initial, pre-dialysis phase, use of drugs, modification of diet and restriction of fluid intake can delay a patient's progression to end-stage renal failure. However, the loss of homeostatic function results in an accumulation of waste products, fluid retention and a distortion of electrolyte levels. Therefore, most patients with severe chronic renal failure will eventually require some form of renal replacement therapy.

The primary aim of renal replacement therapy is to correct the accumulation of toxins, electrolytes and fluid. The main treatment options for chronic renal failure are:

- Haemodialysis
- Peritoneal dialysis
- Haemofiltration
- Haemodiafiltration
- Transplantation

The first four will be discussed in this article and transplantation will be covered in the next.

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HAEMODIALYSIS

The use of semi-permeable membranes was first discovered by a Scottish chemist, Thomas Graham, in the 1850s. Problems with developing suitable vascular access delayed its introduction as a useful treatment.¹ However, haemodialysis has been available as a treatment for chronic renal disease since the 1960s. Most patients in the United Kingdom have dialysis in hospital-based units, although it can be performed at home or in a nurse-led satellite unit. Hospital-based units also provide dialysis services for acute renal failure patients.

Haemodialysis works by a combination of diffusion (the movement of solutes in a fluid from an area of high concentration to an area of low concentration across a semi-permeable membrane) and ultrafiltration (the movement of fluid under pressure across a semi-permeable membrane). Excess fluid is removed by ultrafiltration and waste products by diffusion. Essential minerals (eg, calcium and bicarbonate) are also replaced by diffusion.² Panel 1 describes the methods of gaining vascular access for haemodialysis.

Blood is removed from the arterial site and pumped through the haemodialysis

Panel 1: Vascular access for haemodialysis

Fistula A fistula is the surgical connection of a vein and an artery that allows blood into the venous system at arterial pressure close to the surface of the skin. This was first introduced in 1966 and is the preferred option.³ It takes about three months to "mature" and for the vein to be ready for use. Therefore, it should be planned in advance — unfortunately, this does not always happen.⁴ Ideally, the patient should have a good vascular system but this is not always the case, especially in the elderly who are making up an increasing propor-

tion of the haemodialysis population.⁵ The femoral vein can also be used but there is a greater risk of infection at this site.

Temporary or permanent catheter Catheters are usually placed into the subclavian or jugular vein. The latter is preferred as fewer complications, such as kinking leading to flow problems, occur.³ Catheters can also be placed in the femoral vein if there are problems with other veins, such as infection.

machine via a dialyser, where diffusion and ultrafiltration occur. The dialyser allows the free movement of low molecular weight molecules (less than 5kDa) but restricts the passage of larger molecules and blood.² Blood is then returned to the patient via the venous site.

Blood and dialysate flow in opposite directions to optimise the removal of waste products. Pumps are needed to produce a high enough flow rate for blood to go round the extracorporeal circuit. As dialysis progresses, its efficiency is decreased because the concentration gradient across the membrane in the dialyser is reduced.

There are many different dialysers available but the more biocompatible the dialyser, the fewer long-term side effects a patient is likely to suffer. The most biocompatible dialysers are steam sterilised and are made of a synthetic material, such as polysulfone. It has not been determined whether short-term complications (eg, hypotension, headaches and muscle cramps) are related to bioincompatibility or to the rate of fluid and urea removal.^{6,7}

An interaction occurs between angiotensin converting enzyme inhibitors and high-flux polyacrylonitrile membranes, which can lead to anaphylaxis caused by bradykinin formation.⁸

Dialysis fluid consists of a concentrated solution of electrolytes dissolved in water. Different types vary only in the quantities of electrolytes they contain (eg, low or high calcium or potassium concentrations depending on the patient's requirements). Most units will keep their chronic haemodialysis patients on the same dialysis fluid.

The water used to dilute the dialysate must be purer than drinking water, because patients are exposed to approximately 360L of water each week, and any impurities could pass across the semi-permeable membrane in the dialyser and cause adverse effects.^{9,10}

Before entering the dialysis machine, water passes through a reverse osmosis system to remove any aluminium. Aluminium enters the water supply as part of water treatment processes and has been shown to accumulate in people with renal failure. Signs of aluminium toxicity have been reported to include dementia and bone dis-

ease. It is important to recognise that aluminium levels might be higher in patients who take aluminium hydroxide as a phosphate binder. The water is purified to remove bacteria and other potential toxins.

Anticoagulation is usually necessary to keep blood flowing. Heparin is used to maintain anticoagulation in most patients during dialysis and the dose is dependent on the response of the patient. Most units use conventional heparin. Low molecular weight heparin can be used but is more expensive. In patients with bleeding complications, a continuous infusion of epoprostenol can be used as an anticoagulant, or heparin-free dialysis might be considered.²

When people first start on dialysis, they have short, frequent sessions because the body will have adjusted to having large quantities of waste products in the blood. If these are removed too rapidly, a disequilibrium syndrome occurs, which causes headache, nausea and vomiting and, in severe cases, confusion and convulsions.² The time spent on haemodialysis is gradually increased to between three and six hours, three times a week, depending on the patient's blood results, size and residual urine output.

The patient's weight is measured before and after dialysis. The "after" weight should be as close to the patient's "dry" weight as possible (ie, the body weight without excess fluid). Patients are advised to limit their fluid intake between dialysis sessions, sometimes to as little as 500ml per day, depending on their urine output. This can be difficult,

especially for younger patients. If people have problems tolerating fluid removal during dialysis, ultrafiltration profiling or sodium profiling can be attempted. This involves taking more fluid off at the beginning of dialysis so that the body has time to normalise before dialysis is finished, or altering the sodium content of the dialysate fluid during dialysis. These processes can reduce the incidence of dizziness and cramps caused by fluid removal but might exacerbate thirst, which does not help the patient's efforts at fluid restriction.¹¹

Inadequate dialysis and poor nutritional intake are associated with increased mortality and morbidity. Inadequate dialysis can also play a major role in erythropoietin resistance, resulting in worsening of anaemia. Table 1 lists some of the complications associated with haemodialysis.

There are two main methods of determining the adequacy of dialysis:

- Urea reduction ratio (URR)
- Urea kinetic modeling (UKM)

URR (as the name suggests) is the difference in urea levels pre- and post-dialysis expressed as a percentage. A URR of greater than 65 per cent indicates that dialysis has been adequate. The URR is not ideal, because it does not take into account the effect of residual renal function or dietary intake.

UKM is a more complex calculation of urea removal and takes into account Kt/V (ie, urea clearance per minute [K], time on dialysis [t] and how much urea is to be

TABLE 1: COMPLICATIONS ASSOCIATED WITH HAEMODIALYSIS^{2,12,13}

Complication	Reason	Remedy
Hypotension	Too much fluid removed too quickly.	Give at least 100ml bolus of sodium chloride 0.9 per cent via the haemodialysis machine. Raise the patient's feet above the head. Reduce the rate of fluid removal.
Cramps	Can be related to hypotension or to removal of too much fluid.	Give a bolus of 50–100ml sodium chloride 0.9 per cent or quinine sulphate tablets. Reassess the patient's weight.
Chest/back pain	Usually caused by activation of complement but angina should be excluded.	Changing to a more biocompatible dialyser can help, otherwise, give paracetamol.
Pruritis	Dry skin, hyperphosphataemia, uraemic toxins or allergic reaction to heparin or dialyser membrane.	Give antihistamines and moisturising lotions or change the dialyser.
Infection	Increased manipulations and skin penetration. Dialysis patients have impaired immune response.	Commence antibiotics, mainly anti-staphylococcal agents.
Anaemia	Blood loss, inadequate dialysis, excessive bleeding post dialysis, iron or erythropoietin deficiency.	Give erythropoietin and iron either IV or orally. Reduce heparin dose.

cleared [V]), protein catabolic rate, nutritional status and residual renal function. However, it is more accurate than URR and can indicate how much dialysis a patient requires.

Renal Association standards state that a Kt/V greater than 1.2 equates to good dialysis for three times a week dialysis. If dialysis is only done twice a week then a Kt/V greater than 1.8 is required.¹⁴

PERITONEAL DIALYSIS

Peritoneal dialysis (PD) was first introduced in 1975 and has had varying popularity.¹⁵ By the end of 1997, there were 120,000 people on peritoneal dialysis worldwide, which represented 15 per cent of the total dialysis population.¹⁶

In the UK, 50 per cent of dialysis patients are on this form of renal replacement therapy. It is preferred in children, patients with diabetes and people with unstable cardiovascular disease. PD is also used in patients who can manage their condition independently, or those who live a significant distance from a dialysis centre.

Like haemodialysis, PD works by diffusion, osmosis and convection. A solution is infused into the peritoneal cavity, where the patient's peritoneum acts as the semi-permeable membrane. The peritoneal membrane is a thin, highly vascular membrane with a surface area of 1 to 2m². Diffusion and convection of solutes occurs between capillary blood and the dialysis solution in the peritoneal cavity, and osmosis removes excess fluid.¹⁷

Access to the peritoneal cavity is via a catheter inserted through the abdominal wall into the peritoneum at the midline below the umbilicus. The catheter is usually made of silicon rubber and is flexible and non-irritant. It is secured by one or two dacron cuffs, which facilitate fibrous growth in the tunneled section.¹⁷

Peritoneal dialysis is not as aggressive as haemodialysis and does not leave the patient feeling fatigued at the end of each session. Unfortunately, it is not as efficient as dialysis at removing large molecular weight molecules, such as phosphate, and is, therefore, not suitable for all patients.

The dialysate used for peritoneal dialysis usually contains glucose as the osmotic agent, and traditionally comes in three strengths — 1.36 per cent (weak), 2.27 per cent (medium) and 3.86 per cent (strong). The solution also contains lactate, sodium, potassium and calcium.

The consultant and peritoneal dialysis nurse decide what prescription is most suitable for an individual, depending on the result of initial adequacy tests (the efficiency of the process) and the patient's blood results. Adjustment of the prescription takes place as blood results change and the patient's condition alters.

The adequacy of the peritoneal dialysis process is determined using peritoneal equi-

librium tests (PETs). These give a measure of the net ultrafiltration rate, which is dependent on the permeability of the membrane and its efficiency at exchange. PETs are calculated as either a creatinine clearance or Kt/V estimation. The calculation takes into account any residual renal function and allows the patient to be classified as a "high", "average" or "low" transporter. The form of peritoneal dialysis offered is dependent upon this result. PETs also allow patients who are receiving suboptimal treatment to be identified.

Renal Association standards state that renal units should aim for a Kt/V of 1.7 or a creatinine clearance of 50L.¹⁴ Recent studies in the United States and Canada have suggested that Kt/V should be nearer 2.0, or that a creatinine clearance greater than 60L per 1.73m² body surface area per week should be the target.¹⁸

There are two main forms of peritoneal dialysis, continuous ambulatory (CAPD) and automated (APD).

Continuous ambulatory peritoneal dialysis CAPD is usually performed manually by the patient at least four times each day.

Prewarmed dialysate is run into the peritoneum via the catheter and allowed to remain in place for about four hours (the dwell time). The fluid is then drained out and replaced with fresh dialysate. Fluid from a further bag is allowed to dwell in the peritoneal cavity overnight. The optimum dialysate volume that the body can tolerate is 2.5L per 1.73m² body surface area. If the body surface area is greater than 2m² then a fill volume of 3 to 3.5L can be tolerated. The volume of fill is reduced if there is a history of hernia, pleural leak or if the patient experiences abdominal pain.^{15,19}

Automated peritoneal dialysis APD is similar to CAPD, except that the exchanges are

done by a machine overnight. Two to 3L of fluid are drained into the peritoneum by a machine, left for about an hour and a half, then drained out and replaced with fresh dialysate. This process is repeated throughout the night until the total prescription volume has been reached (ie, the volume of fluid that the patients needs for adequate dialysis).

APD is a more expensive procedure than CAPD but many patients find it more socially acceptable. It allows the patient to lead a normal life during the day. Dwell times are shorter than with CAPD, and fluid from an extra bag can be run in at the end of dialysis and kept in during the day. Also, larger total volumes can be used because intraperitoneal pressure is lower when lying down. It is a good dialysis method for high transporters. Equilibrium is reached rapidly in high transporters after dialysate has been run into the peritoneal cavity.

Tidal peritoneal dialysis is a variant of APD. Dwell times are considerably shorter with this method because only about half of the fluid is drained out and replaced at each exchange. During the day the peritoneum is kept dry. The high flow rate achieved with this method leads to better diffusion because an equilibrium gradient is always present.¹⁹

COMPLICATIONS OF PD

Peritoneal dialysis of any type is not suitable for people who have had a lot of abdominal surgery and, in any case, it tends to last no longer than eight years.

There are many potential complications that can befall a patient receiving treatment with PD. As with most medical procedures, many of the complications listed below can be prevented by good operative and post-operative care, and close long-term follow-up. This involves a multidisciplinary approach. Patients should be fully involved

Panel 2: Signs and symptoms of peritonitis²²

Patients with peritonitis will present with at least one, but normally several, of the following:

- cloudy dialysis effluent
- slow drainage at exchange
- reduced volume of effluent
- abdominal pain or discomfort
- pyrexia

in their own care and must be aware of the causes of complications.

Infection Prophylactic antibiotic therapy An antibiotic providing Gram positive cover is given to prevent post-operative exit site or wound infection when the catheter is inserted. The antibiotic chosen should have activity against *Staphylococcus aureus* and *Staph epidermidis* and is normally vancomycin. There is little hard evidence to support this approach but it is considered prudent and is currently recommended.²⁰

Exit site infection The main causes of exit site infection are that the patient has poor technique when exchanging bags, that the patient causes trauma to the catheter site when exchanging bags, or that the fluid exchange programme via the catheter has been started too soon after insertion. Exit site infection is characterised by erythema of the skin and purulent drainage fluid.²⁰

Swabs are taken to confirm the presence of infection and to ascertain the causative organism. However, treatment of the infected exit site is usually commenced empirically. It is assumed initially that the causative organism is a Gram positive skin contaminant (these account for 50 per cent of cases), and treatment is started with an anti-staphylococcal agent until bacterial cultures have been grown.

If the contaminant is thought to be Gram negative, it is normally assumed initially to be *Pseudomonas*, and treatment is commenced with ciprofloxacin for 10 to 14 days. Therapy is altered depending on culture and sensitivity results.

It is important that the exit site is cleaned thoroughly at least daily to prevent deterioration. Chlorhexidine or mupirocin are used in some centres.

Peritonitis Peritonitis is a bacterial or fungal infection that causes inflammation of the peritoneal membrane and it is a major complication of peritoneal dialysis. It is often caused by external contamination eg, from poor exchange technique. The causative organism is normally a skin contaminant, but,

more rarely, can come from the bowel or spread from concurrent infections, such as respiratory infections. An episode of peritonitis occurs on average once every 24–36 months per patient.²¹

When a patient presents to a unit with suspected peritonitis, samples of any cloudy effluent are sent for microscopy, Gram stain and culture and sensitivity testing. A white cell count greater than 100/ml confirms the diagnosis of peritonitis. Treatment is commenced empirically because results from Gram staining, and culture and sensitivity reporting, take 48–72 hours to return. A number of combinations of antibiotics have been recommended depending on local conditions and resistance patterns.²²

The aim of treatment is first to treat Gram positive organisms (mainly *Staph epidermidis* or *Staph aureus*) with agents such as vancomycin or a first generation cephalosporin, and secondly Gram negative organisms, such as *Escherichia coli*, with agents such as ceftazidime or an aminoglycoside. The use of a combination of cephalosporin and aminoglycoside is preferred, because they have synergistic activity against staphylococci and because some Gram positive organisms, such as enterococci, are more susceptible to aminoglycosides.

Incidence reporting has shown that about 60 per cent of peritonitis episodes are caused by Gram positive organisms, and that Gram negative organisms account for 20 per cent. Fungal peritonitis accounts for 5 per cent of cases and in the remaining 15 per cent no organism can be identified.

Once the causative organism has been identified, it is normal to stop any inappropriate antibiotics and continue with appropriate monotherapy, where possible. Detection of multiple Gram negative organisms (aerobic and anaerobic) means that bowel perforation might have occurred, necessitating surgical referral. Antibiotics can either be added to peritoneal dialysis fluid (intraperitoneal, IP administration) or be given intravenously. It is normal for a patient with peritonitis to show clinical signs of improvement after five to seven days.

If the organism isolated is *Staph aureus*

or *Staph epidermidis* and response to treatment is poor, rifampicin 600mg daily for three weeks can be given. If *Pseudomonas* is isolated, then an anti-pseudomonal agent, such as piperacillin, should be given in addition to an aminoglycoside.

Fungal peritonitis is a rare complication of PD treatment, and is normally caused by yeasts, especially *Candida* spp. Treatment with IP fluconazole and oral flucytosine (only available on a named-patient basis) is common. However, treatment with antifungals is usually unsuccessful and catheter removal is normally necessary.

During a suspected peritonitis episode, initial exchanges with heparin 500 units/L should be given until the fluid runs clear.

The Renal Association has recommended that all CAPD patients use a disconnect system as standard, because it has been proved to reduce the incidence of CAPD peritonitis.¹⁴ With a disconnect system, the patient does not need to remain attached to a drainage bag between dialysis sessions. In the past, after a patient had drained CAPD fluid into the peritoneum, the bag remained connected to the catheter. After four hours, the bag was then unrolled and used to drain the fluid back out of the peritoneum. A new bag was then attached and the process repeated. Because the bag remained connected to the catheter between sessions, there was an increased risk of infection. The Renal Association also recommends the auditing of infection rates on renal units, and has set a standard of less than one episode of peritonitis every 18 months as the minimum acceptable level of infection. In addition, it says that the initial cure rate of peritonitis should be greater than 80 per cent.

Patients have an important role in detecting the outbreak of an episode of peritonitis and should be trained to recognise signs and symptoms (see Panel 2) and to be aware of the appropriate response to them.

Recurrent cases of peritonitis are a major reason why patients transfer to haemodialysis,¹⁶ because the peritoneal membrane becomes fibrosed, adhesions form and the dialysis process becomes inefficient.

Blocked catheters When the catheter becomes blocked, and the cause is not related to its position, treatment with urokinase is recommended. A normal dose is 5,000 units instilled into the catheter for two to four hours. The blockage is usually caused by fibrin.

Other complications *Hernia* Hernias commonly occur when the volume of exchange is 2L or more because of the resultant 2kg load in the peritoneal cavity.

Haemoperitoneum Haemoperitoneum is normally caused by rupture of small blood vessels in the peritoneum and presents as blood in the fluid. Microscopy shows a high red cell count and a low white cell count. The bleeding settles spontaneously but patients who are required to add heparin to the fluid in their bags routinely are normally advised to stop.

Acute hydrothorax Acute hydrothorax presents as acute breathlessness. This rare complication occurs when PD fluid leaks through the diaphragm into the pleural cavity. Analysis of the fluid in the pleural cavity confirms the presence of PD fluid. Initial treatment is to drain the peritoneal fluid from the abdomen. A significant hydrothorax will require direct drainage of the fluid from the chest cavity.

SOCIAL IMPLICATIONS OF CAPD

The social implications for CAPD patients should not be underestimated. Patients have to carry out exchanges four or five times a day, each one of which takes 30 to 40 minutes to perform and must be done in a clean area. This can put considerable pressure on the person in their place of work.

HAEMOFILTRATION

Haemofiltration tends to be used as a short-term treatment in acute intensive care settings²³ and is much "gentler" than haemodialysis. It is performed over a longer time or it can be continuous. It is more suitable than haemodialysis for people with an unstable cardiovascular condition. This method of dialysis is also preferred for fluid-overloaded patients, because excess fluid can be removed gradually. It can also be used to remove fluid in fluid-restricted patients who need enteral or parenteral nutrition or who are receiving intravenous antibiotics.²⁴ Permeable hollow fibre dialysers, known as haemofilters, and a special filtration fluid are used. Haemofiltration works by convection (movement of solutes in fluid across a membrane) and ultrafiltration, so it removes extracellular fluid with toxins.

Haemofiltration fluid is added to filtered blood at a haemofilter, so diluting any waste products. Haemofiltration fluid is a balanced electrolyte solution that is available with or without potassium (eg, Haemafiltrisol and Monosol). It is usually lactate-based, because lactate is metabolised to bicarbonate, which is used to correct underlying metabolic acidosis.

It is thought that haemofiltration results in a higher rate of removal of molecules with a large molecular weight but lower removal of small molecules eg, potassium and urea, than haemodialysis.² Access is mainly via a central line.

HAEMODIAFILTRATION

As the name suggests, haemodiafiltration is a combination of haemodialysis and haemofiltration ie, small and large molecule clearance.² Blood is withdrawn and passes through a highly permeable dialyser removing much greater volumes of extracellular fluid than haemodialysis. Haemofiltration substitution fluid and the filtered blood are then returned to the patient. This method has advantages in the long term because it removes larger substances, such as beta₂-microglobulin, but has the potential hazards of regular large infusions of haemofiltration fluid (eg, sodium and lactate accumulation).

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