Kidney Dialysis

Introduction to Anatomy and Physiology

The kidneys are located in the abdominal cavity either side of the spine, just below the the ribcage. The right kidney is positioned slightly lower in the body, and also closer to the spine due the presence of the liver. They are bean shaped and divided into 18 lobes which each contain the outer renal cortex and the inner renal medulla. These sections themselves are made up of nephrons, which drain into a collecting duct. Nephrons are made up of two parts: a renal corpuscle, where blood plasma is filtered, and a renal tubule, into which the filtered fluid passes. There are two main types of nephrons in the kidney: the more superficial cortical nephron (which makes up 80-85% of the nephrons), and the juxtamedullary (or deep) nephron, which makes up 15-20% of the nephrons. The kidneys are under the control of the sympathetic branch of the autonomic (otherwise known as involuntary) nervous system. Blood is supplied through the renal artery, and leaves via the renal vein. Urine which is produced by the kidneys is transported along the ureter into the bladder, where it is stored prior to urination.

Kidney Function
The kidneys have several functions, with the most well known being the filtration of blood and the production of urine (between 1.2 and 2 litres of urine per day). The two kidneys receive 20-25% of the total cardiac output from the heart, approximately 1.200 ml/min. Such a high rate is needed to maintain the diffusion gradient required for ultrafiltration and reabsorption, the two processes by which the kidneys produce urine. The kidneys are very efficient at filtration, and manage to reclaim and recycle most of the water that they filter, as well as around 1,300 g of sodium chloride and 180 g of glucose every day. The kidneys produce around 180 litres of filtrate a day; fortunately most of this is then reabsorbed, leaving 1.2 - 2 litres of urine. The amount of urine produced can be varied by the kidneys to assist in maintaining a constant body water level and mineral ion concentration.

In addition to this function, the kidneys are also the site of synthesis of several minerals, including vitamin D. They also have an important endocrine function: they are able to detect low levels of oxygen in the blood, upon which they stimulate the production of red blood cells in the bone marrow, via a hormone known as erythropoietin. The kidneys also indirectly regulate blood pressure by initiating the production of a series of enzymes. They do this by converting the precursor hormone prorenin into renin, when low blood pressure is detected. This cycle leads to blood vessels constricting, thereby increasing blood pressure. The hormone aldosterone is also released in this situation, causing the tubules in the kidney's nephrons to increase the reabsorption of water and sodium into the blood, which in turn leads to the excretion of potassium from the body, in order to maintain the blood's chemical balance. This chain of events leads to an increase in the volume of extracellular fluid in the body, thereby further increasing blood pressure.

**Diseases Which Warrant Kidney Dialysis**

Dialysis is the mainstay of treatment for acute kidney injuries (AKI), and also more commonly for the later stages of chronic kidney disease (CKD). It is used to keep the patient alive and healthy while the patient waits for a kidney to become available for transplantation.

**Stages**

Chronic kidney disease has five commonly regarded stages.[2] Most CKD patients are at stage 1-3 due to general wear and tear on the body during life. The medical profession starts to pay attention once stage 3 is hit; at this point regular screening occurs. At stage 4, the patient is put forward for consideration and preparation for dialysis therapy. At stage 5, also referred to as end stage kidney disease, dialysis is commenced and the patient may also be listed for a kidney replacement. It is estimated that 8.8% of the population in the UK suffers from symptomatic chronic kidney disease.[3]

Patients are suffering from end-stage renal failure when about 90% of their kidney function has been lost. At this stage they are filtering about 10-15 % of the amount of urine that their kidneys would normally process in any given time, and are producing substantially smaller volumes of urine as a result. There will be a build up in the blood stream of waste products normally excreted by the kidneys (including nitrogenous compounds, and creatinine).

**Causes**

The most common causes of CKD include:

1. Diabetes – More commonly type II than type I.
2. Glomerulonephritis – A term used to describe a broad range of kidney diseases, but most commonly 'immunoglobulin A nephropathy'.
3. Unknown – 20% of cases in the UK have no obvious cause. These are known as 'idiopathic' cases in the medical profession.

Other causes have been observed, such as adult polycystic kidney disease, or even more rarely due to parasites such as pinworm.

**Diagnosis**

Commonly, the diagnosis of CKD is usually made during the screening of people with known risk factors for kidney problems, such as raised blood pressure or diabetes. It is also frequently diagnosed when patients are symptomatic of anaemia or cardiovascular disease. Initial diagnostic tests normally include a blood test for creatinine, which is a breakdown product of muscle metabolism. An elevated level of this compound is indicative of a lower glomerular filtration rate (GFR). A urine sample is also taken and analysed for the presence of protein, as well as poorly concentrated urine, as these both show that the kidneys are functioning incorrectly. To confirm the diagnosis, medical imaging is often used and commonly a kidney biopsy is also performed to identify if the decrease in kidney capability is reversible.

**History of Dialysis**

Dialysis was originally invented by Willem Johan Kolff in 1943, but was initially unsuccessful as it could not allow for the removal of excess fluid.[4] The original machine was created with scrap, including salvaged cars, washing machine parts and sausage skins. This was due to sparsity of resources during the occupation of the Netherlands during World War II. The machine did not successfully treat anyone until 1945, when one female patient recovered, all previous patients had died prior to this. Kolff never patented his invention and instead donated his machines to hospitals and researchers around the world, in order to help improve them. One of these machines was improved upon by Dr. Nils Alwall, who enclosed it in a stainless steel case allowing excess fluid to be drained by negative pressure. This became the first practical kidney dialysis machine, and successfully treated its first patient on 3rd September 1946.

**Dialysis - What's Available and How it Works**
Patients suffering from end-stage renal failure require kidney dialysis therapy, otherwise known as 'renal replacement therapy'. Dialysis literally means 'cleaning the blood', and involves the separation of large solutes from smaller solutes in the blood, through a selectively permeable membrane, as shown in the diagram below. The blue solutes and red blood cells remain in the blood, whilst the purple, yellow and green solutes move across the yellow membrane by diffusion, encouraged by a concentration gradient. Excess fluid is removed by a process known as 'ultrafiltration', and is literally driven across the membrane by hydrostatic pressure.

Haemodialysis

There are three main components to a haemodialysis machine - the hemodialysers (artificial kidney), the dialysis membrane, and the dialysate. The schematic diagram below shows a basic outline of how such a machine might work.
Blood removed from the patient is delivered to the haemodialyser, inside which, the blood flows through the dialysis membrane. The blood flows through this machine at a very low rate.

2. This membrane is selectively permeable and contains pores large enough to allow the diffusion of small solutes across it. The patient’s blood is then effectively bathed in a special solution called the dialysate (separated only by the dialysis membrane).

3. The blood and the dialysate move in opposite directions, thereby forming a countercurrent exchange system, and aiding in the transfer of molecules across the dialysis membrane.

4. This dialysate is specially formulated to maintain concentration gradients between itself and the patient’s blood. Therefore, waste products can diffuse from the blood into the dialysate, and substances required by the body can diffuse from the dialysate into the blood.

Examples of waste products include - urea, creatinine, uric acid, and excess phosphate, potassium and sulphate ions. Examples of substances required by the body include: glucose and bicarbonate ions.

The cleaned and ‘revitalised’ blood is then returned to the patient. The dialysate, complete with the waste products removed from the patient’s blood, and devoid of the substances it has transferred to the patient’s blood, is then discarded.

Patients typically require this treatment for about 6-12 hours per week, and this is normally split into three sessions. Some patients elect for shorter, but more frequent treatments, as this may better fit their lifestyle.

For people undergoing regular haemodialysis treatments, a ‘fistula’ or ‘graft’ is normally surgically created in the patient’s arm. This aids the connection of the dialysis machine to the patient, and provides faster and easier access to the patient’s blood.

**Haemofiltration**

This technique is similar to the process of haemodialysis as described above, but makes use of some slightly different principles, and is used when heavier molecules (with a higher molecular weight) need to be cleared from the patient. In this process, no dialysate is used, but instead the blood is pumped through a dialyser and a pressure gradient is applied. Water then moves quickly across the dialysis membrane as a result of this, dragging with it the larger waste molecules that normal haemodialysis may leave behind. Any water or salts lost from the blood during this process, which the patient needs, are replaced by an equal volume of ‘substitution fluid’, before being returned to the patient.

This technique is impractical for long term management of stable CKD patients, as it takes much longer to achieve the same clearance of waste substances. Also, due to the effects of the substitution fluid, the patient will be more cardiovascularly stable, and this technique is therefore more suited to critically ill patients (in an intensive care setting, for example). This technique would therefore be more commonly used on a younger otherwise more healthy patient, suffering from a short term and reversible case of acute kidney failure. Things that could cause this would include a sudden drop in blood pressure, poisoning, or kidney stones.

The image below shows an example of what a typical haemofiltration machine might look like:
Haemodiafiltration

This third technique is a combination of the first two techniques - i.e. haemodialysis combined with haemofiltration. There are various permutations of this combination, with recent evidence suggesting that intermittent haemodiafiltration gives better long term results in an outpatient setting, when compared with patients receiving regular haemodialysis.

Peritoneal Dialysis

This technique makes use of the patient’s peritoneum (the membrane surrounding the abdominal cavity and organs) as the selectively permeable membrane, in a procedure known as an 'exchange'. The peritoneum is rich in blood vessels, and is therefore ideally suited to carrying out this procedure.

There are actually two types of peritoneal dialysis available to patients, both of which the patient can carry out at home after suitable training. This type of dialysis involves having a permanent 'access point' to the patient's abdomen. This usually takes the form of a surgically implanted catheter, just below the belly button. The two techniques are described in more detail below.

Continuous Ambulatory Peritoneal dialysis (CAPD)

1. Dialysate is infused into the patient’s abdomen.
2. 4-6 hours later this fluid is then drained out of the peritoneum via a catheter in the abdominal wall.
3. The fluid is then replaced with fresh solution, the equipment is disconnected, and the exchange is finished.
4. This process is painless, and takes about 30-40 minutes to complete. As you can imagine for patients undergoing this treatment for the first few times, the process the abdomen being filled with dialysate can be quite strange and uncomfortable at first.
5. The patient may then undertake normal activities, all whilst dialysis is continually occurring between the peritoneal blood vessels and the dialysate.
6. The dialysate is changed at regular intervals and is continually present in the abdomen.\[12\]

Automated Peritoneal dialysis (APD)

This technique is similar to CAPD, except it involves a machine filtering the patient's blood when asleep at home. The patient is connected to an APD machine which performs a numbers of exchanges during the night, and requires a time window of around 8-10 hours in order to complete this successfully.

Side Effects and Complications

Since there are a relatively small number of kidney donors, unfortunately not every CKD patient can receive a donor's kidney through transplant surgery. As was described above, they can, however, rely on a dialysis machine to replace the function of their impaired kidneys. Unfortunately, as with most therapeutic procedures, this can cause patients to suffer from side effects. These side effects will differ depending on the length of dialysis therapy, the duration of each session, and their frequency.

In the Short-Term

Patients who begin kidney dialysis are initially 2-3 times more likely to experience vomiting, convulsions, low blood pressure, tiredness and stress, all due to a sudden change in the hydration and mineral status of the body.

Generally, as patients become more familiar with dialysis, these symptoms begin to ease after about 3 - 6 months. However, for some patients, carbonated dialysate is used to relax the body.

In the Long-Term

For long-term dialysis patients, it is much more likely that complications and physical deterioration will occur. These can include:

Cardiac Insufficiency

Accumulation of sodium and water in the body is main cause of cardiac insufficiency in most patients. As more water and sodium stays inside the body the total circulating blood volume also increases, resulting in an increased cardiac activation, which in turn leads to an increase in stroke volume and heart rate. If this status continues for long period of time, the tissues of the heart become exhausted and begin to exhibit decreased functionality. As water and sodium are the main causes of this, patients need to limit their water and sodium intake, as well as control their body weight and blood pressure, by keeping a close eye on their diet.

Hypertension
Much like cardiac insufficiency, hypertension is caused by excessive intake of water and sodium in the diet. Once hypertension has been present for a protracted period, the resistance of blood vessels tends to increase. This increased resistance can lead to cardiac insufficiency and ultimately cerebral haemorrhage. The following steps are often recommended in order to prevent hypertension: limiting water, sodium, and high calorie food (especially foods with a high fat content), regular blood pressure checks, and regular moderate exercise.

**Hyperkaleamia (excessive blood potassium level)**

As patients cannot excrete potassium into their urine, the concentration of potassium in the blood has a tendency to increase steadily in CKD patients. An extremely high level of potassium in the blood can lead to critical damage in the body (including abnormalities in the heart rate and rhythm). Therefore, patients should try to decrease the amount of potassium rich foods that they eat, as well as making sure that they undergo sufficient dialysis procedures, and are administered appropriate medications to help decrease the potassium level.

**Carpal Tunnel Syndrome**

Carpal tunnel syndrome is a condition that causes pain, nerve conduction failure and paraesthesia (pins and needles) as a result of lack of blood flow to the median nerve. This is caused by high pressure in carpal tunnel, which is bordered by the transverse carpal ligament, as shown in the figure above. This syndrome is much worse in dialysis patients than others, in whom it also has a higher rate of relapse and deformation of the median nerve than normal patients. The main cause has not been found, but stacking of amyloid protein is suspected to be the main reason. There are two types of treatment: conservative management, or surgery.

Drugs, including pain killers, may be used, and anti-inflammatory doses of steroids may be injected into the carpal tunnel. In addition to this, an external cast or splint may be used to hold the tunnel in position, and thus minimise the occurrence of symptoms.

For patients who suffer unmanageable pain, and for whom therefore conservative management is considered a failure, surgical treatment then indicated. The surgery is a relatively simple procedure, taking around half an hour. During the procedure, the surgeon will cut transverse carpal ligament, thereby relieving pressure on the median nerve.

**During dialysis**

The actual process of dialysis occurs outside the body (apart from peritoneal dialysis), and the body struggles to maintain homeostasis when a rapidly altered blood volume is redistributed back into it. This can lead to unexpected reactions in the body occurring. It is therefore important that patients are monitored by medical staff whilst dialysis is occurring.

**Dialysis Disequilibrium**

While dialysis is effective at removing waste compounds in the blood quickly, it takes longer to remove waste substances from the brain. As a result of this, the osmotic pressure in brain can increase, causing the brain to absorb water and become swollen. This obviously dangerous condition can cause neurological side effects in the short-term. But the good news is that these tend to be reversible, and are eased once the waste substances in the brain are eliminated and are diffused or actively transported into the blood.

**Arrhythmia**
An electrolyte imbalance in the blood, due to CKD for example, can cause fatal disturbances in heart rate and rhythm. In fact, 10% of deaths in dialysis patients are actually caused by cardiac arrest. Therefore monitoring of the heart's electrical activity (as assessed by an electrocardiogram, or ECG) is essential when undergoing dialysis. The image above shows both a normal ECG trace, and also a trace for a patient suffering from atrial fibrillation.

When potassium concentration in the blood is excessively higher or lower than the normal level, too much water is drawn out of the blood, also anaemia may result. This commonly happens to patients who have a concurrent heart disease. In this situation, the following therapeutic interventions are indicated: oxygen treatment, anti-arrhythmic agents, and the control of potassium concentration.

Irregular blood pressure
The haemodialyser draws around 150 - 250 ml of blood per minute from the patient, and this is independent of the patient's heart activity. Some patient's blood pressure can drop suddenly during dialysis therapy. This can also happen when the patient is over-hydrated. In either case, the fluid imbalance is corrected by administering fluid therapy, or by decreasing the flow rate, respectively. The graph above depicts an image of irregular blood pressure that could be seen in a patient undergoing dialysis therapy. Very rarely, antihypertensive medications may also be prescribed to help decrease a patient's blood pressure.

Future Developments
The current dialysis options available to CKD patients replace the function of kidney very well. However, there are a few things that could be improved upon for the patient's safety and comfort. Three such developments will be discussed in this section. High-flux haemodialysis and nano fibre dialysis techniques have been invented in order to prevent patients lying recumbent on a hospital bed for long periods of time. Another novel technique is the production of the artificial 'bionic kidney', which could be a fundamental solution to CKD in itself.

High-Flux Haemodialysis
High-flux haemodialysis uses a dialysis membrane which has an efficiency 10 times higher than the low-flux ones currently used. This high-flux membrane not only filters water and minerals more quickly, but it is also more efficient at removing larger molecules from the body. The figure above shows that a high-flux membrane may be almost as efficient as a human kidney at filtering a patient's blood. However, so far it has not been clinically proven, but there are some early signs of improvement to a patient's dialysis experience.

Nano-Fibre Technology
One of the main problems with current haemodialysis techniques is that patients are required to lie in bed for 3-4 hours three times a week, which is very time consuming. However a 16 g nano-fibre mesh based system is a 'cheaper and wearable' alternative to dialysis, and continually filters the blood whilst
being attached to the patient’s skin. The nano-fibres consist of two parts: ethylene vinyl alcohol and different types of zeolite. More work needs to be done to improve the ‘compactness’ and portability of this technology in order to make it truly portable.

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References


