NAME: OJAMERUAYE OGHENEFEJIRO

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COURSE: RENAL PHYSIOLOGY

DEPARTMENT: MEDICINE AND SURGERY

ASSIGNMENT

1. Discuss the pathophysiological process involves in renal failure?

2. With the aid of suitable diagrams discuss the types of dialysis you know?

ANSWERS

1. PATHOPHYSIOLOGICAL PROCESS OF RENAL FAILURE

Pathophysiology seeks to explain the functional changes that are occurring within an individual due to a disease or pathologic state. Renal failure is defined as a significant loss of renal function in both kidneys to the point where less than 10 to 20% of normal GFR remains. • Renal failure may occur as an acute and rapidly progressing process or may present as a chronic form in which there is a progressive loss of renal function over a number of years. • Acute renal failure has an abrupt onset and is potentially reversible. • Chronic failure progresses slowly over at least three months and can lead to permanent renal failure.

PATHOPHYSILOGY

Initially, regardless of the primary cause of nephron loss, some usually survive or are less severely damaged. These nephrons then adapt and enlarge, and clearance per nephron markedly increases. If the initiating process is diffuse, sudden, and severe, such as in some patients with rapidly progressive glomerulonephritis (crescentic glomerulonephritis), acute or subacute renal failure may ensue with the rapid development of ESRD. In most patients, however, disease progression is more gradual and nephron adaptation is possible. Adapted nephrons enhance the ability of the kidney to postpone uremia, but ultimately the adaptation process leads to the demise of these nephrons.

Decreased renal function interferes with the kidneys' ability to maintain fluid and electrolyte homeostasis. The ability to concentrate urine declines early and is followed by decreases in ability to excrete excess phosphate, acid, and potassium. When renal failure is advanced (glomerular filtration rate [GFR] ≤ 15 mL/min/1.73 m2), the ability to effectively dilute or concentrate urine is lost; thus, urine osmolality is usually fixed at about 300 to 320 mOsm/kg, close to that of plasma (275 to 295 mOsm/kg), and urinary volume does not respond readily to variations in water intake.

The following changes takes place physiologically in the body due to renal failure:

a) Fluid and Electrolyte Derangement:

- Sodium

In a normal individual, more than 25,000mmol of sodium ions are filtered daily with < 1% being excreted. CRF can be associated with sodium retention, sodium depletion or normal sodium balance and is influenced by factors such as diuretic use and cardiac function. However, despite a diminishing GFR, sodium and water balance are well maintained by increased fractional excretion of sodium in urine and a normal response to thirst. Thus, the plasma sodium

concentration is typically normal, and hypervolemia is infrequent unless dietary intake of sodium or water is very restricted or excessive. Heart failure can occur due to sodium and water overload, particularly in patients with decreased cardiac reserve.

- Calcium and Phosphate

Abnormalities of calcium, phosphate, parathyroid hormone (PTH), and vitamin D metabolism can occur, as can renal osteodystrophy. Decreased renal production of calcitriol (1,25(OH)2D, the active vitamin D hormone) contributes to hypocalcaemia. Decreased renal excretion of phosphate results in hyperphosphatemia. Secondary hyperparathyroidism is common and can develop in renal failure before abnormalities in calcium or phosphate concentrations occur. For this reason, monitoring PTH in patients with moderate CKD, even before hyperphosphatemia occurs, has been recommended.

> Renal osteodystrophy: (abnormal bone mineralization resulting from hyperparathyroidism, calcitriol deficiency, elevated serum phosphate, or low or normal serum calcium) usually takes the form of increased bone turnover due to hyper-parathyroid bone disease (osteitis fibrosa) but can also involve decreased bone turnover due to adynamic bone disease (with increased parathyroid suppression) or osteomalacia. Calcitriol deficiency may cause osteopenia or osteomalacia.

- Potassium and magnesium

Adaptive processes increase potassium secretion in the distal nephron (collecting tubules) and also in the gut. Whilst a wide range of plasma potassium concentrations can be encountered dependent on factors such as diuretic use, it tends to be elevated. Acute changes present the greatest threats to life. A range of drugs may cause acute hyperkalaemia such as β-blockers, potassium-sparing diuretics (e.g. spironolactone), ACE inhibitors, angiotensin antagonists, NSAIDs and nephrotoxins such as aminoglycosides and cyclosporins. Extracellular acidosis causes an exchange of intracellular potassium for extracellular hydrogen ions in an attempt to maintain electrical neutrality. In acute acidosis, the serum potassium will rise 0.5 mmol litre–1 for each 0.1 unit decrease in ph. For this reason, hypercarbia should be avoided during general anaesthesia.

Magnesium is handled by the kidney much like potassium. Reduced excretion may cause hypermagnesemia, muscle weakness and potentiate non-depolarising muscle relaxants.

- Creatinine and urea

Plasma concentrations of creatinine and urea (which are highly dependent on glomerular filtration) begin a hyperbolic rise as GFR diminishes. These changes are minimal early on. When the GFR falls below 15 mL/min/1.73 m2 (normal > 90 mL/min/1.73 m2), creatinine and urea levels are high and are usually associated with systemic manifestations (uremia). Urea and creatinine are not major contributors to the uremic symptoms; they are markers for many other substances (some not yet well defined) that cause the symptoms.

- Acidosis

Chronic metabolic acidosis is a common feature of renal failure. The inability to secrete protons and buffers (e.g. phosphate) or to regenerate bicarbonate limits the clearance of hydrogen ions. Furthermore, reduction in glutamine utilisation reduces ammonia production and secretion into the proximal tubule. Retention of organic anions causes a progressive increase in the anion gap and a further fall in plasma bicarbonate concentration. Although

plasma bicarbonate concentrations rarely fall below 12–15mmol litre–1, there is little reserve to counter acute acidosis caused by ketoacidosis or sepsis.

b) Cardiovascular and pulmonary abnormalities

Cardiovascular abnormalities are common in Chronic renal failure and are responsible for 48% of deaths in these patients. Systemic hypertension is the most common with an incidence approaching 80%, although it is often not a feature of sodium-wasting nephropathies such as polycystic kidney disease or papillary necrosis. Plasma volume expansion resulting from sodium and water retention is the most frequent cause of hypertension; it may be improved significantly by dialysis. Some patients may require β-blockers, ACE inhibitors, α-antagonists and vasodilators to control their blood pressure adequately. Alteration in the control of renin and angiotensin secretion may also contribute to hypertension in 30% of patients. Ischaemic heart disease (IHD) is a frequent cause of mortality in patients with CRF. Accelerated atherosclerosis results from a decreased plasma triglyceride clearance, hypertension and fluid overload causing left ventricular hypertrophy and failure.

c) Neurological abnormalities

Many patients with CRF have abnormalities in central (CNS) and peripheral nervous system function. There is a wide spectrum of CNS changes. for example, from mild personality alterations to asterixis (i.e. lapse of posture, usually manifest by bilateral flapping tremor), myoclonus, encephalopathy and convulsions. Peripheral neuropathy is common in advanced stages of the disease. Initially, it presents as a distal 'glove and stocking'sensory loss but then progresses to motor changes. Both dialysis and renal transplantation may improve the neuropathy. The presence of a peripheral neuropathy should alert the anaesthetist to the presence of an autonomic neuropathy with delayed gastric emptying, postural hypotension and silent myocardial ischaemia. Two types of neurological disturbances are unique to patients on dialysis. Dialysis dementia with dyspraxia, myoclonus and dementia occurs in patients on dialysis for many years and may be related to aluminium toxicity. The dialysis disequilibrium syndrome is associated with rapid initial reduction in plasma urea concentrations at the start of dialysis.

d) Anemia

Anemia is characteristic of moderate to advanced CKD (≥ stage 3). The anemia of CKD is normochromic-normocytic, with an Hct of 20 to 30% (35 to 40% in patients with polycystic kidney disease). It is usually caused by deficient erythropoietin production due to a reduction of functional renal mass (see Overview of Decreased Erythropoiesis). Other causes include deficiencies of iron, folate, and vitamin B12.

e) Endocrine disturbances

Changes in parathyroid function and lipid clearance have been noted above. Glucose tolerance is impaired but there is a reduced requirement for exogenous insulin in diabetic patients, probably related to the reduced metabolism of insulin by the failing kidney. Patients with CRF have abnormalities of temperature regulation with reduced basal metabolic rate and a tendency to hypothermia. This is may by important when assessing fever.

f) Immune function

Sepsis is a leading cause of death in patients with CRF. Inhibition of cell-mediated immunity and humoral defence mechanisms occurs, with little improvement following dialysis. There is an increased production of pro-inflammatory cytokines suggesting that activation of monocytes may play a role in uremic immune dysfunction. Superficial infections are common in fistula and

catheter sites; wound healing is poor. The incidence of viral hepatitis B has decreased somewhat following the introduction of erythropoietin and hepatitis B vaccination. There is also an increased incidence of hepatitis C infection in patients on haemodialysis and, although there is often little effect on liver function, it is of concern in patients undergoing renal transplantation and immunosuppression.

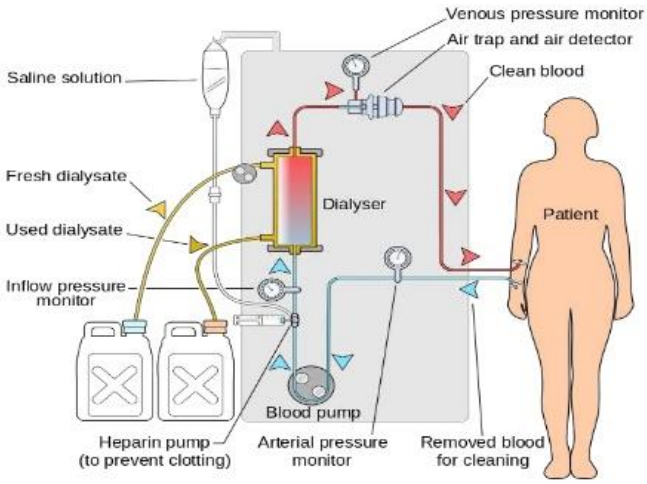
TYPES OF DIALYSIS

In medicine, dialysis is the process of removing excess water, solutes, and toxins from the blood in people whose kidneys can no longer perform these functions naturally. Dialysis is for patients who suffer from damaged, injured or impaired kidneys. A patient who suffers from chronic kidney disease or renal failure in its late stages is likely to be put on a dialysis treatment. Kidney failure, however, is not always permanent. In that case, dialysis may be used as a treatment for a limited period of time until the kidneys are able to naturally function optimally.

There are three primary and two secondary types of dialysis: hemodialysis (primary), peritoneal dialysis (primary), hemofiltration (primary), hemodiafiltration (secondary) and intestinal dialysis (secondary).

HEMODIALYSIS

PROCEDURE:



Hemodialysis is a therapy that filters waste, removes extra fluid and balances electrolytes (sodium, potassium, bicarbonate, chloride, calcium, magnesium and phosphate). In hemodialysis, blood is removed from the body and filtered through a filter called a dialyzer, or artificial kidney, and the filtered blood is returned to the body. To perform hemodialysis, a minor surgery is usually needed to create a vascular access in the patient's body to get the blood from the body to the dialyzer and back into the body. There are 3 types of vascular access:

- AV (arteriovenous) fistula: The AV fistula is the safest type of vascular access. It can last for years and is least likely to get infections or blood clots. A surgeon connects an artery (a large

blood vessel that carries blood from your heart) and a vein (a blood vessel that carries blood to your heart) under the skin in your arm. Usually, they do the AV fistula in your non-dominant arm. For example, if you are right-handed, you would probably get your fistula in your left arm.

Because the fistula needs time to heal after surgery, it's best to get an AV fistula 2–3 months before you need to start dialysis. After 2-3 months, the fistula will be stronger than a normal artery or vein to allow needles to be put in and taken out many times a week.

- AV graft: An AV graft is the next best vascular access option. It's more likely to have problems with infections and blood clots. A surgeon uses a plastic tube to connect an artery and vein under the skin in your arm. It's best to get an AV graft 2–3 weeks before you start dialysis.
- Catheter: A catheter is a Y-shaped plastic tube. Catheters are more likely to have problems with infection, blood clots, and scarring. One end connects to a large vein that is deeper inside your body. The other two ends come out through your skin. There are 2 types of catheters:

-A venous catheter connects to a vein in your neck, chest, or leg and hangs outside your body from an opening in your skin. If you need to start dialysis right away, your doctor may recommend a venous catheter because it can be placed and used the same day. But it should only be used for short periods of time.

-A tunnelled catheter most often connects to a vein in your neck. It is safer and can be used for longer periods of time than a venous catheter.

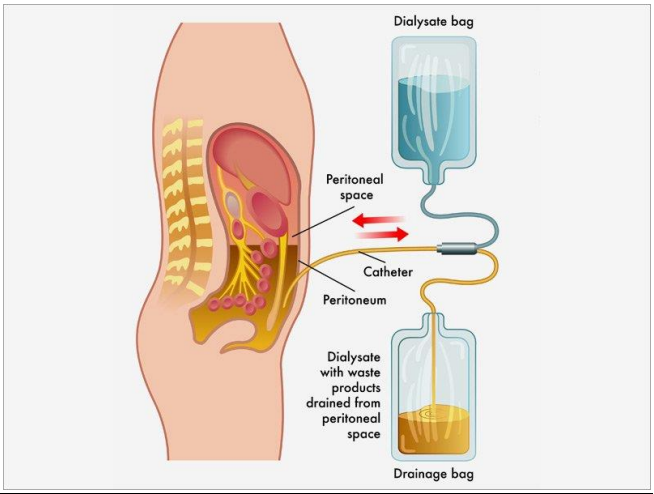
During hemodialysis, a nurse checks vital signs and gets the patient's weight. The patient's weight will indicate how much excess fluid the patient needs to have removed during the treatment. The patient is then connected to the machine.

Blood never actually goes through the dialysis machine. The machine is like a big computer and a pump. It keeps track of blood flow, blood pressure, the amount of fluid removed, and other vital information. It also mixes the dialysate, or dialysis solution, which is the fluid bath that goes into the dialyzer. This fluid helps pull toxins from the blood. The dialysis machine has a blood pump that keeps the blood flowing by creating a pumping action on the blood tubes that carry the blood from the body to the dialyzer and back to the body.

The dialyzer, or filter, is the key to hemodialysis. The dialyzer is a hollow plastic tube about a foot long and three inches in diameter that contains many tiny filters. There are two sections in the dialyzer: the section for dialysate, and the section for the blood. The two sections are divided by a semipermeable membrane to prevent mixing. The membrane allows the dialysate and waste to pass through but does not allow blood cells to pass through. The dialysis solution is then flushed down the drain along with the waste. The electrolytes in the dialysis solution help balance the electrolytes in the patient's blood. Once it is filtered, it is then returned to the patient's body.

Hemodialysis treatments usually last three to five hours and are performed three times per week. However, hemodialysis treatment can also be completed in shorter, more frequent sessions. Most hemodialysis treatments are performed at a hospital, doctor's office, or dialysis centre. The length of treatment depends on your body size, the amount of waste in your body, and the current state of your health.

PERITONEAL DIALYSIS



In peritoneal dialysis, wastes and water are removed from the blood inside the body using the peritoneum as a natural semipermeable membrane. Peritoneal dialysis involves surgery to implant a peritoneal dialysis (PD) catheter into your abdomen. In peritoneal dialysis, a soft tube called a catheter is used to fill the abdominal cavity with a cleansing liquid called dialysate solution. The walls of the abdominal cavity are lined with a membrane called the peritoneum, which allows waste products and extra fluid to pass from your blood into the dialysate solution. The solution contains a sugar called dextrose that will pull extra fluid into the abdominal cavity. These wastes and fluid then leave the body when the dialysate solution is drained, and that used solution is then discarded. The process of draining and filling is called an "exchange" and may be done a few or several times each day, depending on the individual patient's needs. Peritoneal dialysis can be performed in the home, usually while the child sleeps, without a health professional present. Training is available under this circumstance.

The elimination of unwanted water, or ultrafiltration, occurs through osmosis. The dialysis solution has a high concentration of glucose, and this causes osmotic pressure. The pressure causes the fluid to move from the blood into the dialysate. As a result, more fluid is drained than is introduced.

Peritoneal dialysis is less efficient than hemodialysis. It takes longer periods, and it removes around the same amount of total waste product, salt, and water as hemodialysis. However, peritoneal dialysis gives patients more freedom and independence, because it can be done at home instead of going to the clinic several times each week. It can also be done while traveling with a minimum of specialized equipment.

There are numerous types of peritoneal dialysis, but the main types are:

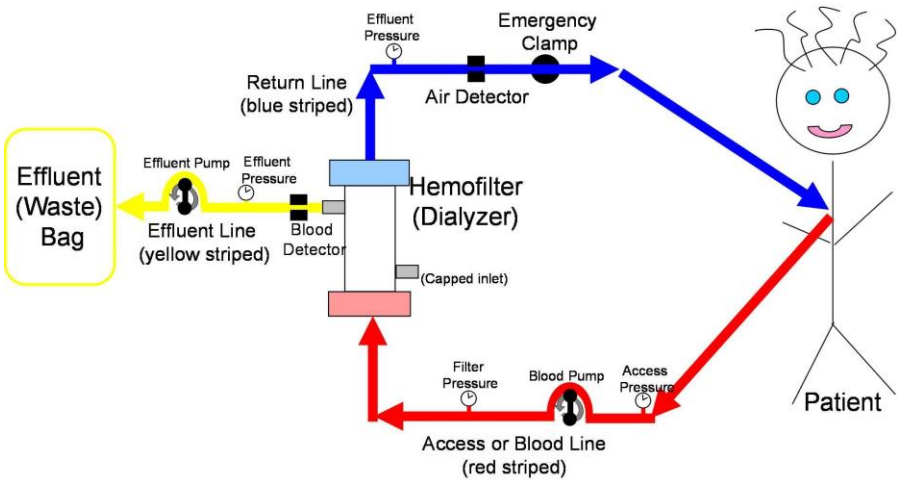
- Continuous ambulatory peritoneal dialysis (CAPD)
- Continuous cyclic peritoneal dialysis (CCPD)

The basic treatment is commonly shared between the two types. The differences are in the number of treatments required and the way they are carried out.

- Continuous ambulatory peritoneal dialysis (CAPD) is the only type of dialysis done without the use of a machine. In this type of treatment, the patient or caregiver fills and drains the dialysate solution multiple times in the day through the catheter. This is called an exchange and is done 3-5 times a day, with each exchange taking 45 minutes. During this time the patient can go about doing their daily activities care-free.

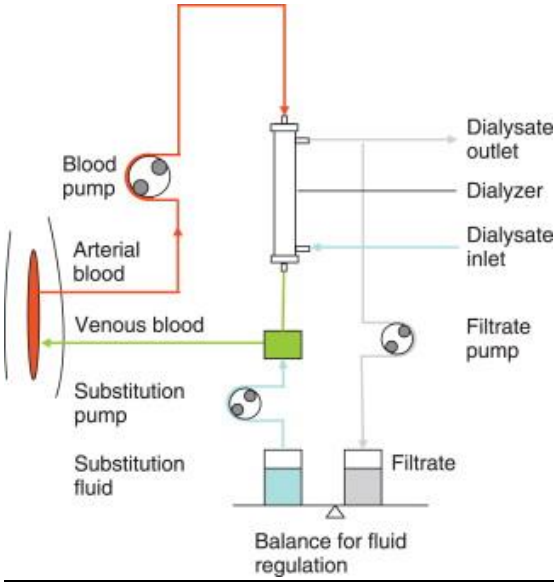
- Continuous cyclic peritoneal dialysis (CCPD) makes use of a machine to cycle the fluids in and out of the patient's abdomen. The treatment is generally carried out every night while the patient sleeps with 10-12-hour duration. It is ideal for infants, children and the elderly due to its convenience and comfort.

HEMOFILTRATION



This therapy is used primarily in the intensive care unit for people with acute kidney failure. It's also known as Continuous Renal Replacement Therapy. Hemofiltration is a similar treatment to hemodialysis, but it makes use of a different principle. The blood is pumped through a dialyzer or "hemofilter" as in dialysis, but no dialysate is used. A machine passes the blood through tubing. A filter then removes waste products and water. The blood is returned to the body, along with replacement fluid. Hemofiltration works by removing large volumes of plasma water across the dialyzer membrane using a pressure gradient, or transmembrane pressure. The lost plasma volume is replenished with concurrent intravenous administration of a physiologic replacement fluid. The removal of plasma water under pressure essentially "drags" solute with it, leading to solute removal and is referred to as convection. By this mechanism, middle molecule clearance is superior to dialysis; hence, many clinicians have proposed that hemofiltration is the preferred method of RRT in septic AKI. The major disadvantage of hemofiltration is cost. Replacement fluid, because it is administered intravenously, needs to be ultrapure and is therefore more expensive compared with dialysis fluid. This procedure is performed 12 to 24 hours a day, generally every day.

HEMODIAFILTRATION



Hemodiafiltration is a combination of hemodialysis and hemofiltration, thus used to purify the blood from toxins when the kidney is not working normally and also used to treat acute kidney injury (AKI). Hemodiafiltration combines diffusive and convective solute removal in a single therapy by ultra-filtering 20% or more of the blood volume processed using a high flux hemodialyzer and maintaining fluid balance by infusing sterile nonpyrogenic replacement fluid directly into the patient's blood. Compared with standard hemodialysis, HDF removes more middle-molecular-weight solutes. Some, though not all, studies have suggested that HDF is associated with improved clinical outcomes, providing adequate convection volumes are achieved. However, HDF is more complex than standard hemodialysis and places increased demands on the user and outpatient dialysis center

INTESTINAL DIALYSIS

In intestinal dialysis, the diet is supplemented with soluble fibers such as acacia gum, which is digested by colonic flora, thereby increasing the amount of nitrogen that is eliminated as fecal waste. Apparently when acacia fibers are added to a low protein diet in children with advanced CKD who do not have access to dialysis, their serum BUN levels were slightly lower, and they experienced a decrease in uremic symptoms. Admittedly, this would appear to be a much less viable option than PD or HD, but in situations of limited resources it may be valuable.