PRE COURSE

You finally arrive back at base after a long stretch of calls and standbys, to have the tones sound “Code 4 for an unresponsive male patient”. You proceed to the call where upon entering the scene, you find a middle aged male patient named Gerry, in bed, looking pale, diaphoretic, not acting appropriately. He is attached to a device on the bedside table with large IV bags hanging. You ask his family what seems to be the problem, and they state that all day the patient had been complaining of lethargy, weakness and decreased sensation in his extremities. He started his dialysis treatment, but then began to act very weird and not making sense.

The patient’s family tells you that he is on peritoneal dialysis for end stage renal disease and it has been a few days since his last treatment as he became stuck out of town with none of his equipment.

Chronic Renal Failure (CRF) was the 10th leading cause of death in Canada between 2007 and 2009. Over 3 million adults have some form of kidney disease. In Ontario alone, 10000 people are on dialysis and there are over 1000 people waiting on the kidney transplant list. In 2010, 537 transplants were done. Hospitals, on average, spend approximately $500 million dollars a year on dialysis. The mortality rate alone of a patient on dialysis is 20% more than the average and 30% more if the patient is within their first year of dialysis.

As with all medical treatments, more and more we are finding patients with Chronic Renal Failure and on dialysis, both in the home and in-hospital, within our communities. As with the growing population of patients that are within in our communities, paramedic’s knowledge base in anatomy, physiology and the pathophysiology behind renal failure needs to grow in order to understand what is happening in these patients and how we can best treat them with the tools that are available to us.

The Anatomy and Physiology Refresher: The Kidneys

The kidneys are located within the retroperitoneal space at the level of T12-L3 and the adrenal glands rest on superior aspect of the kidneys. The kidneys are responsible for the homeostatic regulation of the volumes and composition of the body fluids. This includes:

- Filtering blood plasma, separating wastes from useful chemicals and eliminating waste
- Regulate blood volume and pressures through conservation/waste of water
- Regulates osmolality of body fluids by controlling relative amounts of water and solutes
- Secretes renin which activates hormonal mechanisms that control blood pressure and electrolyte balance
- Secretes hormone erythropoietin that controls red blood cell count and oxygen carrying capacity
- Functions with the lungs to regulate PCO₂ and Acid-Base Balance

Within the kidneys, there are approximately 1 million nephrons, and there are three main areas of the nephron that are responsible for the actions of the kidneys, the renal arteries, corpuscles and tubules.
The renal arteries within the nephrons divide into afferent and efferent arterioles that will form a round capillary bed called the glomerulus, where urine production begins with capillary filtration. The renal corpuscle is a capsule that encloses the glomerulus and collects glomerular filtrate from the glomerular capillaries. The renal tubule is the duct that leads away from the glomerular capsule and is divided into four main regions:

- The Proximal Convoluted Tubule: majority of absorption happens here
- The Nephron Loop “Loop of Henle”: active transport of salts
- Distal Convoluted Tubule: where ‘renal auto regulation” happens. Contains juxtaglomerular apparatus that enables the nephrons to monitor and stabilize its own performance and compensate for fluctuations in blood pressure.
- The Collecting Duct: several Distal Convoluted Tubules drain into one of these and is responsible for the majority of water reabsorption

### How urine is made within the body

There are four processes that occur in order to make urine.

**Glomerular Filtration**

The process in which water and some solutes (glucose, amino acids, nitrogenous wastes and some electrolytes) in the blood plasma pass from the capillaries of the glomerulus into capsular space of the nephron. It creates a plasma-like filtrate of the blood. The driving force behind this is the high pressure gradient from the glomerulus to the Bowman Space. This pressure depends primarily on renal blood flow and is controlled by the combined resistances of renal afferent and efferent arterioles. This makes the kidneys very susceptible to hypertension, and systemic hypertension promotes atherosclerosis of renal blood vessels, which decrease renal blood supply and causes renal failure.

The ability of filtration to happen is measured by the Glomerular Filtration Rate (GFR). The GFR is the amount of filtrate that is formed per minute by the two kidneys combined. The average GFR for an adult should be between 90-120mL/min. It requires precise control to maintain and is done through three methods:

a. Renal auto regulation: the ability of the kidneys to maintain a relatively stable GFR in spite of changes in arterial blood pressure. It utilizes the dilation and constriction of the afferent and efferent arterioles based on the patient’s blood pressure. The GFR cannot be maintained in extreme blood pressure ranges (MAP outside of 80-170mmHg).

b. Sympathetic Control: SNS stimulation affects the afferent arterioles, causing them to constrict (decreases GFR and urine output) which allows for blood to be re-directed to other vital organs.

c. Renin-Angiotensin-Aldosterone System: stimulates widespread vasoconstriction, raising the men arterial pressure (MAP) and has a profound effect on the efferent arterioles to help maintain renal blood flow and glomerular blood pressure. It increases tubular reabsorption of water and stimulates the adrenal cortex to produce aldosterone which causes sodium and water retention.
Tubular Reabsorption
This occurs in the Proximal Convoluted Tubule where it reabsorbs approximately 65% of glomerular filtrate including useful solutes such as sodium, glucose, water and protein. There is a maximum amount of solutes that can be brought back into the blood due to the limited number of transport proteins. This is why we see glucose present in the urine in the setting of hyperglycemia.

Tubular Secretion
This occurs in the Proximal Convoluted Tubule and the Loop of Henle where the renal tubule extracts wastes such as urea, ammonia, hydrogen ions, bicarbonate to maintain the acid base balance and secretes it into the tubular fluid. Within the Loop of Henle, the collecting duct concentrates the urine and conserves water. However, reabsorption of further salts, such as sodium, potassium and chloride allows the fluid to become diluted as it enters the distal convoluted tubule.
Once in the Distal Convoluted Tubule (DCT) and Collecting Duct (CD), there is a great deal of fluid reabsorption which is subjected to hormonal control including:

a. Aldosterone senses the sodium and serum potassium concentration. The DCT and CD will reabsorb sodium, pulling chloride and water with it and wasting potassium.
b. Atrial Natriuretic Factor inhibits sodium and water reabsorption.
c. Antidiuretic Hormone makes the collecting duct more permeable to water to concentrate the urine

Water Conservation
The Collecting duct reabsorbs water and concentrates the urine as the medullary portion of the collecting duct is only permeable to water.
The urine is then collected from the tubules into a funnel-like renal pelvis and then flows through a ureter and into the bladder.
**Renin-Angiotensin-Aldosterone System (RAAS)**

Renin is released via the juxtaglomerular cells in the kidneys when renal blood flow is reduced, either from a loss in blood volume or a drop in blood pressure. Renin stimulates the conversion of Angiotensinogen to Angiotensin I. Angiotensin I circulates and through the actions of the Angiotensin Converting Enzyme mainly in the lung capillaries, causes Angiotensin I to become Angiotensin II. Angiotensin II has two actions to increase blood pressure, it directly acts on blood vessels to cause vasoconstriction and it also stimulates the secretion of the hormone aldosterone from the adrenal cortex. Aldosterone causes the tubules of the kidneys to increase the reabsorption of sodium, chloride and the retention of water while potassium is being excreted. This increases the volume of fluid in the body, which also increases blood pressure.

**Renal Failure**

When the kidneys stop their ability to filter the blood and create urine, it begins the process of renal failure. There are two different kinds of renal failure, one being acute renal failure and the other being chronic renal failure. Acute renal failure is defined as an abrupt or rapid decline in renal filtration function; whereas chronic renal failure is defined as the loss of kidney function over time.

**Acute Renal Failure (ARF)**

There are three categories of acute renal failure or acute kidney injury, based on the location of the injury.

**Prerenal**

The patient has an adaptive response to severe volume depletion and hypotension with structurally intact and undamaged nephrons. A reduction in renal blood flow (RBF) causes a decrease in the GFR. This leads to ischemia and cell death (which may occur before frank hypotension). This triggers a cascade of events where chemical mediators are released, coagulopathy begins, and tubular cellular damage allows back leak of glomerular filtrate with further decrease in the GFR. Recovery is dependent upon restoration of RBF through restoration of circulating blood volume. Early normalization means better prognosis for recovery of renal function. This can be caused by any kind of volume loss, including GI (vomiting and diarrhea), renal (diuretics, polyuria) cutaneous damage (burns), internal and external hemorrhage, decrease in renal perfusion in patient with heart failure (PE, AMI) or shock (OD, anesthetics, sepsis, anaphylaxis) or arteriolar vasoconstriction (hypercalcemia, NSAID usage, Norepinephrine, contrast media)
**Intrinsic**
The patient has a response to a cytotoxin, ischemia, or inflammatory insult to the kidney causing structural and functional damage. This includes diseases of the kidney itself, predominantly affecting the glomerulus or tubules which are generally associated with the release of renal afferent vasoconstrictors. Recovery is dependent again upon restoration of RBF. Through removal of the toxins and initiation of therapy for glomerular disease will cause decrease in renal afferent vasoconstriction, increasing RBF. This can be caused by structural injury – renal artery obstruction (thrombosis, emboli, dissection) renal vein obstruction (thrombosis), microangiopathy (DIC, Pre-eclampsia), Cytotoxic (heme pigment in Rhabdomyolysis, ethylene glycol poisoning, mega dosage of Vitamin C), Interstitial causes(drugs – penicillin, NSAID’s, sulfonamides; infection – pyelonephritis; systemic disease – lupus, lymphoma, leukemia)

**Postrenal**
ARF in the postrenal area is due to anything that causes an obstruction to the passage of urine which causes an increase in tubular pressure, which decreases the filtration driving force. The pressure gradient equalizes and maintenance of a depressed GFR depends on renal efferent vasoconstriction. Recovery is still dependent upon restoration of RBF by the rapid relief of the obstruction and will result in a prompt decrease in vasoconstriction. This can be caused by stone disease, tumors, thrombosis or compressive hematoma, fibrosis, mechanical obstructions of urinary collecting system, enlarged prostate.

In ARF, the goal of treatment is to increase the RBF. This is done by providing the patients with fluid, including possible fluid challenges to maintain the patient at euvolemic or hypervolemic states. It has been shown that dialysis may actually delay recovery in acute renal failure. Once RBF is restored, the remaining functional nephrons will increase their filtration and eventually undergo hypertrophy. GFR recovery is dependent on the size of the remaining nephron pool. The prognosis for those with ARF is directly related to the cause and presence/absence of preexisting kidney disease and duration of renal impairment prior to therapeutic intervention. ARF is not completely reversible.

**Chronic Renal Failure (CRF)**
CRF is defined as kidney damage (acute or chronic induced) and decrease GFR of less than 60mL/min for greater than 3 months. In the face of renal injury, regardless of etiology, the kidney has an innate ability to maintain GFR despite progressive destruction of nephrons. The remaining nephrons manifest an ability for hyper filtration and compensatory hypertrophy which is a major cause of progressive renal dysfunction. Once the loss of nephrons and reduction of functional renal mass reaches a certain point, the remaining nephrons begin a process of irreversible sclerosis that leads to a progressive decline in GFR. Chronic renal failure is most commonly an acquired disease process with specific factors that put people at higher risk. There are some genetic pre-dispositions but they are more commonly seen in children.

There are many factors that contribute to chronic renal failure including:
- Diabetes
- Hypertension
- Hyperlipidemia
Nephrotoxins (NSAID'S, IV contrast media)
- Decreased perfusion
- Episodes of acute renal injury increases the risks
- Vascular diseases (renal artery stenosis)
- Glomerular Disease (membranous nephropathy, IDDM, Rheumatoid Arthritis, Hep B/C, Heroin use)
- Tubulointerstitial Disease (infections, medications – allopurinol, sulfonamides)
- Urinary Tract obstruction or dysfunction (kidney stones, tumors, benign prostate hypertrophy)
- Biological process of aging can change the structures and functions of the glomeruli and the renal vasculature

There are five stages of Chronic Renal Failure:

Stage One: Kidney damage with normal or increased GFR (>90mL/min)
Stage Two: Mild reduction in GFR (60-89mL/min)
Stage Three: Moderate reduction in GFR (30-59mL/min)
Stage Four: Severe reduction in GFR (15-29mL/min)
Stage Five: Kidney failure (GFR < 15mL/min), also called End Stage Renal Disease (ESRD)

Generally patients in Stage 1-3 are asymptomatic. In Stage 1 and 2, a decrease in GFR alone does not clinch the diagnosis because GFR may border normal. Other markers of kidney damage (abnormalities in composition of blood, urine or structural abnormalities) establish the diagnosis. Once Stage 4 and 5 are reached, patients will start having clinical manifestations of the endocrine and metabolic disturbances.

Some common complications within advancing CRF are:

- Anemia: this begins early and becomes more severe as there is a shrinking availability of viable renal mass due to decreased renal synthesis of erythropoietin. This causes a decreased production of red blood cells and which causes fatigue, decrease in exercise tolerance, impaired cognitive and immune function, decrease quality of life, development of CAD and new or worsening heart failure.

- Uremia (ESRD): This is generally seen in End Stage Renal Disease as it begins when the kidneys can no longer filter amino acids or proteins and they remain in the blood. This can cause signs and symptoms such as pericarditis, encephalopathy, peripheral neuropathy, restless leg syndrome, GI disturbances (anorexia, N/V/D), integumentary issues (dry skin, pruritus, ecchymosis), failure to thrive and malnutrition.

- Metabolic Acidosis (ESRD): because the kidneys are unable to produce enough ammonia in proximal tubules to excrete endogenous acid into urine (ammonium) there is an accumulation of phosphates, sulfates and other organic anions causing an increase in the anion gap. This has a deleterious effect on protein balance which leads to negative nitrogen balance, increase amino acid oxidation, increase protein degradation.

- Salt and Water Handling Abnormalities: is where total body volume overload results from a failure of sodium and free water to be excreted by the kidneys. This leads to peripheral edema, pulmonary edema and hypertension and is generally seen in patients with GFR < 10mL/min as they have no compensatory mechanisms. This can still happen in patients that have a higher GFR when they have excess intake of sodium and water.
Hyperkalemia: as the patients GFR drops to less than 20-25mL/min, the kidneys have a decreased ability to secrete potassium. This can be observed sooner in those patients with potassium rich diets or have low serum aldosterone. It can be aggravated by an extracellular shift in potassium due to acidemia or lack of insulin.

Treatment Options for CRF
Depending on what stage a patient is in, will depend on the type of treatment the patient requires. There are three general rules to treating CRF:

1. Delay the progression of diagnosed renal failure and treat the underlying conditions as indicated
The rate of progression of CKD depends on many factors, including age, underlying diagnosis, success of implementation of secondary preventative measures and the individual patient. Patient education is also a large factor to delay the progression of diagnosed renal failure and includes the following:
   - Importance of avoiding factors that lead to increase progression
   - Aggressive management of: Blood pressure (Target value of 130/80), hyperlipidemia and glycemic control
   - Natural disease progression including the discussion surrounding different dialytic modalities, options to refuse or discontinue dialysis, renal transplant and the timely placement of vascular access for hemodialysis or peritoneal catheter insertion for peritoneal dialysis
   - Prescribed medications: the potential benefits and the adverse effects, including RAAS (ACEI, ARB’s) blockers among patients with proteinuria
   - Avoidance of nephrotoxins (NSAID’s, aminoglycosides, Contrast dye)
   - Diet (Sodium, Protein and Phosphate restrictions)

2. Treat the pathological manifestations that emerge
Anemia: erythropoiesis stimulating agents
Hyperphosphatemia: dietary phosphate binders and dietary restrictions
Hypocalcemia: Calcium supplements with or without calcitriol
Hyperparathyroidism: calcitriol or vitamin D analogues
Volume Overload: loop diuretics or ultrafiltration
Metabolic Acidosis: oral alkali supplements (Bicarbonate supplements showed slower decline in renal function and a decrease in the rapid disease progression which means decrease in ESRD)

3. Timely planning for long term renal replacement therapy
Following the education regarding the natural disease progression and treatment options, the patient then starts the process of preparing for and undergoing dialysis and or renal transplant.
In February 2014, the Canadian Society of Nephrology changed their clinical practice guidelines for timing of the initiation of chronic dialysis. They stated that there should be a delay in dialysis in patients with CRF without symptoms until the GFR is less than 6mL/min or until the first clinical indication (symptoms of uremia, fluid overload, refractory hyperkalemia or acidemia). They determined that early initiation of dialysis does not increase survival, quality of life or decreased hospital admission. They stated that they highly valued quality of life and as such, saw no use in starting a burdensome treatment that is also resource intensive which does not provide any measurable benefit.
Dialysis

Once the kidneys have failed and are no longer able to function properly, a patient is put on dialysis which is a treatment to remove toxins from the blood. There are two different types of dialysis, Hemodialysis and Peritoneal Dialysis, each with their own strengths and limitations.

Hemodialysis

Blood is withdrawn from the body by a machine and passed through an artificial kidney called a dialyzer. The dialyzer has two spaces, one for blood and one for dialysis fluid (a special liquid that helps remove waste products from the blood). They are separated from each other by a very thin artificial membrane, blood passes on one side of the membrane and dialysis fluid on the other, diffusion through the semi-permeable membrane allows for the removal of wastes. It takes approximately 4-5 hours per treatment and on average; patients require three treatments per week.

Hemodialysis has strengths to the treatment which include:

- Relieves symptoms of uremia
- Works quickly and efficiently
- Requires at least three treatments a week, each four to eight hours
- Most people have suitable blood vessels for establishing an access site

Hemodialysis also has its limitations:

- The patient will have to take medications, learn new food choices, and restrict their intake of fluids
- Access to the bloodstream is with needles, which some people find difficult
- Patients must plan their week around their hemodialysis schedule (although with home hemodialysis, they can plan their treatment schedule around their week)
- Patients may need to travel some distance to the hemodialysis unit
- Some people do not have suitable blood vessels for establishing an access site

There are three different types of access for hemodialysis that are commonly seen in patients.

Arteriovenous (AV) fistula: is where an autologous AV access is created by a connection of a vein to an artery, generally the cephalic vein to the radial artery, where the vein serves as the accessible conduit. It is considered the optimal for long term vascular access for hemodialysis because it provides adequate blood flow, last a long time and has lower complication rates.

Arteriovenous Grafts: is where an artificial prosthetic segment is used to connect the artery and vein together for hemodialysis.
Central Venous Access: is one of the most common vascular accesses where a catheter is inserted in a central vein (Subclavian is common) and the tip of the catheter ends just inside of the right atrium.

On average it takes approximately 3 months or more to have an AV fistula or AV graft established and ready to go for hemodialysis, whereas a CVAD can be done in a more emergent setting if required.

Peritoneal Dialysis
Peritoneal Dialysis (PD) uses the peritoneal membrane inside the abdominal cavity to remove waste and extra fluid from your blood. The peritoneal membrane forms a sac within the abdomen that is called the peritoneal cavity. A flexible catheter is inserted into your peritoneal cavity and through the catheter the peritoneal cavity is filled with a special solution called dialysate. Waste products and extra water from the surrounding blood vessels are drawn through the walls of the peritoneal membrane, which act like a filter, into the peritoneal cavity. Depending on the type of peritoneal dialysis that is being used, will depend on when and how often the fluid is drained and replaced with fresh dialysate. This process is called an exchange.

Continuous Ambulatory Peritoneal Dialysis (CAPD)
Dialysate is hung and through gravity, the peritoneal cavity is filled with fresh fluid. The patient then can go about their daily activities. The patient then does the exchange approximately 4-5 times per day where, prior to replacing the fluid, the peritoneal cavity is allowed to drain, bringing with it all the dialyzed material. This takes approximately 30-40 minutes to complete. This is the most common form of peritoneal dialysis done as it relies on gravity and there are no machines that the patient is required to use.

Continuous Cyclic Peritoneal Dialysis (CCPD)
The patient is attached to a dialysis machine called a Cycler. The peritoneal membrane is still used as the filter to which waste products and extra water are drawn in, however the machine does the exchange multiple times per night as the patient is sleeping. The machine then leaves 2L of fluid in the peritoneal cavity for the day to assist with dialysis. This type of dialysis allows for the patient to have the freedom of all daily activities without the need to stop during the day and do the exchange.

Strengths for peritoneal dialysis include:
- Relieves symptoms of uremia
- Is less stressful on the patient’s body because dialysis is done continuously (i.e. daily) versus intermittently (i.e. three times per week)
- Allows for a more liberal diet
- Frees the from hospital as it is generally done in home
- Makes it easier to travel, especially CAPD, as there are no machines required for the dialysis.
- Gives greater flexibility with the patient’s treatment

There are some limitations as well, and they include:
- Permanent catheter in your abdomen
- Possibility of peritonitis (infection of your peritoneal cavity)
- Dialysis must be a daily part of the patient’s life
- Patients will have to take medications and learn new food choices
- You will need to prevent the catheter from getting wet (no swimming)
- It is not as effective in patients that are obese, have little or no residual kidney function or have had previous abdominal surgeries resulting in adhesions

**Dialysis: Where can you go?**

Patients have various options of where their dialysis can take place, depending on their situation. They can opt for either home dialysis or in-hospital/clinic dialysis.

Options for home dialysis include:
- **Home Hemodialysis**: the patient and a dialysis helper (family, friend, etc.) go through a 6 week training program with the Home Dialysis RN. Utilizing the AV fistula/graft or CVAD, the patient is then free to determine when they are able to do their dialysis during the day while maintaining a regular schedule.
- **Nocturnal Hemodialysis**: is a much slower and gentler type of hemodialysis as it done 6 nights a week for 8-10 hours and can do it alone. This is ideal for patients that do not have the helper for regular Home Hemodialysis.
- **Peritoneal Dialysis** – both CAPD and CCPD are done at home, depending on what type of dialysis best works for the patient.
Patients also have the option of Self-care dialysis where the patient is in a hospital or out-patient clinic and are responsible for their own attaching and detaching from the dialysis machine. There is an RN available at all times, however, they are able to schedule their dialysis around their schedule within the clinic and it is not set times where they have to do the dialysis. The last option for patients undergoing dialysis is the Satellite or In Center (Outpatient clinic or hospital clinic) dialysis. This is for patients that have an increase need for support with activities of daily living. There is a set schedule to which the patient has to schedule their life around. There is often a lot of waiting prior to the treatment and can be described as a less relaxed environment.

Home dialysis is not suitable for every patient, they must be:
- Emotionally and cognitively competent
- Have a stable medical condition
- Have a dependable dialysis care partner/provider available to help
- Have sufficient water, electricity and space available in the home to accommodate the equipment.

The Ontario Renal Network shows that the quality of life is better and patients feel their symptoms are better controlled with home-based dialysis as treatments can be extended and more intensive. There has been an increase in the choice to have home based dialysis because it offers:
- Greater convenience due to the flexible treatment schedule with less need to travel
- More time with family as it improves a patients energy levels and life expectancy
- Patient is able to maintain their independence and manage their own condition
- Due to the more intensive therapy there is a better clearance of toxins, better prognosis in terms of survival, decrease frequency of illness and rehabilitation and better ability to work.
- More cost effective

**Common Complications with Dialysis**

As with any procedure, there are always possible complications that can happen with both peritoneal dialysis and hemodialysis. These can include:
- CAPD associated peritonitis – generally happens once a year in patients with this type of dialysis
- AV Fistula – can have infection at the site, or have clot formation
- AV Graft – increase chance of clot formation and infection and often have to be replaced sooner
- CVAD – will clog easily and become infected much easier

There are also complications that can occur actually during the dialysis procedure, although generally seen in hemodialysis, which can include:
- Hypotension – which is most common and is often due to removing to much fluid or “weight”, the patient taking their anti-hypertensive medications at the wrong time or septicemia
- Muscle Cramps – this can happen any time during dialysis but especially in the middle to end portion. This is due to large amounts of fluid being taken off or sudden changes in electrolytes (rapid sodium removal or decreasing potassium levels)
• Disequilibrium syndrome – systemic and neurological symptoms such as nausea/vomiting, headache, restlessness, hypertension, slurred speech, seizure or coma. This is can be due to fluid shifting into the brain due to electrolytes being taken off and causing cerebral edema, or rapid changes in the patient’s serum electrolyte levels.

Technical issues can occur during dialysis which can include clotting, blood leaks, power failures, hemolysis, air embolism, exsanguination and dialyzer reactions.

Complications can also arise in patients that miss their dialysis, and those can include:
• Anemia and bone disease
• Cerebrovascular complications i.e. stroke
• Cramping and hypotension during next dialysis appointment due to having to remove extra fluid and wastes
• Fluid overload leading to shortness of breath
• Shortened life expectancy
• Severe cardiac complications including arrhythmias and cardiac arrest especially due to hyperkalemia

Let’s go back to Gerry for a minute here......you have assessed Gerry and asked the family about Gerry’s past medical history. The family states that he has ESRD, NIDDM, HTN, hyperlipidemia, MI (2009, 2012) Angioplasty x 3 (2012) and he takes Januvia, Metformin, Ramipril, HCTZ, Metoprolol, Crestor, Multivitamin, Ferrous Gluconate, Omeprazole, Senokot.

Your assessment indicates Gerry is decreased LOA, pale, diaphoretic, he is tachypnic but lungs are clear, nothing else noted on physical exam, catheter in patient’s arm appears well taken care of. Your partner gives you the vitals (HR-60, RR-30, BP 76/40, Temp 36.8, GCS 9, BS 24.6mmol/L) and hands you the ECG: You automatically ask the family “How can we get Gerry off the dialysis machine, we need to get him to the hospital now?”

Dialysis Disconnect
In an emergency setting, there are tools that patients and their families can use to disconnect the patient from the home dialysis machine during a treatment. The patient and the patient’s family are taught and often undergo a 4-6 week training program in order to bring the machine home and learn how to take care of themselves or their loved ones. There are emergency disconnect kits that are with the machine and instructions on proper disconnect procedures to follow to help mitigate the risk of infection and other complications from an emergency disconnect.
Emergency disconnect during a treatment is generally only done when there is a life threatening event happening with the patient. Paramedics are allowed, with a Base Hospital Physician (BHP) patch to disconnect the patient in order to treat their condition. Generally, paramedics should allow family members to do the disconnect, as they have undergone the training, however it can happen where there is no one to help with the disconnect and paramedics are left wondering how to do the procedure. Through a consult with the BHP, the paramedic can disconnect the patient from the dialysis machine and continue their treatment and transport the patient to the hospital for further care.

**Hyperkalemia**

In patients with ESRD, one of the most common causes of life threatening emergencies including sudden cardiac arrest is hyperkalemia. It is also a very treatable problem if caught early enough. Potassium is the primary intracellular electrolyte where 98% remains in the intracellular space and 2% remains in the extracellular space. It plays a crucial function in normal cardiovascular and neuromuscular functions. It maintains the fluid and electrolyte balance, blood pressure, blunts the effects of excess sodium, and reduces bone loss and risk of kidney stones. 90% of potassium is secreted in the urine and 10% is excreted in the feces. Normal serum levels are 3.5-5.0mmol/L with hyperkalemia being defined as a serum level above 5.5mmol/L.

The primary source of potassium is diet. It is absorbed within the small intestine as long as the potassium concentration is higher in the gastrointestinal tract than in the blood. Potassium is generally filtered by the glomerulus with most being reabsorbed in the proximal tubule and Loop of Henle. Even minor variations in the serum potassium level can have a significant impact on cardiovascular and neuromuscular function. This is due to the ratio of intracellular to extracellular potassium being an important determinant of cellular membrane potential, remember that potassium moves because of Na/K/ATPase pump.

Kidneys regulate potassium through potassium and hydrogen ions competing for exchange with sodium ions in the renal tubules. Secondly, aldosterone causes the kidneys to retain sodium which in turn causes retention of water. To retain sodium, the kidneys have to excrete potassium. The patient must have adequate renal function to maintain normal potassium levels.

**Causes of Hyperkalemia**

Hyperkalemia is generally seen in two settings: actual hyperkalemia; where there is an actual increase in potassium levels within the body and relative hyperkalemia; where the serum level of potassium increases due to shifts within the body as it attempts to maintain homeostasis in other settings.

**Relative hyperkalemia**

The body has an ability to maintain homeostasis very well. In specific settings, the body does what it can to maintain this, however, it is often at the expense of other electrolytes or body functions. This can be seen in cases where patients develop metabolic acidosis. As the body decreases its pH level, it becomes more acidic. This means that there are more hydrogen ions circulating systemically. The body attempts to maintain homeostasis by having the cells of the body shift hydrogen ions intracellularly, but because the cells want to maintain their own homeostasis and electrical gradient to the outside, it shifts potassium out of the cell. This works on a one to one basis as hydrogen ions and
potassium ions both have a single positive charge. Therefore, the cell is maintaining its electrical gradient, but is shifting the ions across the cell membrane to allow the body to become less acidic. There are a couple of very common examples of times where patients can end up with metabolic acidosis, Diabetic Ketoacidosis and Tricyclic Antidepressant Overdose (TCA OD). Diabetic Ketoacidosis (DKA) is generally seen in the setting of new onset diabetes, inadequate insulin compliance and in patients with IDDM, times of increased stress (illness, trauma, or surgery). DKA results from a shortage of insulin; in response the body switches to burning fatty acids and producing acidic ketone bodies. This results in a profound electrolyte imbalances, acidosis and dehydration. The metabolic acidosis causes an increase in transport of potassium out of the intracellular space as the body attempts to maintain homeostasis by moving hydrogen ions into the cell. This causes the relative hyperkalemia in that the serum level of potassium is high; however the total body potassium level is the same. This can still cause the cardiac abnormalities as seen in other forms of hyperkalemia.

Tricyclic Antidepressants are utilized in the treatment of major depressive disorders, anxiety disorders or treatment-resistant depression. Some common names are amitriptyline (Elavil) or doxepin. In an overdose setting, they act as sodium channel blockers and cause an anticholinergic surge. They can cause cardiotoxicity, QRS widening and profound hypotension, eventually leading to a metabolic acidosis. It is the same homeostatic capabilities of the body that allow the hydrogen ions to move into the cell and potassium moves out, therefore causing a relative hyperkalemia.

**Actual Hyperkalemia**

**Crush Injury**

A crush injury results from prolonged continuous pressure on large muscle groups. As the pressure builds within the extremity, the skin will only stretch so far. Eventually, the pressure will be transferred from the skin to the vessels and internal structures of the extremity. The skeletal muscle cell contains myoglobin which is responsible for supplying the skeletal and cardiac muscles with oxygen. There are also enzymes that are not generally harmful to the cell unless there is a high calcium level. During a prolonged crush injury, as calcium levels rise, the enzymes become destructive to the cell structure and cause the cell to leak or rupture. Damage to the cell membrane causes further calcium and sodium to rush into the cell which causes myoglobin, potassium, uric acid and phosphorous to leak out of the cell. They are eventually brought into systemic circulation which leads further complications and a process called rhabdomyolysis.

In a crush injury, venous blood flow is stopped but arterial flow may not be and thus significant pressure begins to build within the injured tissue. Inadequate blood flow through the extremity will lead to tissue ischemia which is followed by the development of metabolic acidosis within the injured extremity. Once blood flow is restored, the toxic substrates that have built up are released into systemic circulation. The patient may become metabolically acidotic, which can cause a widespread vasodilation and relative hypotension. Potassium that has leaked out of the cell can cause a patient to become hyperkalemic which, along with the metabolic acidosis, can cause severe arrhythmias leading to cardiac arrest. Myoglobin also rushes into the systemic circulation and combined with the metabolic acidosis, will promote renal failure in patients that survive.

**End Stage Renal Disease and Hyperkalemia**

Patients who have chronic renal failure do not have the ability to excrete potassium efficiently. This will often put them at risk of hyperkalemia. Patients with chronic renal failure, especially those with end
stage renal disease (ESRD) need to follow a strict regimen involving dietary restrictions, appropriate medications and appropriate dialysis treatments to ensure that their serum levels of potassium remain within acceptable ranges. Potential risk factors for times where hyperkalemia can become an issue can include missed dialysis appointments or dietary slips. The main concern for patient with ESRD is medications, specifically antihypertensive medications, certain diuretics, types of analgesia and certain antimicrobial drugs.

Antihypertensive Medications:
- Angiotensin Converting Enzyme inhibitors (ACEI) like Enalapril or ramipril
- Angiotensin Receptor Blockers (ARB’s) including Irbesartan and Losartan

These cause an effect by reducing the production of aldosterone as seen in the next figure. The reduction in aldosterone means less reabsorption of water, less conservation of sodium and less excretion of potassium.

Diuretics, especially the potassium-sparing ones like spironolactone and amiloride, impair the ability of the collecting tubule to secrete potassium, blocks the interaction of aldosterone with the aldosterone receptors and blocks sodium channels in the collecting ducts, all contributing to an increase in serum potassium.

Analgesia medications that can cause hyperkalemia include most NSAID’s. They have two effects that can promote hyperkalemia, they will lower renal renin secretion, which is normally mediated in part by prostaglandins and they impair angiotensin II induced aldosterone release.

Antifungals, such as ketoconazole and fluconazole, inhibit the biosynthesis of adrenal steroids from the adrenal gland, including aldosterone.

Clinical Manifestations of Hyperkalemia

Hyperkalemia, whether mild or severe, can present with life-threatening complications but can also be unrecognized prior to cardiac arrest.
Non-cardiac signs can include altered mental status, confusion, muscle cramps and weakness, muscle hypotonia dyspnea, paresthesia, flaccid paraplegia, paralysis and tetany.
Cardiac signs can include bradycardia, hypotension and specific ECG patterns.

Mild Hyperkalemia
- Serum levels of 5.5-6.5mEq/L
- Tall, tented T waves with narrow base

Moderate Hyperkalemia
- Serum levels of 6.5-8.0mEq/L
- Prolonged PR Interval
- Widening QRS
- Progressive loss of P wave

Severe Hyperkalemia
- >8.0 mEq/L
- No P waves
- Progressive widening of the QRS to Sine wave pattern
- Sine Wave → VF → Asystole

The paramedic should realize that although the patients’ ECG may reflect these changes, not all patients will go through each ECG change as their potassium levels rise. Patients with chronic renal failure, especially in ESRD, can have a baseline serum potassium level that is hyperkalemic. The paramedic may not see any clinical manifestations with serum potassium levels that could be considered severe. The ESRD patient may have an ECG that is just about normal and go into ventricular fibrillation or asystole without ever seeing the widening QRS

Treatment of Hyperkalemia
Hyperkalemia is one of the deadliest electrolyte abnormalities; however, is also one of the more treatable. Treatment should always begin with looking at the patient’s overall clinical picture as the manifestations of hyperkalemia can happen at varying levels and will depend on each patient. It is recommended to definitively start treatment when there are obvious ECG changes present. Treatment
for hyperkalemia should be done in three steps. Step one is to antagonize the effects of potassium on the cardiac cell membranes. Step two is to decrease the serum potassium levels by promoting cellular re-uptake of potassium and step three is to remove potassium from the body.

### Antagonizing the cardiac effects of potassium: Calcium Gluconate

In the setting of hyperkalemia, the resting membrane potential is shifted to a less negative value and in turn moves the resting membrane potential closer to the normal threshold potential. When calcium is given, it shifts the threshold potential to a less negative value which allows for the difference between the resting membrane potential and the threshold potential to go back to the normal 15mV difference. Calcium will also help in cells that have calcium dependent action potentials, such as the SA and AV nodes. It will increase the extracellular concentration of calcium and thus increasing the magnitude of the calcium inward current and allow for increased impulse propagation, thus increasing the heart rate. The effects of calcium occur within 1-3 minutes and last for approximately 30-60 minutes. The preferred dose is 10mL of a 10% solution or 1G of Calcium Gluconate. The usage of calcium gluconate should be limited in patients on Digoxin as the administration of calcium gluconate could potentiate hypercalcemia. Digoxin is a cardiac glycoside, which inhibits the Na-K ATPase pump and therefore increasing the intracellular concentration of sodium. This increase in intracellular sodium inhibits sodium-dependent calcium transport out of the cell, resulting in an increase in intracellular calcium. This can potentially cause an irreversible, non-contractile state.

### Redistribution of potassium into cells

**Beta<sub>2</sub> Antagonist (i.e. Salbutamol)**

Salbutamol temporarily shifts extracellular potassium into the intracellular area by causing a stimulation of the beta<sub>2</sub> receptors, which in turn release catecholamines. This causes an action similar to insulin where it increases the plasma insulin levels which then stimulate the movement of glucose into skeletal muscle and hepatocytes, which in turn stimulates the movement of potassium into the cells. Inhaled beta-adrenergic agonists are more effective at lowering serum potassium levels than oral forms. They can lower the serum potassium levels by 0.5-1.5mEq/L when the preferred dose of 10mg nebulized or 1600mcg MDI is provided.

**Insulin/D50W**

Insulin helps to lower the serum potassium level by shifting potassium into skeletal muscles and hepatocytes. Insulin stimulates the Na-K ATPase pump, which moves potassium intracellularly in exchange for sodium, which is independent of insulin’s effect on glucose. 10 units of intravenous insulin are given and the patient’s blood sugar is closely monitored. D50W may be administered at the same time in normoglycemic patients. If a patient is clearly hyperglycemic, the D50W is routinely not administered. The onset time of the insulin is approximately 20 minutes and can be expected to decrease the serum potassium by 0.6-1.0mEq/L.

**Sodium Bicarbonate**

This is a very controversial medication to administer in the setting of hyperkalemia. There is little evidence to show that it is actually effective in lowering the serum potassium level. The theorized mechanism of action is that it increases the pH of the blood which in turn causes cells to excrete hydrogen ions to the extracellular fluid in an attempt to lower the blood pH. As hydrogen is excreted from the cells, the cells need to maintain their electrical gradient, and as such, will uptake potassium in place of the hydrogen. This should effectively lower the serum potassium level. The average dose of
Sodium Bicarbonate is 1mEq/kg to a maximum dosage of 100mEq IV. Due to the controversial setting of Sodium Bicarbonate being used in hyperkalemia alone, it is recommended that the usage of Sodium Bicarbonate should be reserved for patients that have hyperkalemia and also a history of severe academia (including DKA or TCA overdose)

Removal of the excess potassium from the body

*Furosemide*

Furosemide is a loop diuretic which acts on the loop of Henle. This causes the kidneys to excrete potassium. A dosage of 20-40mg is an effective dose.

*Kayexalate*

Kayexalate is also known as sodium polystyrene sulfonate. This is an ion exchange resin that works through exchanging the intestinal cations, most importantly potassium for sodium, which is released from the resin. The potassium is then excreted in the fecal matter. It is taken generally as an oral formula and once it has entered the intestinal tract is where it is most effective. This is not a quick and efficient way to remove excess potassium from the body so generally it is not seen in the emergent treatment of hyperkalemia. It is generally used as a follow up to acute hyperkalemia treatments.

*Dialysis*

Dialysis is the quickest and most efficient way to remove the excess potassium. Hemodialysis is the most effective, as it lowers both serum and total body potassium, reducing extra- and intracellular potassium. Due to the time it takes to properly remove the potassium, the expense and invasive nature, it is not often the first line treatment to remove excess potassium unless the patient is already on dialysis and has life-threatening hyperkalemia.

Coming back to Gerry, after seeing the ECG and being the astute paramedic you are, and after a stimulating CME where you learned all about hyperkalemia in renal failure patients, you realize that Gerry is suffering from hyperkalemia caused by missed dialysis and improper diet. There are two things that can be done to help Gerry, one is to stabilize the cardiac membrane and two is to shift the potassium back into the cells. You do not carry a medication that will stabilize the cardiac membrane, however you do carry a medication that can assist in the movement of potassium back into the cells, salbutamol. You patch to your BHP and obtain an order for Ventolin 10mg nebulized. You begin treatment and then begin transport code 4 CTAS 1 to the nearest facility.
References


