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**QUESTION 1: Discus the pathophysiological process involved in renal failure**?

Several kidney diseases that lead to renal failure are divided into 2 main categories. They are:

1. Acute kidney injury (AKI)
2. Chronic kidney disease (CKD)

• ACUTE KIDNEY INJURY:

This is the condition in which there is an abrupt loss of kidney function within a few days. The term 'acute renal failure' is usually reserved for severe acute kidney injury where the kidney may abruptly stop working entirely or almost entirely, necessitating renal replacement therapy such as dialysis. Some patients with the AKI may eventually recover nearly normal kidney function.

* For the **Symptoms and Signs**, some are: not enough urine, swelling in your legs, ankles or feet, feeling tired, trouble catching your breath, nausea, pain or pressure in your chest. If the condition is severe, one may fall into coma or have seizures.
* The **CAUSES** of Acute Kidney Injury are divided into 3 main categories, they are:

1. Prerenal AKI; which is a condition that results from decreased blood supply. This condition reflects an abnormality originating outside the kidneys. E.g., pre-renal AKI can be a consequence of heart failure with reduced cardiac output and low blood pressure or conditions associated with diminished blood volume and low blood pressure such as severe haemorrhage.
2. Intrarenal AKI; which is a condition that results from abnormalities within the kidney itself and it includes those that affect the blood vessels, glomeruli, or tubules.
3. Postrenal AKI; which results from obstruction of the urinary collecting system anywhere from the calyces to the outflow from the bladder. The most common causes of obstruction of the urinary tract outside the kidney are kidney stones caused by the precipitation of calcium, urate or cystine.

PRERENAL ACUTE KIDNEY INJURY:

This is caused by decreased blood flow to the kidney. On normal terms, the kidney receives an abundant blood supply of about 1100 ml/min, or about 20-25% of cardiac output. The main purpose of this high blood flow to the kidney is to provide enough plasma for the high rates of glomerular filtration which is needed for effective regulation of body fluid volumes and solute concentrations. However, decreased renal blood flow is usually accompanied by decreased GFR (Glomerular Filtration Rate) and decreased urine output of water and solutes.

Consequently, conditions that lead to/acutely diminish the blood flow to the kidneys usually cause **Oliguria**; which refers to diminished urine output below the level of intake and solutes. This condition causes accumulation of water and solutes in the body fluids. If renal blood flow is markedly reduced, total cessation of urine output can occur, a condition referred to as **Anuria**. There are also other several causes of prerenal AKI and they are: Intravascular volume depletion (Diarrhoea/vomiting, burns, hemorrhage), cardiac failure (myocardial infarction, valvular damage) etc.

As long as renal blood flow does not fall below about 20-25% of normal, AKI can be reversed if the cause for ischemia is corrected before the damage to renal cells has occurred. If the cause of prerenal AKI is not corrected and ischemia of the kidney persists longer than a few hours, this type of renal failure can evolve into intrarenal AKI.

INTRARENAL ACUTE KIDNEY INJURY:

This is the condition caused by abnormalities that originates within the kidney itself. This category can be further divided into 3. This type of classification refers to ***the primary site of injury***, but because the renal vasculature and tubular system are functionally interdependent, damage to the renal blood vessels can lead to tubular damage and the primary tubular damage can lead to the damage of the renal blood vessels.

i. Conditions that injure the glomerular capillaries or other small vessels;

Some of the conditions are Vasculitis (polyarteritis nodosa), cholesterol emboli, malignant hypertension, and acute glomerulonephritis.

-Acute Glomerulonephritis:

This is a type of intrarenal AKI which is caused by an abnormal immune reaction that damages the glomeruli. The damage to the glomeruli occurs 1-3 weeks after an infection elsewhere in the body usually caused by a certain type of group A bata streptococci. This infection may have been a streptococcal sore throat, tonsillitis or even infection to the skin. It is not the infection itself that damages the kidneys, instead, over a few weeks, as antibodies develop against the streptococcal antigen, the antigen and antibodies react with each other to form an insoluble immune complex that becomes entrapped in the glomeruli, especially the basement portion of the glomeruli.

ii. Conditions that cause damage to the renal tubular epithelium.

This means the destruction of the tubules of epithelial cells. It can be due to acute tubular necrosis due to ischemia or acute tubular necrosis due to toxins (heavy metals, ethylene glycol, insecticides, poison mushrooms, carbon tetrachloride.

-Acute Tubular necrosis due to ischemia

The ischemia of the kidney can result from circulatory shock that severely impair the blood supply to the kidneys. Damage to the tubular epithelium occurs when the ischemia is severe enough to stop the supply/delivery of nutrients and oxygen to the renal epithelial cells.

iii. Conditions that cause damage to the renal interstitium; some are acute pyelonephritis, acute allergic interstitial nephritis, etc.

POSTRENAL ACUTE KIDNEY INJURY:

This is caused by abnormalities of lower urinary tract. Sever abnormalities in the lower urinary tract can lead to total blockage or partial blockage of urine flow and therefore lead to AKI even when the blood supply to the kidney and other functions are initially normal.

Although if the urine output of only one kidney is diminished, no major changes in body fluid composition will occur because the contralateral kidney can increases its urine output sufficiently to maintain relatively normal levels of extracellular fluid volume. With this type of renal injury, normal kidney function can be restored if the basic problem is corrected within a few hours.

However, chronic obstruction of the urinary tract that lasts for several days or weeks can lead to irresistible kidney damage. Some of the causes of postrenal AKI include: Bilateral obstruction of the ureters or renal pelvises by large stones of blood clots, bladder obstruction and obstruction of the urethra.

* **PHYSIOLOGICAL EFFECT** OF ACUTE KIDNEY INJURY

A major physiological effect of AKI is the retention of water, waste products of metabolism and electrolytes in the blood and extracellular fluid. This can lead to water and salt overload which in turn can lead to edema and hypertension.

The excessive retention of potassium, however, is a more serious threat to patients with the AKI because increase in plasma potassium concentration (hyperkalemia) above 8mEq/L can be fatal. Because the kidneys are also unable to excrete sufficient hydrogen ions patients with AKI may experience metabolic acidosis which in itself can be lethal or can aggravate the hyperkalemia.

In most severe cases of AKI, complete anuria occurs and the patients die in 8-14 days unless the kidney functions are restored or unless an artificial kidney is used to get rid of the body of excessive retained water, electrolytes and waste products of embolism.

* **TREATMENT** OF ACUTE KIDNEY INJURY:

The treatment for AKI depends on what caused it to happen. While being treated for the problem that caused the AKI, there may also be treatments to prevent problems that can make it harder for the kidneys to heal. Some possible treatments include:

1. Temporary hemodialysis to do the work that your kidneys should be doing, until they can recover.
2. Medicines to control the amounts of vitamins and minerals in your blood.
3. Treatments to keep the right amount of fluid in your blood

The doctor may advise to follow a kidney-friendly diet plan to help the kidneys continue to heal, or may even be referred dietician, who can help make a kidney-friendly diet plan that works for you.

• CHRONIC KIDNEY DISEASE:

This is the condition in which there are progressive losses of functions of more and more nephrons (functional units of the kidney) that gradually decrease overall kidney function.

The CKD is usually defined as the presence of kidney damage or decreased kidney function that persists for a period of time (about 3 months). It is often associated with progressive and irresistible loss of large numbers of functioning nephrons.

* It can be **CAUSED** (Aetiology) by:

1. Metabolic disorders (Diabetics mellitus, Obesity, Amyloidosis)
2. Hypertension
3. Infections (Pyelonephriris, Tuberculosis)
4. Renal Vascular disorders (Atherosclerosis, Nephrosclerosis-hypertension)
5. Congenital disorders (Polycystic disease, congenital absence of the kidney tissue called *renal hypoplasia*) etc.

NOTE THAT:

In general, CKD like AKI (Acute Kidney infection) can occur because of disorders or injuries to the renal vasculature, tubules, lower urinary tract, glomeruli (Glomerulonephritis), renal interstitium (Interstitial nephritis) etc. It can result from any cause of renal dysfunction of sufficient magnitude. The most common causes are: Diabetic nephropathy, hypertensive nephrosclerosis and various primary and secondary glomerulopathies.

* For the **SIGNS and SYMPTOMS**;

Although the patients with mildly diminished renal reserve are asymptomatic (that is, showing no symptoms), even patients with mild-moderate renal insufficiency may have no symptoms despite elevated blood urea nitrogen (BUN) and creatinine. Nocturia is often noted and this is principally due to failure to concentrate urine. Anorexia, nausea, vomiting, weight loss, stomatitis, and an unpleasant taste in the mouth are almost uniformly present. The skin may be yellow-brown. Pruritus may be especially uncomfortable. Under-nutrition leading to generalized tissue wasting is a prominent feature of chronic uremia. In advanced CKD, pericarditis and gastrointestinal ulceration and bleeding may occur. Hypertension is present in > 80% of patients with advanced CKD and is usually related to hypervolemia. Heart failure caused by hypertension or coronary artery disease and renal retention of sodium and water may lead to dependent edema and/or dyspnea.

* **PHYSIOLOGICAL EFFECTS** OF CHRONIC KIDNEY DISEASE:

Chronic kidney disease (CKD) is initially described as '***Diminished renal reserve or renal insufficiency***', which may progress to renal failure (end-stage renal disease). Initially, as renal tissue loses function, there are few noticeable abnormalities because the remaining tissue increases its performance (renal functional adaptation).

* Effect of decreased renal function (CKD) on fluid and electrolytes:

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.

-Creatinine and urea:

The 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 (such as uremia). Urea and creatinine are not major contributors to the uremic symptoms; they are markers for many other substances that cause the symptoms.

-Sodium and water:

Despite a diminishing GFR, sodium and water balance is 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.

* Osteomalacia in Chronic kidney disease

It is caused by decreased production of active vitamin D and by phosphate retention by the kidneys. Prolonged CKD also caused osteomalacia, a condition in which the bones are partially absorbed and therefore, becomes greatly weakened. An important cause of demineralization of the skeleton in CKD is the rise in serum phosphate concentration hat occurs as a result of decreased GFR. This rise in serum phosphate increases binding of phosphate with calcium in the plasma thus decreasing the plasma serum ionized calcium concentration, which in turn, stimulates parathyroid hormone secretion. This secondary hyperparathyroidism then stimulates the release of calcium from bones causing further demineralization of the bones.

* Acidosis in Chronic Kidney Disease:

The body normally produce about 50-80mmol more metabolic acid than metabolic alkali each day. Therefore, when kidney failure occurs, acid accumulates in the body fluids. The buffer of the body fluids normally can buffer 500-1000mmol of acid without lethal increases in extracellular fluid H+ concentration and the phosphate compounds in the bones can buffer an additional few thousand mmol of H+. However, when this buffering power is used up, the blood pH falls drastically and the patient will become comatose and die if the pH falls below about 6.8.

* Anemia in Chronic kidney disease:

Anemia in chronic kidney disease is caused by decreased erythropoietin secretion. Anemia almost always develops in patients with severe CKD. The most important cause of this anemia is decreased renal secretion of erythropoietin which stimulates the bone marrow to produce red blood cells. If the kidneys are seriously damaged, they are unable to form adequate quantities of erythropoietin which leads to diminished red blood cell production and consequent anemia.

The availability of recombinant erythropoietin however has provided a means of treating anemia in patients with CKD.

* Increase in Urea and other non-protein nitrogen (Azotemia):

This non protein nitrogen includes urea, uric acid, creatinine, and a few less important compounds. This non-protein nitrogen in general is the end products of protein metabolism and must be removed from the body to ensure continued normal protein metabolism in the cells. The concentration of this non-protein nitrogen particularly of urea can rise to as high as 10 times normal during 1-2 weeks of total renal failure. With CKD, the concentrations rise approximately in proportion to the degree of reduction in functional nephrons. For this reason, measuring the concentration of these substances especially of urea and creatinine provides an important means for assessing the severity of CKD.

* **TREATMENT** OF CHRONIC KIDNEY DISEASE

1. Control of underlying disorders
2. Possible restriction of dietary protein, phosphate, and potassium
3. Vitamin D supplements
4. Treatment of anemia
5. Treatment of contributing comorbidities (eg, heart failure, diabetes mellitus, nephrolithiasis, prostatic hypertrophy)
6. Doses of all drugs adjusted as needed
7. Dialysis for severely decreased glomerular filtration rate (GFR) if symptoms and signs not adequately managed by medical interventions.
8. Transplantation of a new kidney, if a living kidney donor is available, better long-term outcomes occur when a patient receives the transplanted kidney early.

NOTE THAT:

Underlying disorders and contributory factors must be controlled. In particular, controlling hyperglycemia in patients with diabetic nephropathy and controlling hypertension in all patients substantially slows deterioration of GFR.

**QUESTION 2: With the aid of suitable diagrams, dicuss the types of dialysis you know**?

What is dialysis?

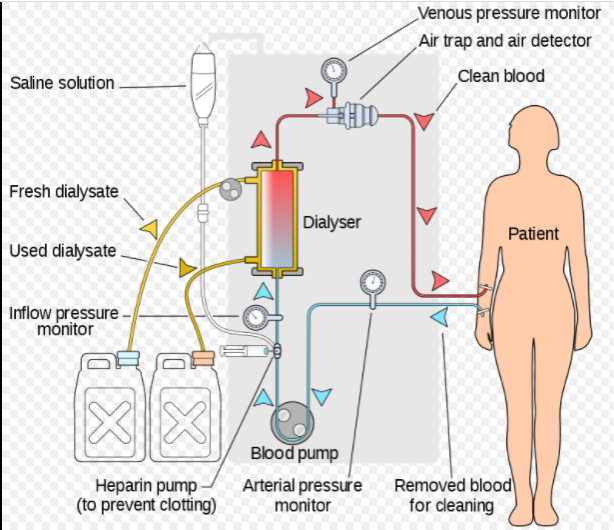
Dialysis in medicine is the process of removing excess water, solutes, and toxins from the blood in people whose kidneys can no longer perform these functions naturally. This is referred to as ***renal replacement therapy***. Dialysis is used in patients with rapidly developing loss of kidney function or slowly worsening kidney function called Acute Kidney Injury (AKI) and Chronic Kidney Disease (CKD) respectively. Kidney dialysis is a procedure that is a substitute for many of the normal functions of the kidneys.

There are 2 main types of Kidney dialysis:

1. Hemodialysis
2. Peritoneal dialysis

* HEMODIALYSIS:

**DIAGRAM**:



**Diagram above showing how the process of Hemodialysis is done.**

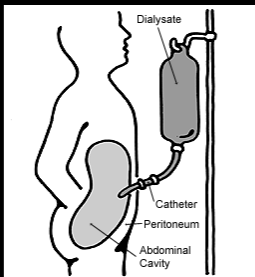
Hemodialysis uses an external machine and a special type of filter to remove excess waste products and water from the blood.

During hemodialysis, blood passes from the patient's body to the dialysis machine through sterile tubing and into a filter called a ***dialysis membrane***. For this procedure, the patient has a specialized vascular tube placed between an artery and a vein in the arm or leg (called a gortex graft). Sometimes, a direct connection is made between an artery and a vein in the arm. This procedure is called a ***Cimino fistula***. Needles are then placed in the graft or fistula and blood passes to the dialysis machine, through the filter and back to the patient. If the patient requires dialysis before a graft or a fistula is placed, a large diameter catheter (hemodialysis catheter) is placed directly into a large vein in the neck or leg in order to perform dialysis. In the dialysis machine, a solution on the other side of the filter receives the waste products from the patient.

Patients generally go to the dialysis unit about three times a week for treatment and before treatment; patients weigh themselves so that excess fluid accumulated since the last dialysis session can be measured. Patients then go to assigned chairs that are like lounge chairs. The area of the graft or fistula (the connection between the artery and vein), is cleaned thoroughly. Two needles are then inserted into the graft or fistula. One takes the blood to the machine where it is cleaned. The other needle allows blood that is returning to the patient to go back into the patient's body. **TREATMENT CAN LAST 2 ½ to 4 ½ HOURS**. During this time, the dialysis staff checks the patient's blood pressure frequently and adjusts the dialysis machine to ensure that the proper amount of fluid is being removed from the patient’s body. On occasion, patients who are very motivated may be able to perform dialysis themselves at home in a process called ***home hemodialysis***.

* PERITONEAL DIALYSIS:

**DIAGRAM**:



**Diagram above showing the process of peritoneal dialysis with the catheter (connected to the dialysate) inserted into the abdominal cavity which is lined by the peritoneum.**

Peritoneal dialysis uses a fluid that is placed into the patient's abdominal cavity through a plastic tube (peritoneal dialysis catheter) to remove excess waste products and fluid from the body.

Peritoneal dialysis uses the patient’s own body tissues inside of the belly (abdominal cavity) to act as *the filter*. The abdominal cavity is lined with a special membrane called the ***peritoneal membrane***. A plastic tube called a *peritoneal dialysis catheter* is placed through the abdominal wall into the abdominal cavity. A special fluid called ***dialysate*** is then flushed into the abdominal cavity and washes around the intestines. The peritoneal membrane acts as a filter between this fluid and the blood stream. By using different types of solutions, waste products and excess water can be removed from the body through this process.

The patient is responsible for maintaining a clean surface on the abdomen and catheter, where treatment is administered, in order to prevent infection. During this process, the patient weighs herself/himself to determine the strength of fluid to be used. The patient then puts on a mask and cleans the peritoneal catheter site. Fluid that has been allowed to stay in the peritoneal cavity while the peritoneal membrane filters waste into the fluid. The fluid and waste are is then drained back into the plastic bag that originally contained the fluid. The patient then disconnects this bag containing waste in the fluid and connects a new bag of solution that is allowed to drain into the peritoneal cavity. Once the fluid is in the body, the new bag is rolled up and placed in the patient's underwear until the next treatment. This procedure **usually takes 30 minutes to accomplish and must be done four to five times a day.**

As an alternative to this treatment, some patients on peritoneal dialysis use a machine called a "**cycler**". This cycler is used every night. Five to six bags of dialysis fluid are used on the cycler and the machine automatically changes the fluid while the patient sleeps. The patient can carry out this process by him/herself.

NOTE THAT:

There are several other forms of dialysis, they are:

1. Hemofiltration:

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 pressure gradient is applied; as a result, water moves across the very permeable membrane rapidly, "dragging" along with it many dissolved substances, including ones with large molecular weights, which are not cleared as well by hemodialysis. Salts and water lost from the blood during this process are replaced with a "substitution fluid" that is infused into the extracorporeal circuit during the treatment.

1. 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).