**EGWU PIUS KEDONOJO**

**17/MHS01/103**

**MBBS 300L**

**PHS 303**

**THE PATHOPHYSIOLOGICAL PROESS INVOLVED IN RENAL FALIURE.**

Severe kidney diseases can be divided into two main categories: (1) Acute renal failure; in which the kidneys abruptly stops working entirely or almost entirely but may eventually recover nearly normal functions.

(2) Chronic renal failure; in which there is progressive loss of function of more and more nephrons that gradually decreases overall kidney function.

Within these two general categories, there are many specific kidney diseases that can affect the kidney blood vessels, glomeruli, tubules, renal interstitium, and parts of the urinary tract outside the kidney, including the ureters and bladder.

**ACUTE RENAL FALIURE**

The causes of acute renal failure can be divided into

three main categories:

1. Acute renal failure resulting from decreased blood supply to the kidneys; this condition is often referred to as prerenal acute renal failure to reflect the fact that the abnormality occurs in a system before the kidneys. This 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 hemorrhage.

2. Intrarenal acute renal failure resulting from abnormalities within the kidney itself, including those that affect the blood vessels, glomeruli, or tubules.

3. Postrenal acute renal failure, resulting 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 precipitation of calcium, urate, or cysteine.

**PRERENAL ACUTE RENAL FAILURE CAUSED BY DECREASED BLOOD FLOW TO THE KIDNEY**

The kidneys normally receive an abundant blood supply of about 1100 ml/min, or about 20 to 25 per cent of the cardiac output. The main purpose of this high blood flow to the kidneys is to provide enough plasma for the high rates of glomerular filtration needed for effective regulation of body fluid volumes and solute concentrations. Therefore, decreased renal blood flow is usually accompanied by decreased GFR and decreased urine output of water and solutes. Consequently, conditions that acutely diminish blood flow to the kidneys usually cause oliguria, which refers to diminished urine output below the level of intake of water and solutes. This 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. As long as renal blood flow does not fall below about20 to 25 per cent of normal, acute renal failure can usually be reversed if the cause of the ischemia is corrected before damage to the renal cells has occurred. Unlike some tissues, the kidney can endure a relatively large reduction in blood flow before actual damage to the renal cells occurs.The reason for this is that as renal blood flow is reduced, the GFR and the amount of sodium chloride filtered by the glomeruli (as well as the filtration rate of water and other electrolytes) are reduced. This decreases the amount of sodium chloride that must be reabsorbed by the tubules, which uses most of the energy and oxygen consumed by the normal kidney. Therefore, as renal blood flow and GFR fall, the requirement for renal oxygen consumption is also reduced. As the GFR approaches zero, oxygen consumption of the kidney approaches the rate that is required to keep the renal tubular cells alive even when they are not reabsorbing sodium. When blood flow is reduced below this basal requirement, which is usually less than 20 to 25 per cent of the normal renal blood flow, the renal cells start to become hypoxic, and further decreases in renal blood flow, if prolonged, will cause damage or even death of the renal cells, especially the tubular epithelial cells. If the cause of prerenal acute renal failure is not corrected and ischemia of the kidney persists longer than a few hours, this type of renal failure can evolve into intrarenal acute renal failure, as discussed later. Acute reduction of renal blood flow is a common cause of acute renal failure in hospitalized patients.

**INTRARENAL ACUTE RENAL FAILURE CAUSED BY ABNORMALITIES WITHIN THE KIDNEY**

Abnormalities that originate within the kidney and that abruptly diminish urine output fall into the general category of intrarenal acute renal failure. This category of acute renal failure can be further divided into:

1. Conditions that injure the glomerular capillaries or other small renal vessels
2. Conditions that damage the renal tubular epithelium
3. Conditions that cause damage to the renal interstitium.

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 primary tubular damage can lead to damage of the renal blood vessels. Causes of renal failure that fall under this category includes:

**Acute Renal Failure Caused by Glomerulonephritis**.

Acute glomerulonephritis is a type of intrarenal acute renal failure usually caused by an abnormal immune reaction that damages the glomeruli. In about 95 per cent of the patients with this disease, damage to the glomeruli occurs 1 to 3 weeks after an infection elsewhere in the body, usually caused by certain types of group A beta streptococci.The infection may have been a streptococcal sore throat, streptococcal tonsillitis, or even streptococcal infection of 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 antibodies and antigen react with each other to form an insoluble immune complex that becomes entrapped in the glomeruli, especially in the basement membrane portion of the glomeruli. Once the immune complex has deposited in the glomeruli, many of the cells of the glomeruli begin to proliferate, but mainly the mesangial cells that lie between the endothelium and the epithelium. In addition, large numbers of white blood cells become entrapped in the glomeruli. Many of the glomeruli become blocked by this inflammatory reaction, and those that are not blocked usually become excessively permeable, allowing both protein and red blood cells to leak from the blood of the glomerular capillaries into the glomerular filtrate. In severe cases, either total or almost complete renal shutdown occurs. The acute inflammation of the glomeruli usually subsides in about 2 weeks, and in most patients, the kidneys return to almost normal function within the next few weeks to few months. Sometimes, however, many of the glomeruli are destroyed beyond repair, and in a small percentage of patients, progressive renal deterioration continues indefinitely, leading to chronic renal failure.

**Tubular necrosis as a cause of acute renal failure**.

Another cause of intrarenal acute renal failure is tubular necrosis, which means destruction of epithelial cells in the tubules. Some common causes of tubular necrosis are:

(1) Severe ischemia and inadequate supply of oxygen and nutrients to the tubular epithelial cells and

(2) Poisons, toxins, or medications that destroy the tubular epithelial cells.

**Acute Tubular Necrosis Caused by Severe Renal Ischemia**.

Severe ischemia of the kidney can result fromcirculatory shock or any other disturbance that severelyimpairs the blood supply to the kidney. If the ischemiais severe enough to seriously impair the delivery ofnutrients and oxygen to the renal tubular epithelialcells, and if the insult is prolonged, damage or eventualdestruction of the epithelial cells can occur. When thishappens, tubular cells “slough off” and plug many of thenephrons, so that there is no urine output from theblocked nephrons; the affected nephrons often fail toexcrete urine even when renal blood flow is restored tonormal, as long as the tubules remain plugged.The mostcommon causes of ischemic damage to the tubularepithelium are the prerenal causes of acute renal failureassociated with circulatory shock.

**Acute Tubular Necrosis Caused by Toxins or Medications.**

There is a long list of renal poisons and medications that can damage the tubular epithelium and cause acute renal failure. Some of these are carbon tetrachloride, heavy metals (such as mercury and lead), ethylene glycol (which is a major component in antifreeze), various insecticides, various medications (such as tetracyclines) used as antibiotics, and cis-platinum, which is used in treating certain cancers. Each of these substances has a specific toxic action on the renal tubular epithelial cells, causing death of many of them. As a result, the epithelial cells slough away from the basement membrane and plug the tubules. In some instances, the basement membrane also is destroyed. If the basement membrane remains intact, new tubular epithelial cells can grow along the surface of the membrane, so that the tubule repairs itself within 10 to 20 days.

**POSTRENAL ACUTE RENAL FAILURE CAUSED BY ABNORMALITIES OF THE LOWER URINARY TRACT**

Multiple abnormalities in the lower urinary tract can block or partially block urine flow and therefore lead to acute renal failure even when the kidneys’ blood supply and other functions are initially normal. If the urine output of only one kidney is diminished, no major change in body fluid composition will occur because the contralateral kidney can increase its urine output sufficiently to maintain relatively normal levels of extracellular electrolytes and solutes as well as normal extracellular fluid volume. With this type of renal failure, normal kidney function can be restored if the basic cause of the problem is corrected within a few hours. But chronic obstruction of the urinary tract, lasting for several days or weeks, can lead to irreversible kidney damage. Some of the causes of postrenal acute failure include:

(1) Bilateral obstruction of the ureters or renal pelvises caused by large stones or blood clots,

(2) Bladder obstruction, and

(3) Obstruction of the urethra.

**CHRONIC RENAL FAILURE:**

**AN IRREVERSIBLE DECREASE**

**IN THE NUMBER OF FUNCTIONAL**

**NEPHRONS**

Chronic renal failure results from progressive and irreversible loss of large numbers of functioning nephrons. Serious clinical symptoms often do not occur until the number of functional nephrons falls to at least 70 to 75 per cent below normal. In fact, relatively normal blood concentrations of most electrolytes and normal body fluid volumes can still be maintained until the number of functioning nephrons decreases below 20 to 25 per cent of normal.

In general, chronic renal failure, like acute renal failure, can occur because of disorders of the blood vessels, glomeruli, tubules, renal interstitium, and lower urinary tract. Despite the wide variety of diseases that can lead to chronic renal failure, the end result is essentially the same—a decrease in the number of functional nephrons.

**VICIOUS CIRCLE OF CHRONIC RENAL**

**FAILURE LEADING TO END-STAGE**

**RENAL DISEASE**

In many cases, an initial insult to the kidney leads to progressive deterioration of kidney function and further loss of nephrons to the point where the person must be placed on dialysis treatment or transplanted with a functional kidney to survive. This condition is referred to as end-stage renal disease. Studies in laboratory animals have shown that surgical removal of large portions of the kidney initially causes adaptive changes in the remaining nephrons that lead to increased blood flow, increased GFR, and increased urine output in the surviving nephrons. The exact mechanisms responsible for these changes are not well understood but involve hypertrophy (growth of the various structures of the surviving nephrons) as well as functional changes that decrease vascular resistance and tubular reabsorption in the surviving nephrons. These adaptive changes permit a person to excrete normal amounts of water and solutes even when kidney mass is reduced to 20 to 25 per cent of normal. Over a period of several years, however, the renal functional changes may lead to further injury of the remaining nephrons, particularly to the glomeruli of these nephrons. The cause of this additional injury is not known, but some investigators believe that it may be related in part to increased pressure or stretch of the remaining glomeruli, which occurs as a result of functional vasodilation or increased blood pressure; the chronic increase in pressure and stretch of the small arterioles and glomeruli are believed to cause sclerosis of these vessels (replacement of normal tissue with connective tissue). These sclerotic lesions can eventually obliterate the glomerulus, leading to further reduction in kidney function, further adaptive changes in the remaining nephrons, and a slowly progressing vicious circle that eventually terminates in end-stage renal disease. The only proven method of slowing down this progressive loss of kidney function is to lower arterial pressure and glomerular hydrostatic pressure, especially by using drugs such as angiotensin-converting enzyme inhibitors or angiotensin II antagonists.

**INJURY TO THE RENAL VASCULATURE AS A**

**CAUSE OF CHRONIC RENAL FAILURE**

Many types of vascular lesions can lead to renal ischemia and death of kidney tissue. The most common of these are (1) atherosclerosis of the larger renal arteries, with progressive sclerotic constriction of the vessels; (2) fibromuscular hyperplasia of one or more of the large arteries, which also causes occlusion of the vessels; and (3) nephrosclerosis, caused by sclerotic lesions of the smaller arteries, arterioles, and glomeruli. Atherosclerotic or hyperplastic lesions of the large arteries frequently affect one kidney more than the other and, therefore, cause unilaterally diminished kidney function. Hypertension often occurs when the artery of one kidney is constricted while the artery of the other kidney is still normal, a condition analogous to “two-kidney” Goldblatt hypertension.

Benign nephrosclerosis, the most common form of kidney disease, is seen to at least some extent in about 70 per cent of postmortem examinations in people who die after the age of 60. This type of vascular lesion occurs in the smaller interlobular arteries and in the afferent arterioles of the kidney. It is believed to begin with leakage of plasma through the intimal membrane of these vessels. This causes fibrinoid deposits to develop in the medial layers of these vessels, followed by progressive thickening of the vessel wall that eventually constricts the vessels and, in some cases, occludes them. Because there is essentially no collateral circulation among the smaller renal arteries, occlusion of one or more of them causes destruction of a comparable number of nephrons. Therefore, much of the kidney tissue becomes replaced by small amounts of fibrous tissue. When sclerosis occurs in the glomeruli, the injury is referred to as glomerulosclerosis.

Nephrosclerosis and glomerulosclerosis occur to some extent in most people after the fourth decade of life, causing about a 10 per cent decrease in the number of functional nephrons each 10 years after age 40. This loss of glomeruli and overall nephron function is reflected by a progressive decrease in both renal blood flow and GFR. Even in “normal” people, kidney plasma flow and GFR decrease by 40 to 50 per cent by age 80.

The frequency and severity of nephrosclerosis and glomerulosclerosis are greatly increased by concurrent hypertension or diabetes mellitus. In fact, diabetes mellitus and hypertension are the two most important causes of end-stage renal disease, as discussed previously. Thus, benign nephrosclerosis in association with severe hypertension can lead to a rapidly progressing malignant nephrosclerosis. The characteristic histological features of malignant nephrosclerosis include large amounts of fibrinoid deposits in the arterioles and progressive thickening of the vessels, with severe ischemia occurring in the affected nephrons. For unknown reasons, the incidence of malignant nephrosclerosis and severe glomerulosclerosis is significantly higher in blacks than in whites of similar ages who have similar degrees of severity of hypertension or diabetes.

**Injury to the Glomeruli as a Cause of Chronic Renal Failure**— Glomerulonephritis Chronic glomerulonephritis can be caused by several diseases that cause inflammation and damage to the capillary loops in the glomeruli of the kidneys. In contrast to the acute form of this disease, chronic glomerulonephritis is a slowly progressive disease that often leads to irreversible renal failure. It may be a primary kidney disease, following acute glomerulonephritis, or it may be secondary to systemic diseases, such as lupus erythematosus.

In most cases, chronic glomerulonephritis begins with accumulation of precipitated antigen-antibody complexes in the glomerular membrane. In contrast to acute glomerulonephritis, streptococcal infections account for only a small percentage of patients with the chronic form of glomerulonephritis. The results of the accumulation of antigen-antibody complex in the glomerular membranes are inflammation, progressive thickening of the membranes, and eventual invasion of the glomeruli by fibrous tissue. In the later stages of the disease, the glomerular capillary filtration coefficient becomes greatly reduced because of decreased numbers of filtering capillaries in the glomerular tufts and because of thickened glomerular membranes. In the final stages of the disease, many glomeruli are replaced by fibrous tissue and are, therefore, unable to filter fluid.

**Injury to the Renal Interstitium as a Cause of Chronic Renal Failure**—

Pyelonephritis Primary or secondary disease of the renal interstitium is referred to as interstitial nephritis. In general, this can result from vascular, glomerular, or tubular damage that destroys individual nephrons, or it can involve primary damage to the renal interstitium by poisons, drugs, and bacterial infections. Renal interstitial injury caused by bacterial infection is called pyelonephritis. The infection can result from different types of bacteria but especially from Escherichia coli that originate from fecal contamination of the urinary tract. These bacteria reach the kidneys either by way of the blood stream or, more commonly, by ascension from the lower urinary tract by way of the ureters to the kidneys. Although the normal bladder is able to clear bacteria readily, there are two general clinical conditions that may interfere with the normal flushing of bacteria from the bladder:

(1) The inability of the bladder to empty completely, leaving residual urine in the bladder, and

(2) The existence of obstruction of urine outflow. With impaired ability to flush bacteria from the bladder, the bacteria multiply and the bladder becomes inflamed, a condition termed cystitis. Once cystitis has occurred, it may remain localized without ascending to the kidney, or in some people, bacteria may reach the renal pelvis because of a pathological condition in which urine is propelled up one or both of the ureters during micturition. This condition is called vesicoureteral reflux and is due to the failure of the bladder wall to occlude the ureter during micturition; as a result, some of the urine is propelled upward toward the kidney, carrying with it bacteria that can reach the renal pelvis and renal medulla, where they can initiate the infection and inflammation associated with pyelonephritis.

Pyelonephritis begins in the renal medulla and therefore usually affects the function of the medulla more than it affects the cortex, at least in the initial stages. Because one of the primary functions of the medulla is to provide the countercurrent mechanism for concentrating urine, patients with pyelonephritis frequently have markedly impaired ability to concentrate the urine.

With long-standing pyelonephritis, invasion of the kidneys by bacteria not only causes damage to the renal medulla interstitium but also results in progressive damage of renal tubules, glomeruli, and other structures throughout the kidney. Consequently, large parts of functional renal tissue are lost, and chronic renal failure can develop.

2**. TYPES OF DIALYSIS**

Severe loss of kidney function either acutely or chronically is a threat to life and requires removal of toxic waste products and restoration of body fluid volume and composition toward normal. This can be accomplished by dialysis.

There are three types of dialysis:

1. Hemodialysis

2. Peritoneal dialysis

3. Continuous Renal Replacement Therapy (CRRT)

**HEMODIALYSIS**

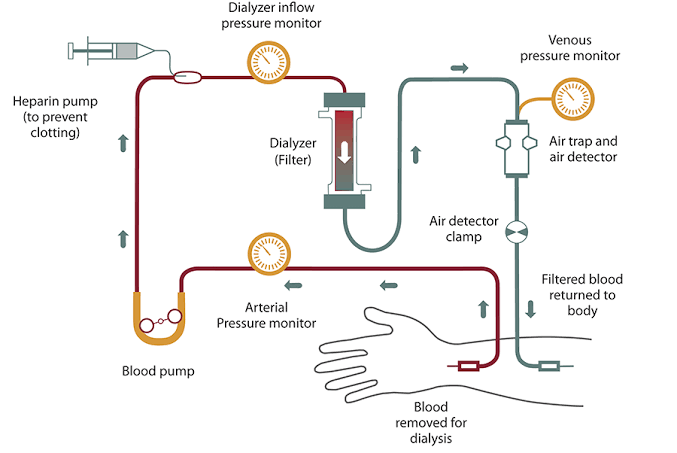
Hemodialysis is the most common type of dialysis. This process uses an artificial kidney (hemodialyzer) to remove waste and extra fluid from the blood. The blood is removed from the body and filtered through the artificial kidney. The filtered blood is then returned to the body with the help of a dialysis machine.

To get the blood to flow to the artificial kidney, the doctor performs a surgery to create an entrance point (vascular access) into the blood vessels. The three types of entrance points are:

* Arteriovenous (AV) fistula. This type connects an artery and a vein. It’s the preferred option.
* AV graft. This type is a looped tube.
* Vascular access catheter. This may be inserted into the large vein in your neck.

Both the AV fistula and AV graft are designed for long-term dialysis treatments. People who receive AV fistulas are healed and ready to begin hemodialysis two to three months after their surgery. People who receive AV grafts are ready in two to three weeks. Catheters are designed for short-term or temporary use.

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. The length of treatment depends on the body size, the amount of waste in the body, and the current state of health.



HEMODIALYSIS

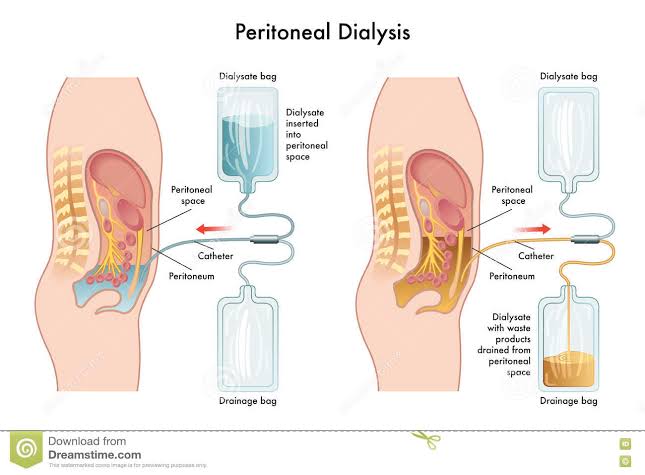
**Peritoneal dialysis**

Peritoneal dialysis involves surgery to implant a peritoneal dialysis (PD) catheter into the abdomen. The catheter helps filter the blood through the peritoneum. During treatment, a special fluid called dialysate flows into the peritoneum. The dialysate absorbs waste. Once the dialysate draws waste out of the bloodstream, it’s drained from the abdomen.

This process takes a few hours and needs to be repeated four to six times per day. However, the exchange of fluids can be performed while the patint sleeping or awake.

There are numerous different types of peritoneal dialysis. The main ones are:

* Continuous ambulatory peritoneal dialysis (CAPD). In CAPD, the abdomen is filled and drained multiple times each day. This method doesn’t require a machine and must be performed while awake.
* Continuous cycling peritoneal dialysis (CCPD). CCPD uses a machine to cycle the fluid in and out of the abdomen. It’s usually done at night while the patient is asleep.
* Intermittent peritoneal dialysis (IPD). This treatment is usually performed in the hospital, though it may be performed at home. It uses the same machine as CCPD, but the process takes longer.



**CONTINUOUS RENAL REPLACEMENT THERAPY (CRRT)**

This therapy is used primarily in the intensive care unit for people with acute kidney failure. It’s also known as hemofiltration. 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. This procedure is performed 12 to 24 hours a day, generally every day.

