17/MHS01/302

MEDICINE AND HEALTH SCIENCE

MEDICINE AND SURGERY

RENAL PHYSIOLOGY

QUESTION 1: Discuss the pathophysiological process involved in renal failure.

ANSWER

Sometimes kidneys are no longer able to filter and clean blood. This can cause unsafe levels of waste products to build up. This id known as kidney (or renal) failure. If untreated, can lead to death. They are two main types of kidney failure:

1. **ACUTE RENAL FAILURE:** The causes of acute renal failure can be divided into three main categories:
   - 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.
   - Intrarenal acute renal failure resulting from abnormalities within the kidney itself, including those that affect the blood vessels, glomeruli, or tubules.
   - Postrenal acute renal failure, resulting from obstruction of the urinary collecting system

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

a. Conditions that injure the glomerular capillaries or other small renal vessels
b. Conditions that damage the renal tubular epithelium, and
c. 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.

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:

- Severe ischemia and inadequate supply of oxygen and nutrients to the tubular epithelial cells.
- 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 from circulatory shock or any other disturbance that severely impairs the blood supply to the kidney. If the ischemia is severe enough to seriously impair the delivery of nutrients and oxygen to the renal tubular epithelial cells, and if the insult is prolonged, damage or eventual destruction of the epithelial cells can occur. When this happens, tubular cells “slough off” and plug many of the nephrons, so that there is no urine output from the blocked nephrons; the affected nephrons often fail to excrete urine even when renal blood flow is restored to normal, as long as the tubules remain plugged. The most common causes of ischemic damage to the tubular epithelium are the prerenal causes of acute renal failure associated 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.

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 about 20 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.

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:

a. Bilateral obstruction of the ureters or renal pelvises caused by large stones or blood clots,
b. Bladder obstruction
c. Obstruction of the urethra.

Signs of acute renal failure

a. Swelling of the hands, feet and face (edema)
b. Internal bleeding
c. Confusion
d. Seizures
e. Coma
f. Abnormal blood and urine tests
g. High blood pressure

2. 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. 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. In the early 1980s, glomerulonephritis in all its various forms was believed to be the most common initiating cause of end-stage renal disease. In recent years, diabetes mellitus and hypertension have become recognized as the leading causes of end-stage renal disease, together accounting for approximately 70 per cent of all chronic renal failure. Excessive weight gain (obesity) appears to be the most important risk factor for the two main causes of end-stage renal disease—diabetes and hypertension.

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

- Atherosclerosis of the larger renal arteries, with progressive sclerotic constriction of the vessels;
- Fibromuscular hyperplasia of one or more of the large arteries, which also causes occlusion of the vessels;
- 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” Gold blatt 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.

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:

- The inability of the bladder to empty completely, leaving residual urine in the bladder, and
- 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 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

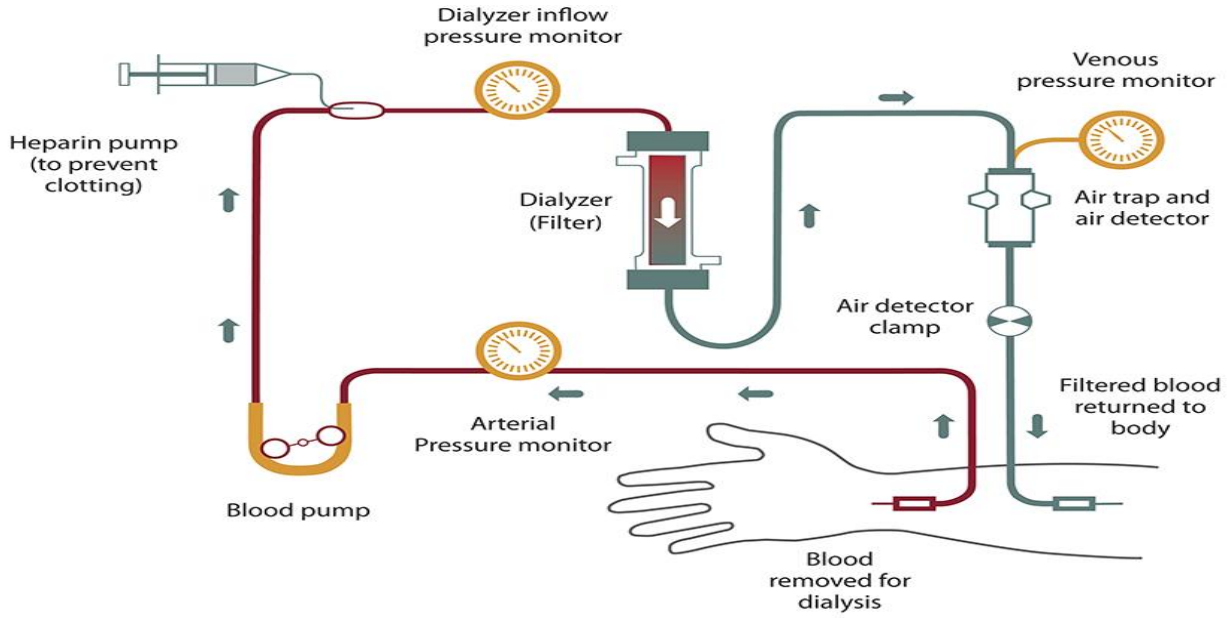
kidney, carrying with it bacteria that can reach the renal pelvis and renal medulla, where they can initiate the infection and inflammation associated with pyelonephritis. Pyelonephritis begins in the renal medulla and therefore usually affects the function of the medulla more than it affects the cortex, 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.

QUESTIUON 2: With the aid of suitable diagrams, discuss the types of dialysis you know.

ANSWER

Dialysis is a way to pump your blood through a machine that filters out the waste and returns the blood to your body. Severe loss of kidney function, either acutely or chronically, is a threat to life or requires removal of toxic waste products and restoration of body fluid volume and composition toward normal. This can be accomplished by dialysis with an artificial kidney. In certain types of acute renal failure, an artificial kidney may be used to tide the patient over until the kidneys resume their function. If the loss of kidney function is irreversible, it is necessary to perform dialysis chronically to maintain life. There are two types of dialysis:

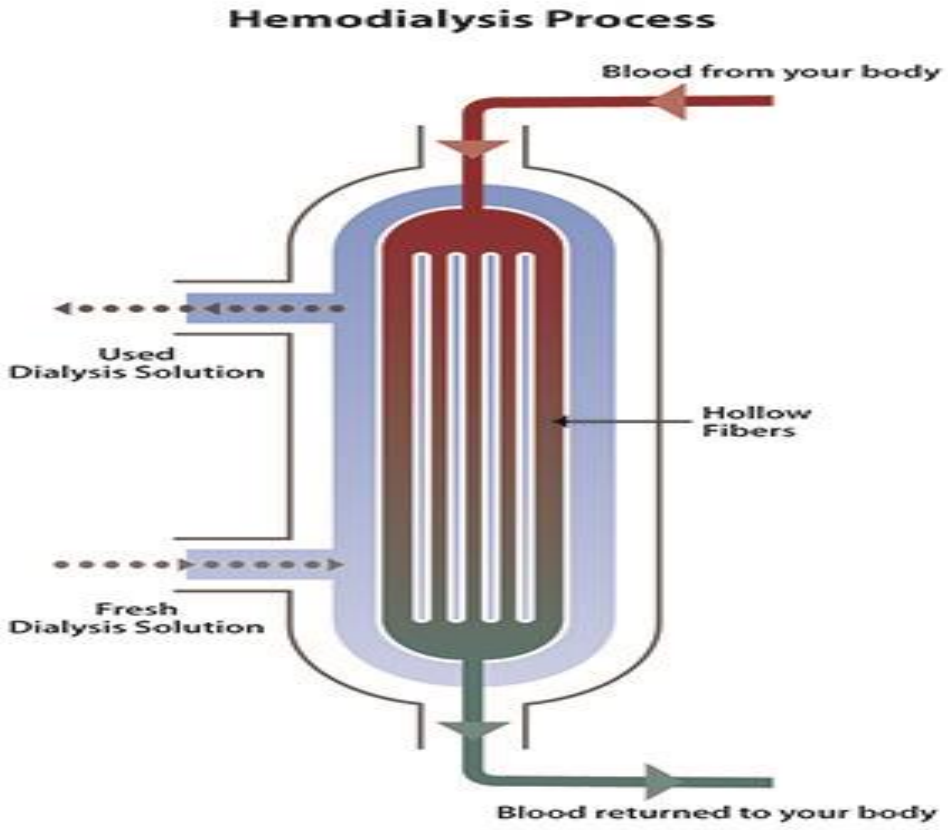
1. **Hemodialysis:**



This is a treatment to filter waste from your blood as your kidneys did when they were healthy. Hemodialysis helps control blood pressure and balance important minerals such as potassium, sodium and calcium in your blood. During hemodialysis, your blood is pumped through a filter called “dialyzer” outside your body. The dialysis machine pumps blood through the filter and returns the blood to your body. During the process, the dialysis machine, checks your blood pressure and controls how quickly

- Blood flows through the filter
- Fluid is removed from your body.

Blood enters at one end of the filter and is forced into many, very thin, hollow fibers. As your blood passes through the hollow fibers, dialysis solution passes in the opposite direction on the outside of the fibers. Waste products from your blood move into the dialysis. Filtered blood remains in the hollow fibers and returns to your body.



In the filter, your blood flows inside hollow fibers that filter out wastes and extra salt and water.

2. **Peritoneal dialysis:** This is a treatment for kidney failure that uses the lining of your abdomen or belly, to filter your blood inside your body. When you start treatment, dialysis solution (water with salt and other additives) flows from a bag through the catheter (soft tube), into

your belly. During peritoneal dialysis, a cleansing tube (dialysate) is circulated through a tube (catheter) inside part of your abdominal cavity. The dialysate absorbs waste products from blood vessels in the abdominal lining and then is drawn back out of the body and discarded.