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RENAL FAILURE

Renal failure, also called end-stage renal disease (ESRD), is the last stage of **chronic kidney disease**. Chronic kidney disease is usually defined as the presence of kidney damage or decreased kidney function that persists for at least 3 months. It is often associated with progressive and irreversible loss of large numbers of functioning nephrons. Serious clinical symptoms usually do not occur until the number of functional nephrons falls to at least 70 to 75 percent below normal. In general, chronic kidney disease 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 kidney disease, the end result is essentially the same—a decrease in the number of functional nephrons. Some of the most important causes of chronic kidney disease and eventually renal failure are;

1. Diabetes mellitus
2. Hypertension
3. Glomerulonephritis
4. Polycystic kidney disease
5. Pyelonephritis
6. Atherosclerosis
7. Urethral constriction
8. Nephrotoxins (analgesics, heavy metals)
9. Tuberculosis

Diabetes Mellitus and Hypertension

In recent years, diabetes mellitus and hypertension have become recognized as the leading causes of ESRD, together accounting for more than 70 percent of all ESRD. Excessive weight gain (obesity) appears to be the most important risk factor for the two main causes of ESRD— diabetes and hypertension. Concurrent diabetes and hypertension greatly increases the frequency and severity of nephrosclerosis and glomerulosclerosis. Benign **nephrosclerosis**, the most common form of kidney disease. 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 leakage 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**. This loss of glomeruli and overall nephron function is reflected by a progressive decrease in both renal blood flow and GFR. Even in healthy people without underlying hypertension or diabetes, renal plasma flow and GFR decrease by 40 to 50 percent by age 80 years.

Atherosclerosis

This is one of the most common vascular lesions that can lead to renal ischemia and death of kidney tissue. Atherosclerosis refers to the hardening of arteries or blood vessels caused by plaques (accumulations of fatty deposits usually cholesterol). Atherosclerosis can occur in the larger renal arteries leading to their constriction. Atherosclerotic 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**.

Glomerulonephritis

Glomerulonephritis refers to inflammation of the glomeruli. 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 **systemic 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. Accumulation of antigen-antibody complex in the glomerular membranes causes 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.

Pyelonephritis

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
- 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 kidney disease can develop.

Nephron Function in Chronic Kidney Disease

Although logically, decreasing the number of functional nephrons, which reduces the GFR, would also cause major decreases in renal excretion of water and solutes. Patients who have lost up to 75 to 80 percent of their nephrons are able to excrete normal amounts of water and electrolytes without serious accumulation of fluid or most electrolytes in the body fluids. Further reduction in the number of nephrons, however, leads to electrolyte and fluid retention, and death usually ensues when the number of nephrons falls below 5 to 10 percent of normal. In contrast to the electrolytes, many of the waste products of metabolism, such as urea and creatinine, accumulate almost in proportion to the number of nephrons that have been destroyed. The reason for this is that substances such as creatinine and urea depend largely on glomerular filtration for their excretion, and they are not reabsorbed as avidly as are the electrolytes.

Effects of Renal Failure on the Body Fluids—Uremia

The effect of chronic kidney disease on the body fluids depends on

- Water and food intake and
- The degree of impairment of renal function.

The important effects include

1. Generalized edema resulting from water and salt retention
2. Acidosis resulting from failure of the kidneys to rid the body of normal acidic products
3. High concentration of the nonprotein nitrogens—especially urea, creatinine, and uric acid—resulting from failure of the body to excrete the metabolic end products of proteins; and
4. High concentrations of other substances excreted by the kidney, including phenols, sulfates, phosphates, potassium, and guanidine bases.

This total condition is called uremia because of the high concentration of urea in the body fluids.

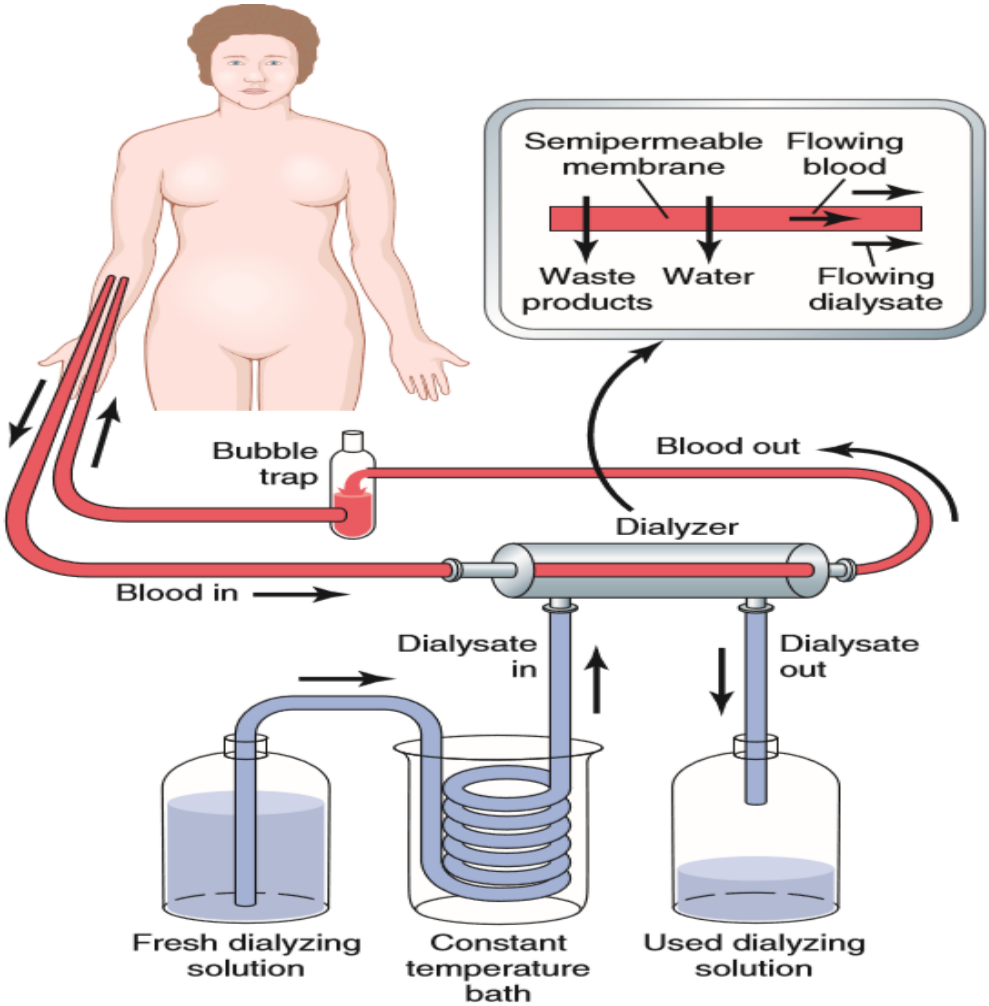
DIALYSIS

The general term dialysis means to separate substances using a permeable membrane. However, in clinical practice, dialysis is a technique used to perform the kidneys' excretory functions during renal failure. In certain types of acute renal failure (following poisoning, circulatory shock) dialysis is done to tide over the patient for a few weeks until the renal damage heals and kidneys resume their normal function. It is also used in patient with chronic renal failure for maintaining the health till the operation of renal transplantation is done. Lives of such patients completely depend upon dialysis.

There are two methods of dialysis;

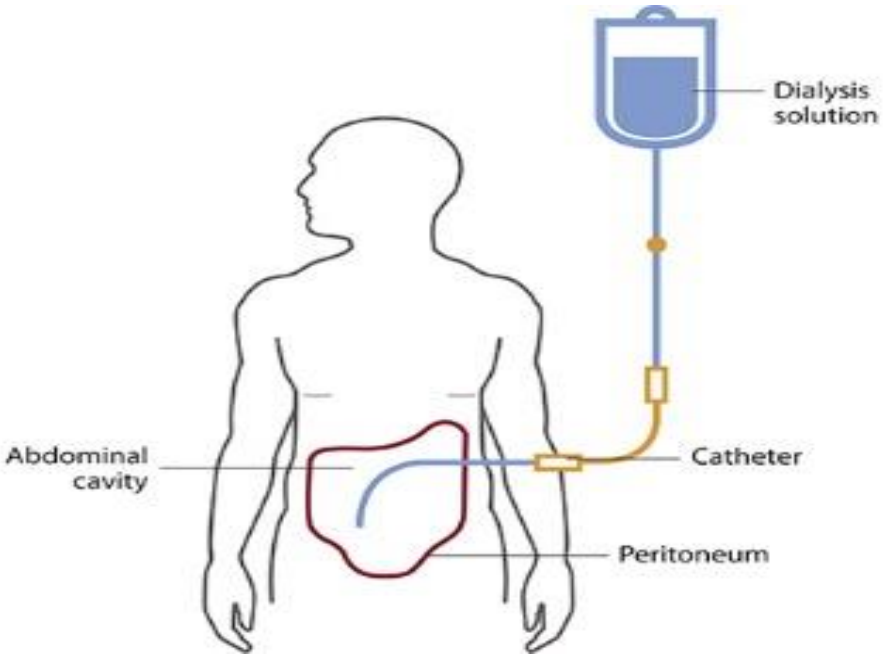
1. Hemodialysis: It utilizes 'artificial kidney' or hemodialyzer. During hemodialysis, blood is pumped from one of the patient's arteries (renal arteries) through tubing that is surrounded by special dialysis fluid. The tubing then conducts the blood back into the patient by way of a vein (basilica vein). The dialysis tubing is typically made of cellophane

that is highly permeable to most solutes but relatively impermeable to protein and completely impermeable to blood cells—characteristics quite similar to those of renal capillaries. The dialysis fluid contains solutes with ionic concentrations similar to or lower than those in normal plasma, and it contains no creatinine, urea, or other substances to be removed from the plasma. As blood flows through the tubing, the concentrations of nonprotein plasma solutes tend to reach diffusion equilibrium with those of the solutes in the bath fluid. For example, if the plasma K+ concentration of the patient is above normal, K+ diffuses out of the blood across the cellophane tubing and into the dialysis fluid. Similarly, waste products and excesses of other substances also diffuse into the dialysis fluid and thus are eliminated from the body. Patients with acute reversible renal failure may require hemodialysis for only days or weeks. Patients with chronic irreversible renal failure require treatment for the rest of their lives. However, unless they receive a kidney transplant, such patients undergo hemodialysis several times a week.



Hemodialysis

2. Peritoneal dialysis: Another way of removing excess substances from the blood is peritoneal dialysis, which uses the lining of the patient's own abdominal cavity (peritoneum) as a dialysis membrane. Fluid is injected via an indwelling plastic tube inserted through the abdominal wall into this cavity and allowed to remain there for hours, during which solutes diffuse into the fluid from the person's blood. The dialysis fluid is then removed and replaced with new fluid. This procedure can be performed several times daily by a patient who is simultaneously doing normal activities. While changing the bags of dialyzing fluid, one must pay attention to the aseptic technique. Also peritoneal catheter site must be taken care of to prevent peritonitis.



Peritoneal dialysis