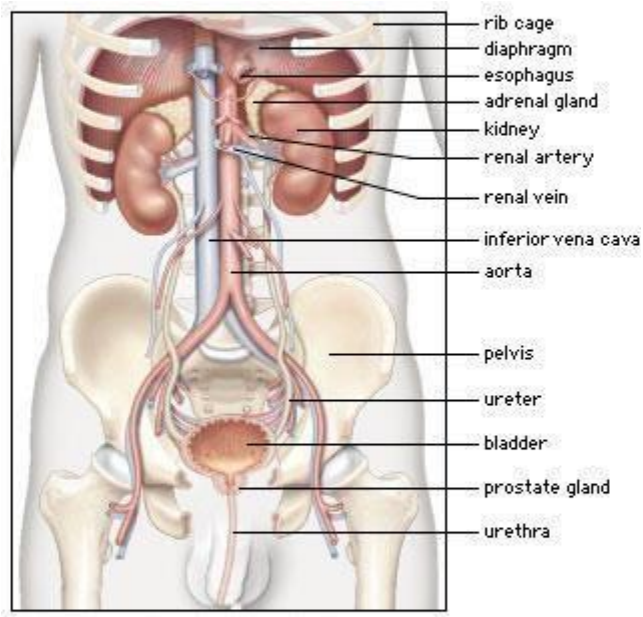
UNIT-1
Introduction to kidney Disease and Renal replacement therapy

LEARNING OBJECTIVE:
1. Basic kidney anatomy
2. Kidney Function and effect of kidney disease
3. Classification of kidney diseases
4. Chronic Kidney Disease

1. Introduction

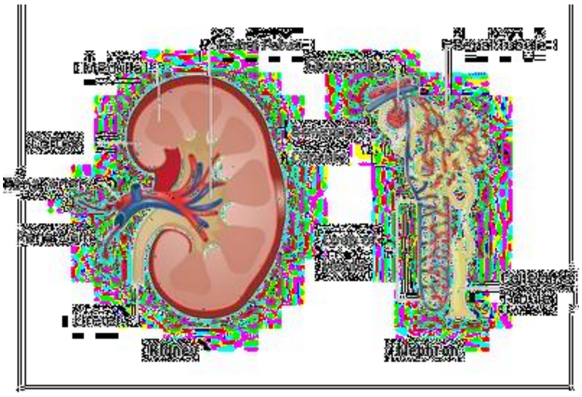
Kidney is one of the most important organ in human body. All vertebretes and some invertebretes have kidney. Human being, as well as all members of all vertebrete species, typically have two kidneys. Human‘s kidneys are dark red in color and have a shape in which one side is convex, or rounded, and the other is concave, or indented. Human‘s kidneys are about 10 to 13 cm long and about 5-7,5 cm wide. Adult human kidneys are about the size of a computer mouse. Kidneys are located beneath the diaphragm and behind the peritoneum. they lie against the rear wall of the abdomen, on either side of the spine. They are situated below the middle of the back, beneath the liver on the right and the spleen on the left.



The most important function of kidneys is the removal of poisonous wastes from the blood. Most of these wastes are nitrogen-containing compounds urea and uric acid. Kidneys ability to carry out it‘s function in removal wastes, depend on the functional unit of the kidney called nephrons. Together with the bladder, two ureters, and the single urethra, the kidneys make up the body‘s urinary system.

2. Structure a. Renal Capsule

Each kidney is encased in a transparent, fibrous membrane called a renal capsule. This membrane protects the kidney against trauma and infection. The capsule is composed of tough fibers, chiefly collagen, and elastin (fibrous proteins), that help to support the kidney mass and protect the vital tissue from injury. The capsule receives its blood supply ultimately from the interlobar arteries, small vessels that branch off from the main renal arteries. These vessels travel through the cortex of the kidney and terminate in the capsule. This membrane is usually 2 to 3 millimeters thick.



b. Renal Cortex

Renal cortex is the outermost layer of the kidney. It is situated between Renal Capsule and Medulla. Upper part of nephron which is Glomerulus and Henle‘s loop are situated in this layer. Renal cortex is a strong tissue that protect the inner layer of the kidney.

c. Renal Medulla (Renal Pyramids)

Renal Medulla lies beneath the Cortex. It is an area that contains between 8 and 18 cone-shaped section known as pyramids, which are formed almost entirely of bundles of microscopic tubules. The tips of these pyramids point toward the center of the kidney. These tubules transport urine from the cortical, or outer, part of the kidney, where urine is produced, to the calyces, or cup-chaped cavities in which urine collects before it passes through the ureter to the bladder. Space between the pyramids filled by cortex and forms structures called renal columns. .

d. Renal Pelvis

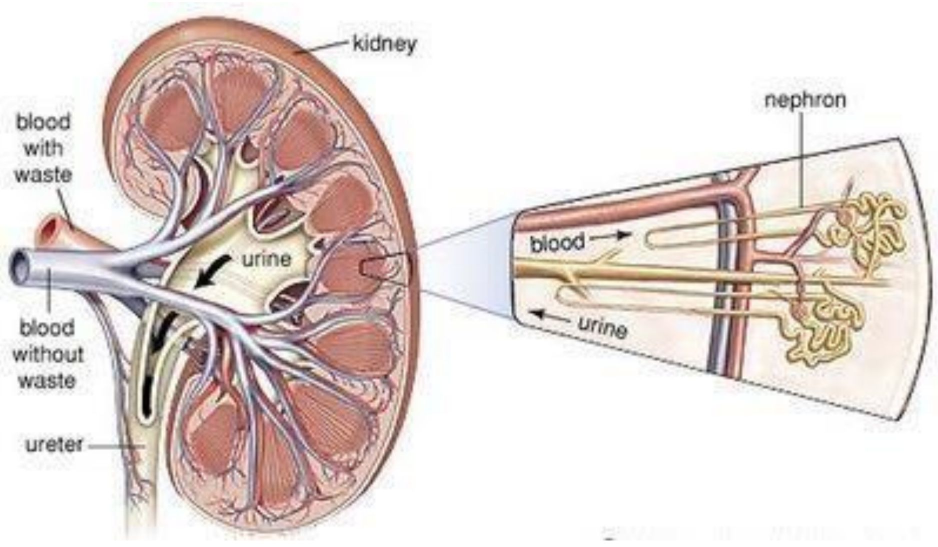
Renal Pelvis is extend in the center of each kidney as the tube through which urine flows from the kidney to the urinary bladder. The shape of renal pelvis is like a funnel that is curved to one side. Renal pelvis is almost completely enclosed in the deep indentation on the concave side of the kidney, the sinus. The large end of the pelvis has roughly cuplike extension, called calyces. The calyces‘ are cavities in which urine collects before it flows on the urinary bladder.

e. Renal Vein and Renal Artery

Two of the body‘s crucial blood vessels, renal vein and renal artery. This two vessel are branch of from the abdominal aorta (the abdominal portion of the major artery leading from the heart) and enter into each kidney by attach to the concave part of the kidney.

At the inner concavity of each kidney there is an opening, known as the hilum, through which the renal artery passes. After passing through the hilum, the renal artery divides ordinarily into two large branches, and each branch divides into a number of smaller arteries, which bring blood to the nephrons, the functioning units of the kidney. Blood that has been processed by the nephrons ultimately reaches the renal vein, which carries it back to the inferior vena cava and to the right side of the heart.

f. Nephron



The most important function of kidneys is to remove waste substances from the blood. Nephrons are the functional unit of the kidney in performing this task. Nephrons produce urine in the process of removing waste and excess substances from the blood. There are about 1.000.000 nephrons in each human kidney. These remarkable structure extend between the cortex and the medulla. Under magnification, nephrons look like tangles of tiny vessels or tubules, but each nephron actually has an orderly arrangement that makes possible filtration of wastes from the blood. Each nephron in the mammalian kidney is about 30-55 mm long. At one end of nephron is closed, expanded and folded into a double-walled cuplike structure. This structure, called the corpuscular capsule, or Bowman‘s capsule. This capsule enclose glomerulus, the nephron‘s primary structure in filtering function.

Structure of nephron explained in detail below:

1). Glomerulus

The glomerulus is the main filter of the nephron and is located within the Bowman's capsule. A glomerulus and its surrounding Bowman's capsule constitute a renal corpuscle, the basic filtration unit of the kidney. From the Bowman‘s Capsule, extends a narrow vessel, called the proximal convoluted tubule. This tubule twists and turns until it drains into a collecting tubule that carries urine toward the renal pelvis.

Glomerulus is a network of extremely thin blood vessels called capillaries. The glomerulus resembles a twisted mass of tiny tubes through which the blood passes. The glomerulus is semipermeable, allowing water and soluble wastes to pass through and be excreted out of the Bowman's capsule as urine. The filtered blood passes out of the glomerulus into the Efferent arteriole to be returned through the medullary plexus to the intralobular vein. A large volume of ultrafiltrate is produced by the glomerulus into the capsule. As this liquid traverses the proximal convoluted tubule, most of its water and salts are reabsorbed, some of the solutes completely and others partially.

A glomerulus is a capillary tuft surrounded by Bowman's capsule in nephrons. It receives its blood supply from an afferent arteriole of the renal circulation. Unlike most other capillary beds, the glomerulus drains into an efferent arteriole rather than a venule. The resistance of the arterioles results in high pressure in the glomerulus aiding the process of ultrafiltration where fluids and soluble materials in the blood are forced out of the capillaries and into Bowman's capsule. The rate at which blood is filtered through all of the glomeruli, and thus the measure of the overall renal function, is the glomerular filtration rate (GFR).

2) Henle's Loop

Henle's Loop is part of renal tubule which become extremely narrow that extending down away from Bowman's capsule and then back up again form a U shape. Surrounding loop of Henle and the other parts of the renal tubule is a network of capillaries, which are formed from a small blood vessel that branches out from glomerulus.

The liquid entering the loop is the solution of salt, urea, and other substances passed along from glomerulus by proximal convoluted tubule. In this tubule, most of the dissolved components needed by the body; particularly glucose, amino acids, and sodium bicarbonate, is reabsorbed into the blood. The first segment of the loop, the descending limb, is permeable to water, and the liquid reaching the bend of the loop is much richer than the blood plasma in salt and urea. As the liquid returns through the ascending limb, sodium chloride diffuses out of the tubule into the surrounding tissue, where its concentration is lower. In the third segment of the loop, the tubule wall can, if necessery, effect further removal of salt, even against the concentration gradient, in an active-transport process requiring the expenditure of energy. In a healty person the reabsorption of salt from the urine exactly maintains the bodily requirement: during periods of low salt intake, none is allowed to escape in the urine, but, in periods of high salt intake, the excess is excreted.

3) Renal Collecting Tubule

Also called Duct of Bellini, any of the long narrow tubes in the kidney that concentrate and transport urine from the nephrons, to larger ducts that connect with the renal calyces. The liquid from the loop of Henle get into the Distal Convoluted Tubule in which reabsorbtion of sodium continues throughout the whole distal tubule. This reabsorbtion extends to the early part of the Renal Collecting Tubule.

Each collecting tubule is about 20-22 milimetres long and 20-50 microns in diameter. The walls of the tubule are composed of cell with hairlike projection, flagellae, in the tube's channel. Motions of the flagellae help to move secretion through the tubes. As the collecting tubes become wider in diameter, the cells increase in height so that the wall becomes thicker.

The function of the collecting tubes are transportation of urine and absorbtion of water. It is thought that the tissue of the kidney's medulla, or inner substance, contains a high concentration of sodium. As the collecting tubule travel through the medulla, the concentration of sodium causes water to be extracted through the tubule walls into the medulla. The water diffuses out between the collecting wall cells until the concentration of sodium is equal in the tubes and outside them. Removal of water from the solution in the tubes serves to concentrate the urine content and conserve body water.

3. Kidney Functions:

1. Urine Production And Blood Filtration:

1) Blood with waste enters the kidney through the renal artery. The artery divides into smaller and smaller blood vessels, called arterioles, eventually ending in the tiny capillaries of the glomerulus in each of the Nephrons.

2) The Blood in kidney get into glomerulus through Affarent Arteriole. In glomerulus, blood travel through twist and turn capilaries. The capillary walls here are quite thin, and the blood pressure within the capillaries is high. The result is that water, along with any substances that may be dissolved in it—typically salts, glucose or sugar, amino acids, and the waste products urea and uric acid—are pushed out through the thin capillary walls, where they are collected in Bowman's capsule. Larger particles in the blood, such as red blood cells and protein molecules, are too bulky to pass through the capillary walls and they remain in the bloodstream. The blood, which is now filtered, leaves the glomerulus through Everent Arteriole, which branches into the meshlike network of blood vessels around the renal tubule. The blood then exits the kidney through the renal vein. Approximately 180 liters (about 50 gallons) of blood moves through the two kidneys every day.

3) Urine production begins with the substances that the blood leaves behind during its passage through the kidney—the water, salts, and other substances collected from the glomerulus in Bowman‘s capsule. This liquid, called glomerular filtrate, moves from Bowman‘s capsule through Proximal Convoluted Tubule. As the filtrate flows through the renal tubule, the network of blood vessels surrounding the tubule reabsorbs much of the water, salt, and virtually all of the nutrients, especially glucose and amino acids, that were removed in the glomerulus. This important process, called tubular reabsorption, enables the body to selectively keep the substances it needs while ridding itself of wastes. Eventually, about 99 percent of the water, salt, and other nutrients is reabsorbed. This process happens in Henle‘s Loop. the kidneys filter each day, about 1.5 liters (1.3 qt) of urine are produced.

2. Body’s Water Volume Regulator:

Other kidney ‘s essential function is to regulate the amount of water contained in the blood. This process is influenced by antidiuretic hormone (ADH), also called vasopressin, which is produced in the hypothalamus (a part of the brain that regulates many internal function) and stored in the nearby pituitary gland. Receptors in the brain monitor the blood‘s water concentration. When the amount of salt and other substance in the blood becomes to high, the pituitary gland release ADH into the bloodstream.

3. Blood Pressure Regulator:

Regulating blood pressure is linked to the kidneys' ability to excrete enough sodium chloride (salt) to maintain normal sodium balance, extracellular fluid volume and blood volume. Kidney disease is the most common cause of secondary hypertension (high blood pressure). Even minor disruptions in kidney function play a role in most (if not all) cases of high blood pressure and increased injury to the kidneys. This injury can eventually cause malignant hypertension, stroke or even death.

4. Body’s Acid Base Balance:

The kidney also adjusts the body‘s acid base balance to prevent such blood disorders as acidosis and alkalosis, both of which impair the functioning of the central nerveous system. If the blood is too acidic, meaning that there is an excess of hydrogen ions, the kidney moves these ions to the urine through the process of tubular secretion.

5. Production of Hormones:

- Erythropoietin
- Calcitriol

4. Classification of kidney diseases:

Glomerular diseases :Diabetes, systemic autoimmune diseases, systemic infections, drugs, neoplasia (including amyloidosis) Diffuse, focal or crescentic proliferative GN; focal and segmental glomerulosclerosis, membranous nephropathy, minimal change disease

Tubulointerstitial diseases: Systemic infections, autoimmune, sarcoidosis, drugs, urate, environmental toxins (lead, aristolochic acid), neoplasia (myeloma) Urinary-tract infections, stones, obstruction

Vascular diseases: Atherosclerosis, hypertension, ischemia, cholesterol emboli, systemic vasculitis, thrombotic microangiopathy, systemic sclerosis ANCA-associated renal limited vasculitis, fibromuscular dysplasia

Cystic and congenital diseases: Polycystic kidney disease, Alport syndrome, Fabry disease Renal dysplasia, medullary cystic disease, podocytopathie.

6. Effects of kidney disease:

Hyperkalemia: The ability to maintain potassium (K) excretion at near-normal levels is generally maintained in chronic kidney disease as long as both aldosterone secretion and distal flow are maintained. Another defense against potassium retention in patients with chronic kidney disease is increased potassium excretion in the GI tract, which also is under control of aldosterone.

Therefore, hyperkalemia usually develops when the GFR falls to less than 20-25 mL/min because of the decreased ability of the kidneys to excrete potassium. It can be observed sooner in patients who ingest a potassium-rich diet or if serum aldosterone levels are low, such as in type IV renal tubular acidosis commonly observed in people with diabetes or with use of angiotensin-converting enzyme (ACE) inhibitors or nonsteroidal anti-inflammatory drugs (NSAIDs).

Metabolic acidosis: Metabolic acidosis often is a mixture of normal anion gap and increased anion gap; the latter is observed generally with chronic kidney disease stage 5 but with the anion gap generally not higher than 20 mEq/L. In chronic kidney disease, the kidneys are unable to produce enough ammonia in the proximal tubules to excrete the endogenous acid into the urine in the form of ammonium. In chronic kidney disease stage 5, accumulation of phosphates, sulfates, and other organic anions are the cause of the increase in anion gap.

Metabolic acidosis has been shown to have deleterious effects on protein balance, leading to the following:

- Negative nitrogen balance
- Increased protein degradation
- Increased essential amino acid oxidation
- Reduced albumin synthesis
- Lack of adaptation to a low protein diet

Hence, metabolic acidosis is associated with protein-energy malnutrition, loss of lean body mass, and muscle weakness. The mechanism for reducing protein may include effects on adenosine triphosphate (ATP)–dependent ubiquitin proteasomes and increased activity of branched chain keto acid dehydrogenases.

Salt and water handling abnormalities: Salt and water handling by the kidney is altered in chronic kidney disease. Extracellular volume expansion and total-body volume overload results from failure of sodium and free water excretion. This generally becomes clinically manifest when the GFR falls to less than 10-15 mL/min, when compensatory mechanisms have become exhausted.

As kidney function declines further, sodium retention and extracellular volume expansion lead to peripheral edema and, not uncommonly, pulmonary edema and hypertension. At a higher GFR, excess sodium and water intake could result in a similar picture if the ingested amounts of sodium and water exceed the available potential for compensatory excretion.

Anemia: Normochromic normocytic anemia principally develops from decreased renal synthesis of erythropoietin, the hormone responsible for bone marrow stimulation for red blood cell (RBC) production. It starts early in the course of disease and becomes more severe as the GFR progressively decreases with the availability of less viable renal mass.

Bone disease: Renal bone disease is a common complication of chronic kidney disease. It results in both skeletal complications (eg, abnormality of bone turnover, mineralization, linear growth) and extraskeletal complications (eg, vascular or soft tissue calcification).

Different types of bone disease occur with chronic kidney disease, as follows:

- High-turnover bone disease due to high parathyroid hormone (PTH) levels
- Low-turnover bone disease (adynamic bone disease)
- Defective mineralization (osteomalacia)
- Mixed disease
- Beta-2-microglobulin associated bone disease

Chronic kidney disease: Most kidney problems, however, happen slowly. A person may have ―silent‖ kidney disease for years. Gradual loss of kidney function is called chronic kidney disease (CKD) or chronic renal insufficiency. People with CKD may go on to develop permanent kidney failure. They also have a high risk of death from a stroke or heart attack.

Chronic kidney disease is when one suffers from gradual and usually permanent loss of kidney function over time. This happens gradually over time, usually months to years. Chronic kidney disease is divided into five stages of increasing severity (see Table 1 below). Stage 5 chronic kidney failure is also referred to as end-stage renal disease, wherein there is total or near-total loss of kidney function and patients need dialysis or transplantation to stay alive. The term "renal" refers to the kidney, so another name for kidney failure is "renal failure." Mild kidney disease is often called renal insufficiency.

TABLE 1

Stage	Description	GFR* mL/min/1.73m^2
1	Slight kidney damage with normal or increased filtration	More than 90
2	Mild decrease in kidney function	60-89
3	Moderate decrease in kidney function	30-59
4	Severe decrease in kidney function	15-29
5	Kidney failure requiring dialysis or transplantation	Less than 15

TABLE 1: Stages of Chronic Kidney Disease

Although chronic kidney disease sometimes results from primary diseases of the kidneys themselves, the major causes are diabetes and high blood pressure.

- Type 1 and type 2 diabetes mellitus cause a condition called diabetic nephropathy, which is the leading cause of kidney disease in the United States.
- High blood pressure (hypertension), if not controlled, can damage the kidneys over time.
- Glomerulonephritis is the inflammation and damage of the filtration system of the kidneys and can cause kidney failure. Postinfectious conditions and lupus are among the many causes of glomerulonephritis.
- Polycystic kidney disease is an example of a hereditary cause of chronic kidney disease wherein both kidneys have multiple cysts.
- Use of analgesics such as acetaminophen (Tylenol) and ibuprofen (Motrin, Advil) regularly over long durations of time can cause analgesic nephropathy, another cause of kidney disease. Certain other medications can also damage the kidneys.
- Clogging and hardening of the arteries (atherosclerosis) leading to the kidneys causes a condition called ischemic nephropathy, which is another cause of progressive kidney damage.
- Obstruction of the flow of urine by stones, an enlarged prostate, strictures (narrowings), or cancers may also cause kidney disease.
- Other causes of chronic kidney disease include HIV infection, sickle cell disease, heroin abuse, amyloidosis, kidney stones, chronic kidney infections, and certain cancers.

If you have any of the following conditions, you are at higher-than-normal risk of developing chronic renal disease. Your kidney functions may need to be monitored regularly.

- Diabetes mellitus type 1 or 2
- High blood pressure
- High cholesterol
- Heart disease
- Liver disease
- Kidney disease
- Amyloidosis
- Sickle cell disease
- Systemic Lupus erythematosus
- Vascular diseases such as arteritis, vasculitis, or fibromuscular dysplasia
- Vesicoureteral reflux (a urinary tract problem in which urine travels the wrong way)
- Problems of the joints or muscles that require regular use of anti-inflammatory medications
- If you have a family history of kidney disease.

Chronic Kidney Disease Symptoms:

The kidneys are remarkable in their ability to compensate for problems in their function. That is why chronic kidney disease may progress without symptoms for a long time until only very minimal kidney function is left.

Because the kidneys perform so many functions for the body, kidney disease can affect the body in a large number of different ways. Symptoms vary greatly. Several different body systems may be affected. Notably, most patients have no decrease in urine output even with very advanced chronic kidney disease.

- Fatigue and weakness (from anemia or accumulation of waste products in the body)
- Loss of appetite, nausea and vomiting
- Need to urinate frequently, especially at night
- Swelling of the legs and puffiness around the eyes (fluid retention)
- Itching, easy bruising, and pale skin (from anemia)
- Headaches, numbness in the feet or hands (peripheral neuropathy), disturbed sleep, altered mental status (encephalopathy from the accumulation of waste products or uremic poisons), and restless legs syndrome
- High blood pressure, chest pain due to pericarditis (inflammation around the heart)
- Shortness of breath from fluid in lungs
- Bleeding (poor blood clotting)
- Bone pain and fractures
- Decreased sexual interest and erectile dysfunction

Tests: Chronic kidney disease usually causes no symptoms in its early stages. Only lab tests can detect any developing problems. Anyone at increased risk for chronic kidney disease should be routinely tested for development of this disease.

- Urine, blood, and imaging tests (x-rays) are used to detect kidney disease, as well as to follow its progress.
- All of these tests have limitations. They are often used together to develop a picture of the nature and extent of the kidney disease.

- In general, this testing can be performed on an outpatient basis.

Prevention:

Chronic kidney disease cannot be prevented in most situations. You may be able to protect your kidneys from damage, or slow the progression of the disease by controlling your underlying conditions.

- Kidney disease is usually advanced by the time symptoms appear. If you are at high risk of developing chronic kidney disease, see your healthcare provider as recommended for screening tests.

If you have a chronic condition such as diabetes, high blood pressure, or high cholesterol, follow the treatment recommendations of your healthcare provider. See your healthcare provider regularly for monitoring. Aggressive treatment of these diseases is essential

UNIT-2

LEARNING OBJECTIVE

- Acute kidney injury
- Common kidney disease

ACUTE KIDNEY INJURY:

Acute kidney injury, previously known as acute renal failure, encompasses a wide spectrum of injury to the kidneys, not just kidney failure. The definition of acute kidney injury has changed in recent years, and detection is now mostly based on monitoring creatinine levels, with or without urine output. Acute kidney injury is increasingly being seen in primary care in people without any acute illness, and awareness of the condition needs to be raised among primary care health professionals. Acute kidney injury is seen in 13–18% of all people admitted to hospital, with older adults being particularly affected. These patients are usually under the care of healthcare professionals practising in specialties other than nephrology, who may not always be familiar with the optimum care of patients with acute kidney injury. The number of inpatients affected by acute kidney injury means that it has a major impact on healthcare resources

Identifying acute kidney injury in patients with acute illness:

Investigate for acute kidney injury, by measuring serum creatinine and comparing with baseline, in adults with acute illness if any of the following are likely or present:

- chronic kidney disease (adults with an estimated glomerular filtration rate [eGFR] less than 60 ml/min/1.73 m 2 are at particular risk)
- heart failure
- liver disease
- diabetes history of acute kidney injury oliguria (urine output less than 0.5 ml/kg/hour)
- neurological or cognitive impairment or disability, which may mean limited access to fluids because of reliance on a carer hypovolaemia use of drugs with nephrotoxic potential (such as non-steroidal anti-inflammatory drugs [NSAIDs],
- aminoglycosides
- angiotensin-converting enzyme [ACE] inhibitors, angiotensin II receptor antagonists [ARBs] and diuretics) within the past week, especially if hypovolaemic use of iodinated contrast agents within the past week symptoms or history of urological obstruction, or conditions that may lead to obstruction sepsis deteriorating early warning scores.

Detecting acute kidney injury :Monitor serum creatinine regularly[2] in all adults, children and young people with or at risk of acute kidney injury

Risk factor: Anyone can get AKI. Most of the time, AKI happens in people who are already sick and in the hospital. People who are in the intensive care unit (ICU) are even more likely than people who are in other units of the hospital to have AKI. This is because people who need to be in the ICU are already very sick. Other things that can increase your risk of having AKI include:

- Being age 65 or above
- Having a kidney disease or kidney problem
- Having high blood pressure
- Having a chronic disease, such as heart disease, liver disease or diabetes
- Having peripheral artery disease (a condition that makes it hard for your blood to get to your arms and legs

Symtomps:

- Not enough urine
- Swelling in your legs, ankles or feet
- Feeling tired
- Trouble catching your breath
- Feeling confused
- Nausea
- Pain or pressure in your chest

Cause: Acute kidney injury (AKI) usually happens when your kidneys are damaged suddenly. The damage that leads to AKI may be caused by:

- Not enough blood flowing through your kidneys
- An injury directly to your kidneys or a problem with your kidneys
- A blockage in your ureters, the tubes that take urine from your kidneys to your bladder

Some examples of problems that can cause you to have too little blood flowing through your kidneys are:

- Low blood pressure
- Bleeding too much
- Having severe diarrhea
- Heart disease or heart attack
- Infection
- Liver failure
- Using NSAIDs (non-steroidal anti-inflammatory drugs), such as aspirin, ibuprofen and naproxen
- Serious burns
- Being very dehydrated (not having enough fluid in your body)
- Severe allergic reaction

Some examples of problems that can cause direct damage to your kidneys are:

- Blood clots in or around the kidneys
- Diseases that affect the kidneys, such as glomerulonephritis and lupus
- Infection
- Certain medicines, such as some chemotherapy drugs, some antibiotics and contrast dyes used during CT scans, MRI scans and other imaging tests
- Alcohol or drug abuse
- Some blood or blood vessel disorders

Some examples of problems that could cause a blockage in your urinary tract are:

- Some cancers
- Blood clots in or around the kidneys
- Kidney stones
- Bladder problems
- Enlarged prostate (in men)

Treatment: The treatment for AKI depends on what caused it to happen. Most people need to stay in the hospital during treatment and until their kidneys recover. While you are being treated for the problem that caused your AKI, you may also have treatments to prevent problems that can make it harder for your kidneys to heal. Some possible treatments include:

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

Prevention:

Because AKI happens suddenly, it can be hard to predict or prevent it. But taking good care of your kidneys can help prevent AKI, chronic kidney disease (CKD) and kidney failure/ESRD. Follow these general rules to keep your kidneys as healthy as possible:

- Work with your doctor to manage diabetes and high blood pressure.
- Live healthy! Eat a diet low in salt and fat, exercise for 30 minutes at least five days per week, limit alcohol and take all prescription medicines as your doctor tells you to.
- If you take over-the-counter pain medicines, such as aspirin or ibuprofen, do not take more than is recommended on the package. Taking too much of these medicines can hurt your kidneys and can cause AKI.

Some Common Kidney Desease:

1. Pyelonephritis

infection and inflammation of the kidney tissue and the renal pelvis (the cavity formed by the expansion of the upper end of the ureter, the tube that conveys urine to the bladder). The infection is usually bacterial. The most common type of renal disorder, pyelonephritis may be chronic or acute. Acute pyelonephritis generally affects one specific region of the kidney, leaving the rest of the kidney structure untouched. In many instances pyelonephritis develops without any apparent precipitating cause. Any obstruction to the flow of blood or urine, however, may make the kidneys more susceptible to infection, and fecal soiling of the urethral opening is thought to increase the incidence of the disease in infants (the urethra is the channel for urine from the bladder to the outside). Women may suffer injury of the urinary passages during intercourse or pregnancy, and catheterization (mechanical draining of urine) can cause infection.

2. Glomerulonephritis

Glomerulonephritis, another common kidney disease, is characterized by inflammation of some of the kidney's glomeruli. This condition may occur when the body‘s immune system is impaired. Antibodies and other substances form large particles in the bloodstream that become trapped in the glomeruli. This causes inflammation and prevents the glomeruli from working properly. Symptoms may include blood in the urine, swelling of body tissues, and the presence of protein in the urine, as determined by laboratory tests. Glomerulonephritis often clears up without treatment. When treatment is necessary, it may include a special diet, immunosuppressant drugs, or plasmapheresis, a procedure that removes the portion of the blood that contains antibodies.

Glomerulonephritis is the disorder commonly known as nephritis, or Bright's disease. The primary impact of the disease is on the vessels of the glomerular tuft. The suffix ―itis‖ suggests an inflammatory lesion, and glomerulonephritis is indeed associated with infection, in the limited sense that it may begin soon after a streptococcal infection and may be aggravated in its later course by infections of various kinds. Nevertheless, there is convincing evidence that glomerulonephritis does not represent a direct attack on the kidney by an infective agent; it appears to be, rather, an immunologic disorder, in the sense of the formation of antibodies in response to the presence of a foreign protein (antigen) elsewhere in the body; these form antigen–antibody complexes that lodge in the glomerular tuft or, in a small number of cases, themselves become deposited on the capillary glomerular walls. In each case the antibody or the antigen–antibody complex reaches the kidney via the circulation, and the mechanism is usually referred to as circulating complex disease.

3. Kidney Stone

also called Renal Calculus, plural Renal Calculi, concretion of minerals and organic matter that forms in the kidneys. Such stones may become so large as to impair normal renal function. Urine contains many salts in solution and if the concentration of mineral salts becomes excessive, the excess salt precipitates as solid particles called stones. Kidney stones are classified as primary if they form without apparent cause, such as an infection or obstruction. They are classified as secondary if they develop after a renal infection or disorder.

Certain circumstances increase the likelihood of stone formation. Either a reduction in fluid volume or a surge in mineral concentration can be enough to upset the delicate balance between the liquid and its solutes. Once a stone starts developing, it generally continues to grow. A nucleus for precipitation of urinary salts can be a clump of bacteria, degenerated tissue, sloughed-off cells, or a tiny blood clot. Minerals start collecting around the foreign particle and encrusting it. As the stone increases in size, the surface area available for additional mineral deposition is continually increased.
Smaller kidney stones can pass out of the body on their own, although this can be painful. Larger stones may require surgery, or they may be broken into smaller pieces with sound waves in a procedure called ultrasonic lithotripsy.

4. Kidney Failure

also called Renal Failure, partial or complete loss of kidney function. Kidney failure is classified as acute (when the onset is sudden) or chronic.

Acute kidney failure results in reduced output of urine, abnormally high levels of nitrogenous substances, potassium, sulfates, and phosphates in the blood, and abnormally low blood levels of sodium, calcium, and carbon dioxide (see uremia). Ordinarily the affected person recovers in six weeks or less.

Causes of kidney failure include destruction of the tubules in the kidney by drugs or organic solvents such as carbon tetrachloride, acetone, and ethylene glycol; exposure to compounds of metals such as mercury, lead, and uranium; physical injuries or major surgery causing much loss of blood or an increase in blood pressure; severe burns; and incompatible blood transfusions. Renal failure can also result from diseases that destroy the cortex (outer substance) of the kidney; from severe bacterial infections of the kidney; from diabetes that causes destruction of the medulla (the inner substance) of the kidney; and from overabundance of calcium salts in the kidneys.

Blockage of the renal arteries, liver diseases, and obstruction of the urinary tract produce acute failure; on rare occasions, kidney failure can occur without apparent symptoms. Complications that arise from kidney failure include heart failure, pulmonary edema, and an overabundance of potassium in the body.

Chronic renal failure is usually the result of prolonged diseases of the kidney. In chronic failure the blood becomes more acidic than normal and there can be loss of calcium from the bones. Nerve degeneration can also occur.

UNIT-3

LEARNING OBJECTIVES

- Lab assessment of kidney disease
- RRT

General Laboratory assessment of Kidney Disease:
Laboratory tests for renal function:

- Urinalysis Volume Haematuria, proteinuria, glycosuria, bacteriuria Specific gravity Osmolality Urinary sodium Fractional excretion of sodium Microscopy
- Creatinine clearance
- Free water clearance
- Serum urea and creatinine
- Urine:serum creatinine ratio
- Urine:serum urea ratio
- Tubular function tests
- Proximal tubular function K+ HCO3 PO4 Glucose Amino acids β2-microglobulin
- Distal tubular function Urinary concentrating capacity in response to water deprivation Measurement of urinary acidification
- Renal blood flow
- Endocrine function tests Measurement of erythropoietin production Renin assays Aldosterone assays 1,25-dihydroxicholecalciferol synthesi

Blood tests:

- Estimated Glomerular Filtration Rate (eGFR) - The best measure of your kidney function. It shows how well your kidneys are cleaning your blood. Your eGFR is usually estimated from the results of the creatinine blood test. eGFR is reported in millilitres per minute per 1.73m2 (mL/min/1.73m2). An eGFR of 100 mL/min/1.73m2 is in the normal range, so it is useful to say that 100 mL/min/1.73m2 is equal to ‗100% kidney function'. An eGFR of 50 mL/min/1.73m2 could be called ‗50% kidney function'.
- Creatinine - A waste product made by the muscles. It is usually removed from the blood by the kidneys and passes out in the urine. When your kidneys aren't working well, creatinine stays in the blood. Creatinine varies with age, gender and body weight, so it's not an accurate way of measuring overall kidney function. When on dialysis, creatinine levels are always high.
- Urea - A waste product made as the body breaks down protein. High urea levels suggest decreased kidney function.

Urine tests:

- Albumin:Creatinine Ratio (ACR) - Used to measure the amount of albumin (a kind of protein) that leaks into your urine when your kidneys are damaged. A small or ‗micro' amount of albumin in the urine is called microalbuminuria, and a larger, ‗macro', amount is called macroalbuminuria.
- Urinalysis - The examination of your urine sample to detect medical conditions like kidney and liver disease, diabetes and urinary tract infections. This can be a visual examination for colour and clearness. A chemically treated strip or dipstick is used to test for pH, sugar (glucose), blood, bacteria, or waste products. A urine sample can be sent to a laboratory for examination under a microscope or to grow a culture (sample test) if an infection is suspected.

Renal replacement therapy:

It is estimated that a third of patients in the critical care setting have an AKI2 and approximately 5% will require renal replacement therapy (RRT).3 The hospital mortality in patients with an AKI requiring RRT is as high as 60%.4 The initial management of AKI involves treating the underlying cause, stopping nephrotoxic drugs and ensuring that the patient is euvolaemic, with an adequate mean arterial blood pressure. However, no specific treatments have been shown to reverse the course of AKI, so RRT forms the basis of further management.

Replacement Therapy Includes:

dialysis (hemodialysis or peritoneal dialysis), hemofiltration, and hemodiafiltration, which are various ways of filtration of blood with or without machines.

Renal replacement therapy also includes kidney transplantation, which is the ultimate form of replacement in that the old kidney is replaced by a donor kidney.

Haemodialysis :involves blood being pumped through an extracorporeal system that contains a dialyser. Blood flows through the dialyser in one compartment, separated from crystalloid solution (dialysate) in a second compartment, by a semipermeable membrane. Solutes move across the membrane, down their concentration gradient (i.e. from high concentration to low) from one compartment of the dialyser to the other (Fick`s law of diffusion). For example, bicarbonate moves from dialysate to blood whereas urea and potassium move from blood to dialysate. In order to maintain these essential concentration gradients and enhance the efficiency of the system the dialysate flows in the opposite direction to the flow of blood (countercurrent). When removal of water is required, the hydrostatic pressure on the blood side of the membrane is increased in order to force water molecules into the dialysate compartmen

Haemodiafiltration: is a combination of filtration and dialysis. There is no evidence to suggest that CVVDF has a survival benefit when compared to CVVH, but if may be a useful way of increasing clearance of small solutes

Haemofiltration: involves blood being pumped through an extracorporeal system that contains a semi-permeable membrane. The hydrostatic pressure that is created on the blood-side of the filter drives plasma water across the filter. This process is referred to as ultrafiltration. Molecules that are small enough to pass through the membrane are dragged across the membrane with the water by the process of convection. The filtered fluid (ultrafiltrate) is discarded and a replacement fluid is added in an adjustable fashion, according to the desired fluid balance

INDICATIONS FOR RRT

Indications for RRT are: 1.Acute kidney injury (AKI) with:

- Fluid overload (unresponsive to diuretics)
- Hyperkalemia ($K^+ > 6.5$)
- Severe metabolic acidosis ($pH < 7.1$)
- Rapidly climbing urea/creatinine (or urea > 30mmol.L-1)
- Symptomatic uraemia:encephalopathy, pericarditis, bleeding, nausea, pruritus
- Oliguria/anuria

2. Overdose with a dialysable drug or toxin:

Some drugs are removed by RRT but some are not. As a general rule, drugs are cleared by RRT if they are water soluble and not highly protein bound

3. Severe sepsis:

Recent studies have investigated the role of haemofiltration in removal of inflammatory mediators in patients with severe sepsis and septic shock

Type of RRT:

1. Continuous renal replacement therapy (CRRT)

- continuous hemodialysis (CHD)
  - continuous arteriovenous hemodialysis (CAVHD)
  - continuous venovenous hemodialysis (CVVHD)
- continuous hemofiltration (CHF)
  - continuous arteriovenous hemofiltration (CAVH or CAVHF)
  - continuous venovenous hemofiltration (CVVH or CVVHF)
- continuous hemodiafiltration (CHDF)
  - continuous arteriovenous hemodiafiltration (CAVHDF)
  - continuous venovenous hemodiafiltration (CVVHDF)

2. Intermittent renal replacement therapy (IRRT)

- intermittent hemodialysis (IHD)
  - intermittent venovenous hemodialysis (IVVHD)
- intermittent hemofiltration (IHF)
  - intermittent venovenous hemofiltration (IVVH or IVVHF)
- intermittent hemodiafiltration (IHDF)
  - intermittent venovenous hemodiafiltration (IVVHDF)

Kidney transplantation:

Kidney transplantation or renal transplantation is the organ transplant of a kidney into a patient with end-stage renal disease. Kidney transplantation is typically classified as deceased-donor (formerly known as cadaveric) or living-donor transplantation depending on the source of the donor organ.

Common Causes of End-Stage Renal Disease

Diabetes mellitus

High blood pressure

Glomerulonephritis

Polycystic Kidney Disease

Severe anatomical problems of the urinary tract

Indications:

The indication for kidney transplantation is end-stage renal disease (ESRD), regardless of the primary cause. This is defined as a glomerular filtration rate < 15 ml/min/1.73 m^2.

Common diseases leading to ESRD include malignant hypertension, infections, diabetes mellitus, and focal segmental glomerulosclerosis; genetic causes include polycystic kidney disease, a number of inborn errors of metabolism, and autoimmune conditions such as lupus.

Diabetes is the most common known cause of kidney transplantation, accounting for approximately 25% of those in the US. The majority of renal transplant recipients are on dialysis (peritoneal dialysis or hemodialysis) at the time of transplantation. However, individuals with chronic kidney disease who have a living donor available may undergo pre-emptive transplantation before dialysis is needed. If a patient is put on the waiting list for a deceased donor transplant early enough, they may also be transplanted pre-dialysis.

Contraindications :

Contraindications include both cardiac and pulmonary insufficiency, as well as hepatic disease and some cancers. Concurrent tobacco use and morbid obesity are also among the indicators putting a patient at a higher risk for surgical complications.

Sources of kidneys:

Living donors

Sometimes family members, including brothers, sisters, parents, children (18 years or older), uncles, aunts, cousins, or a spouse or close friend may wish to donate a kidney. That person is called a "living donor." The donor must be in excellent health, well informed about transplantation, and able to give informed consent. Any healthy person can donate a kidney safely.

Deceased donors

A deceased donor kidney comes from a person who has suffered brain death. The Uniform Anatomical Gift Act allows everyone to consent to organ donation for transplantation at the time of death and allows families to provide such permission as well. After permission for donation is granted, the kidneys are removed and stored until a recipient has been selected.

Transplant Evaluation Process:

Regardless of the type of kidney transplant-living donor or deceased donor-special blood tests are needed to find out what type of blood and tissue is present. These test results help to match a donor kidney to the recipient.

Blood Type Testing*:*

If the recipient blood type is A Donor blood type must be A or O

If the recipient blood type is B Donor blood type must be B or O

If the recipient blood type is O Donor blood type must be O

If the recipient blood type is AB Donor blood type can be A, B, AB, or O

The AB blood type is the easiest to match because that individual accepts all other blood types.

Blood type O is the hardest to match. Although people with blood type O can donate to all types, they can only receive kidneys from blood type O donors. For example, if a patient

with blood type O received a kidney from a donor with blood type A, the body would recognize the donor kidney as foreign and destroy it.

Tissue Typing:

The second test, which is a blood test for human leukocyte antigens (HLA), is called tissue typing. Antigens are markers found on many cells of the body that distinguish each individual as unique. These markers are inherited from the parents. Both recipients and any potential donors have tissue typing performed during the evaluation process.

To receive a kidney where recipient's markers and the donor's markers all are the same is a "perfect match" kidney. Perfect match transplants have the best chance of working for many years. Most perfect match kidney transplants come from siblings.

Although tissue typing is done despite partial or absent HLA match with some degree of "mismatch" between the recipient and donor.

Crossmatch:

The crossmatch is done by mixing the recipient's blood with cells from the donor. If the crossmatch is positive, it means that there are antibodies against the donor. The recipient should not receive this particular kidney unless a special treatment is done before transplantation to reduce the antibody levels. If the crossmatch is negative, it means the recipient does not have antibodies to the donor and that they are eligible to receive this kidney.

Pre-transplant Period:

This period refers to the time that a patient is on the deceased donor waiting list or prior to the completion of the evaluation of a potential living donor. The recipient undergoes testing to ensure the safety of the operation and the ability to tolerate the anti-rejection medication necessary after transplantation.

Procedure:

Transplant Surgery

The transplant surgery is performed under general anesthesia. The operation usually takes 2-4 hours. This type of operation is a heterotopic transplant meaning the kidney is placed in a different location than the existing kidneys. (Liver and heart transplants are orthotopic transplants, in which the diseased organ is removed and the transplanted organ is placed in the same location.) The kidney transplant is placed in the front (anterior) part of the lower abdomen, in the pelvis.

The original kidneys are not usually removed unless they are causing severe problems such as uncontrollable high blood pressure, frequent kidney infections, or are greatly enlarged. The artery that carries blood to the kidney and the vein that carries blood away is surgically connected to the artery and vein already existing in the pelvis of the recipient. The ureter, or tube, that carries urine from the kidney is connected to the bladder. Recovery in the hospital is usually 3-7 days.

Complications can occur with any surgery. The following complications do not occur often but can include:

- Bleeding, infection, or wound healing problems.
- Difficulty with blood circulation to the kidney or problem with flow of urine from the kidney.
- These complications may require another operation to correct them.

UNIT-4

LEARNING OBJECTIVE:

- Haemodialysis
- Peritoneal dialysis

Dialysis:

In end-stage renal disease, kidney functions can be replaced only by dialysis or by kidney transplantation. See the Transplant section for more information about transplants. There are two types of dialysis 1) haemodialysis and 2) peritoneal dialysis.

Haemodialysis:

Haemodialysis involves circulation of blood through a filter on a dialysis machine. Blood is cleansed of waste products and excess water. The acid levels and the concentration of various minerals such as sodium and potassium in the blood are normalized. The blood is then returned to the body.

- Long-term dialysis requires access to a blood vessel so that the machine has a way to remove and return blood to the body. This may be in the form of a dialysis catheter or an arteriovenous fistula or graft.
- A catheter may be either temporary or permanent. These catheters are either placed in the neck or the groin into a large blood vessel. These catheters are prone to infection and may also cause blood vessels to clot or narrow.
- The preferred access for hemodialysis is an arteriovenous fistula wherein an artery is directly joined to a vein. The vein takes two to four months to enlarge and mature before it can be used for dialysis. Once matured, two needles are placed into the vein for dialysis. One needle is used to draw blood and run through the dialysis machine. The second needle is to return the cleansed blood.
- An arteriovenous graft is placed in patients who have small veins or in whom a fistula has failed to develop. The graft is made of artificial material and the dialysis needles are inserted into the graft directly.
- These venous access devices usually can be placed with local anesthesia on an outpatient basis.
- Hemodialysis typically takes three to five hours and is needed three times a week.
- You will need to travel to a dialysis center for hemodialysis.
- Home hemodialysis is possible in some situations. A care partner is needed to assist you with the dialysis treatments. A family member or close friend are the usual options, though occasionally patients may hire a professional to assist with dialysis. Home hemodialysis may be performed as traditional three times a week treatments, long nocturnal (overnight) hemodialysis, or short daily hemodialysis. Daily hemodialysis and long nocturnal hemodialysis offer advantages in quality of life and better control of high blood pressure, anemia, and bone disease.

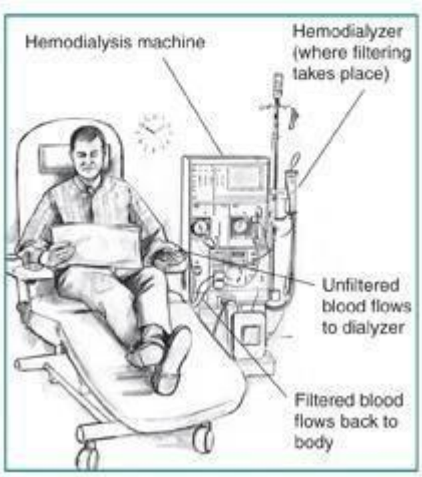


Fig: hemodialysis

Peritoneal dialysis:

Peritoneal dialysis utilizes the lining membrane (peritoneum) of the abdomen as a filter to clean blood and remove excess fluid. A catheter is implanted into the abdomen by a minor surgical procedure. Peritoneal dialysis may be performed manually or by using a machine to perform the dialysis at night.

- About 2 to 3 liters of dialysis fluid are infused into the abdominal cavity through this catheter. This fluid contains substances that pull wastes and excess water out of neighboring tissues.
- The fluid is allowed to dwell for two to several hours before being drained, taking the unwanted wastes and water with it.
- The fluid typically needs to be exchanged four to five times a day.
- Peritoneal dialysis offers much more freedom compared to hemodialysis since patients do not need to come to a dialysis center for their treatment. You can carry out many of your usual activities while undergoing this treatment. This may be the preferable therapy for children.

Most patients are candidates for both hemodialysis and peritoneal dialysis. There are little differences in outcomes between the two procedures. Your physician may recommend one kind of dialysis over the other based on your medical and surgical history. It is best to choose your modality of dialysis after understanding both procedures and matching them to your life style, daily activities, schedule, distance from the dialysis unit, support system, and personal preference.

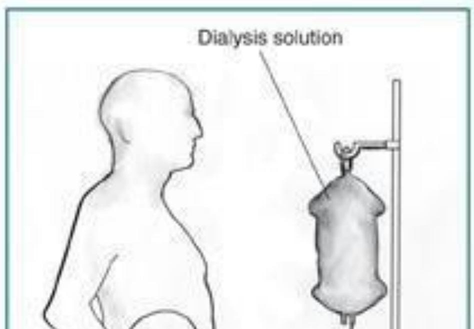


Fig: Peritoneal dialysis