DEPARTMENT OF ELECTRONICS AND COMMUNICATION ENGINEERING

CBM352 Human Assist Devices

UNIT-III ARTIFICIAL KIDNEY

3.1 Indication and Principle of Haemodialysis

1.1.1 Physiology of Kidney:

i. The urinary system of man which is the excretory system consists of kidney, ureters, urinary bladder and urethera.
ii. The kidney is the chief excretory organ which helps in removal of nitrogenous waste materials. Ammonia and urea are chief nitrogenous wastes produced during metabolism. Both urea and ammonia are taken to the kidney by the blood stream and the kidney excrete urea and ammonia in the urine along with uric acid, salts and water.

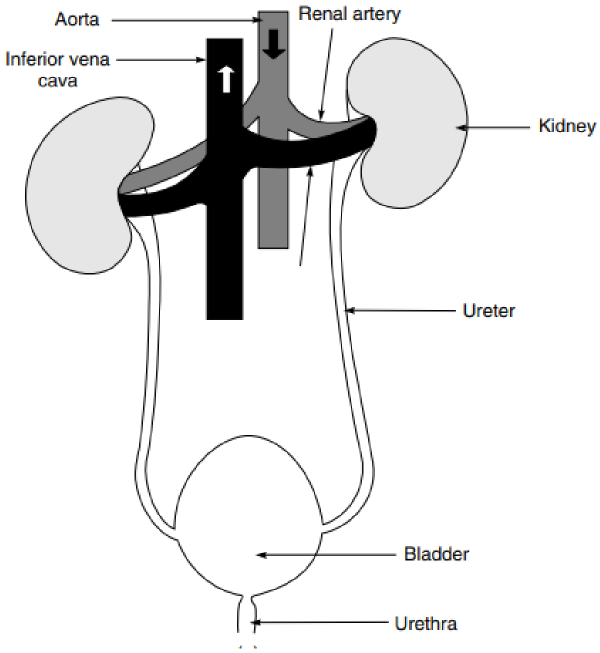


Fig. 3.1.1 Kidneys and their connection to other organs of the body

iii. The kidneys are dark red, bean shaped paired structures placed one or either side of the median vertebral column in the lumbar region. Each kidney is about 11 cm in length, 6 cm is breadth and 3 cm in thickness. Each kidney of the human adult weights about 150 gms and is about the size of a clenched fist.

iv. The right kidney is on a slightly lower level than the left. This is because the right side of the abdominal cavity is occupied by the liver.

v. Each kidney of the human is covered by a tough transparent membrane, the fibrous capsule. Outer surface of the kidney is convex while the inner is concave.

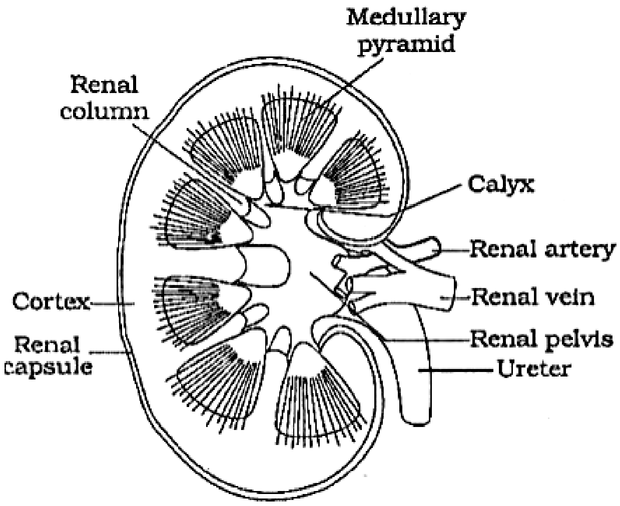


Fig. 3.1.2 Longitudinal Section of Kidney

vi. The two major regions of the kidney are the outer dark cortex and pale inner medulla. The medulla is divided into multiple cone shaped masses of tissue called renal pyramids. The base of each pyramid originates at the border between the cortex and medulla. (The medulla is divided into multiple cone shaped masses of tissue called renal pyramids.)

vii. The base of each pyramid originates at the border between the cortex and medulla and it terminates in the papilla, which projects into the space of the renal pelvis, a funnel shaped continuation of the upper end of the ureter. Each kidney is made of a number of nephrons. These nephrons are structural and functional units of the kidneys.

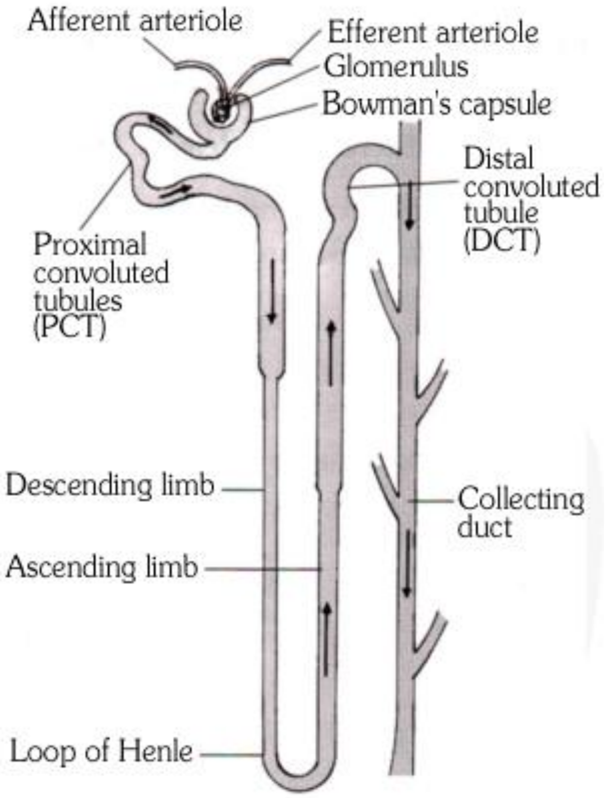


Fig. 3.1.3 Structure of Nephron

viii. An individual nephron consists of a cup shaped malphigian corpuscle and a renal tubule. The head part of the malphigian corpuscle lie in the cortex region of the kidney, and the renal tubules are placed on the medulla.

ix. The malphigian corpuscle consists of a round cup shaped structure called Bowman's capsule. The wall of the Bowman's capsule comprises of a ball of finely divided blood capillaries called the glomerulus. The wall of the Bowman's capsule consists of a single layer of flat cells having minute pores.

x. From the malphigian corpuscles arises the renal tubule. The renal tubule is partly convoluted and partly straight. The renal tubule can be distinguished into 3 regions namely

 (i) Proximal convoluted tubule
 (ii) Henle's loop
 (iii) Distal convoluted tubule

xi. Proximal convoluted tubule in composed of a single layer of columnar epithelial cells. The proximal convoluted tubule extends in the form of a hair pin like structure called Henle's loop. Henle's loop continues in the from of distal convoluted tubule which leads to a collecting tube. The collecting tubules open into a larger tubule called the duct of Bellini which in turn opens into the pelvis.

1.1.2 Indication and Principle of Haemodialysis:

Hemodialysis is a procedure where a dialysis machine and a special filter called an artificial kidney, or a dialyzer, are used to clean the blood.

- Hemodialysis initiation is needed for acute illness associated with:
  - Acute kidney injury
  - Uremic encephalopathy
  - Pericarditis
  - Life-threatening hyperkalemia
  - Refractory acidosis
  - Hypervolemia causing end-organ complications (e.g., pulmonary edema)
  - Failure to thrive and malnutrition
  - Peripheral neuropathy
  - Intractable gastrointestinal symptoms
  - Asymptomatic patients with a GFR of 5 to 9 mL/min/1.73 m^2
  - Any toxic ingestion

Dialysis is a life saving process. The decision to carry out dialysis may be made in the case of either chronic or acute illness.

- **<u>Acute or sudden illness</u>**

Examples of acute conditions where dialysis may be used include:

- **Metabolic acidosis** or a change of the blood pH to acidic. Usually, this condition can be treated by neutralizing the acidic blood with sodium bicarbonate. However, dialysis may be needed in cases where this is impractical or if there is a risk of fluid overload.

- **Electrolyte imbalance** such as severe hyperkalemia where the blood level of potassium is raised.

- **Overload of fluid** in the body that diuretics cannot relieve.

- **Acute poisoning** where the harmful substance can be removed by dialysis. Lithium, a drug used to treat mood disorders and the pain reliever aspirin are two examples of drugs that can be removed using dialysis

- **Uremia** - Certain complications of the condition uremia where urea and other waste material builds up in the blood. Such complications include pericarditis (inflammation of the pericardium in the heart), encephalopathy or a disease affecting brain function and gastrointestinal tract bleeding.

- **Chronic or long-term illness:**

- Renal failure where symptoms are manifesting
- In the case of a lowered glomerular filtration rate (GFR) that has dropped to less than 10-15 mls/min/1.73m2, although in diabetics dialysis is started before this stage is reached.
- In cases of low GFR where medication is unable to control fluid overload and rising levels of serum potassium or phosphorus.

- However, dialysis may be needed in cases where this is impractical or if there is a risk of fluid overload. Electrolyte imbalance such as severe hyperkalemia where the blood level of potassium is raised. Overload of fluid in the body that diuretics cannot relieve.
- It is generally patients with **Stage 5 CKD** that are considered candidates to start dialysis therapy or be considered for kidney transplantation. Once dialysis or transplantation is felt to be necessary, this is called End Stage Renal Disease (ESRD).
- The top two indicators: **Kt/V and URR**
  Kt/V should be at least 1.2 or above—Kt/V stands for clearance multiplied by time divided by volume. This ratio allows your doctor to understand how well waste has been removed by your dialysis treatment. URR should be at least 65%—URR stands for urea reduction ratio.

Principle of Haemodialysis:

Dialysis is a technique of removing toxic substances in blood using a machine when the kidneys are unable to perform their excretory function. The dialysis machine, which is also called an artificial kidney, is used for this purpose.

Blood from an artery of an arm of the patient is passed through the dialysis machine, which removes urea and excess salts. The blood is then passed back to the patient's body through a vein.

1.1.3 Principles of dialysis with an artificial kidney

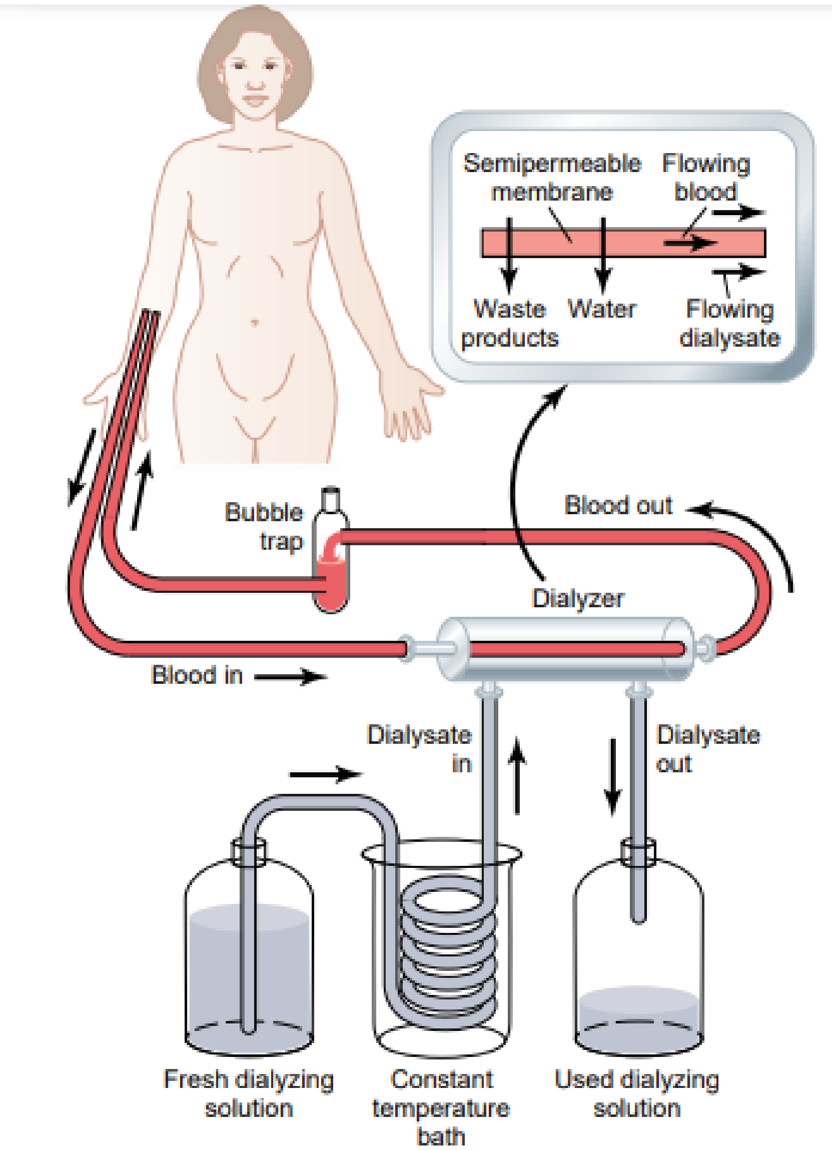


Fig. 3.1.4 Principles of dialysis with an artificial kidney

1. Figure shows the components of one type of artificial kidney in which blood flows continually between two thin membranes of cellophane; outside the membrane is a dialyzing fluid. The cellophane is porous enough to allow the constituents of the plasma, except the plasma proteins, to diffuse in both directions—from plasma into the dialyzing fluid or from the dialyzing fluid back into the plasma. If the concentration of a substance is greater in the plasma

than in the dialyzing fluid, there will be a net transfer of the substance from the plasma into the dialyzing fluid.

2. The rate of movement of solute across the dialyzing membrane depends on

    (1) the concentration gradient of the solute between the two solutions,

    (2) the permeability of the membrane to the solute,

    (3) the surface area of the membrane, and

    (4) the length of time that the blood and fluid remain in contact with the membrane.

3. Thus, the maximum rate of solute transfer occurs initially when the concentration gradient is greatest (when dialysis is begun) and slows down as the concentration gradient is dissipated. In a flowing system, as is the case with "hemodialysis," in which blood and dialysate fluid flow through the artificial kidney, the dissipation of the concentration gradient can be reduced and diffusion of solute across the membrane can be optimized by increasing the flow rate of the blood, the dialyzing fluid, or both.

4. In normal operation of the artificial kidney, blood flows continually or intermittently back into the vein. The total amount of blood in the artificial kidney at any one time is usually less than 500 milliliters, the rate of flow may be several hundred milliliters per minute, and the total diffusion surface area is between 0.6 and 2.5 square meters.

5. To prevent coagulation of the blood in the artificial kidney, a small amount of heparin is infused into the blood as it enters the artificial kidney. In addition to diffusion of solutes, mass transfer of solutes and water can be produced by applying a hydrostatic pressure to force the fluid and solutes across the membranes of the dialyzer; such filtration is called bulk flow.

1.1.4 Dialysate (Or) Dialyzing Fluid:

- Dialysis machines employ a proportioning system that mixes an acid concentrate with a bicarbonate concentrate and purified water. This allows for the generation of a dialysate with a physiologic pH and minimizes the possibility of forming a precipitate between bicarbonate containing alkaline solutions and calcium.

- The acid concentrate contains dextrose and is the source of electrolytes including potassium, calcium, magnesium, and acetic (or citric) acid.
- High dialysate sodium concentrations can lead to sodium loading, increased thirst, and subsequent high weight gains and hypertension.
- Sodium is removed from the patient both by ultrafiltration (for patients with large weight gains) and by diffusion
- Concentrations of ions and other substances in dialyzing fluid are not the same as the concentrations in normal plasma or in uremic plasma. Instead, they are adjusted to levels that are needed to cause appropriate movement of water and solutes through the membrane during dialysis.
- Note that there is no phosphate, urea, urate, sulfate, or creatinine in the dialyzing fluid; however, these are present in high concentrations in the uremic blood. Therefore, when a uremic patient is dialyzed, these substances are lost in large quantities into the dialyzing fluid.
- The effectiveness of the artificial kidney can be expressed in terms of the amount of plasma that is cleared of different substances each minute, is the primary means for expressing the functional effectiveness of the kidneys themselves to rid the body of unwanted substances.
- Most artificial kidneys can clear urea from the plasma at a rate of **100 to 225 ml/min**, which shows that at least for the excretion of urea, the artificial kidney can function about twice as rapidly as two normal kidneys together, whose urea clearance is only 70 ml/min. Yet the artificial kidney is used for only 4 to 6 hours per day, three times a week. Therefore, the overall plasma clearance is still considerably limited when the artificial kidney replaces the normal kidneys.
- Also, it is important to keep in mind that the artificial kidney cannot replace some of the other functions of the kidneys, such as secretion of erythropoietin, which is necessary for red blood cell production.

1.1.5 Functions of Artificial Kidney:

1. Artificial kidney temporarily replaces the function of kidney and thus will reduce the accumulation of waste products and remove toxic substance from the body.
2. It receives the patients blood via a cannulated artery through a plastic tube.

3. The dialysate is an electrolyte solution of suitable composition and the dialysis takes place across a membrane of cellophane.
4. The return of the dialyzed blood is by another plastic tube to an appropriate vein.
5. The dialyzing membrane has perforations which are extremely small (Fig. 3.1.5) and are invisible to the naked eye.
6. Waste products in the blood are able to pass through these minute perforations into the dialysate fluid from where they are immediately washed away.
7. The perforations in the dialysis membrane have an average diameter of 50 Å with an estimated range of 30 Å to 90 Å.
8. The waste products pass through the membrane because of the existence of a concentration gradient across the membrane.
9. The dialysate fluid is free of waste product molecules and, therefore, those in the blood would tend to distribute themselves evenly throughout the blood and the dialysate. This movement of waste product molecules from the blood to the dialysate results in cleaning of the blood.
10. The volume of body fluid cannot be controlled by dialysis. Instead, ultra-filtration across the membrane is employed. For this, a positive pressure is applied to the blood compartment or a negative pressure established in the dialysate compartment. Either way, fluid—both water and electrolytes—will move from the blood compartment to the dialysate, which is subsequently discarded.
11. The degree of ultra-filtration depends both on the pressure difference across the membrane and the ultra-filtration characteristics of the membrane.
12. The artificial kidney is thus simply a membrane separation device that serves as a mass exchanger during clinical use. It is unable to perform any of the synthetic or metabolic functions of the normal kidney and, therefore, cannot correct abnormalities that result from the loss of these functions. The only use of the artificial kidney in replacing renal function, therefore, is the transfer of poisonous substances from the blood to the dialysate, so that they might be eliminated from the body.

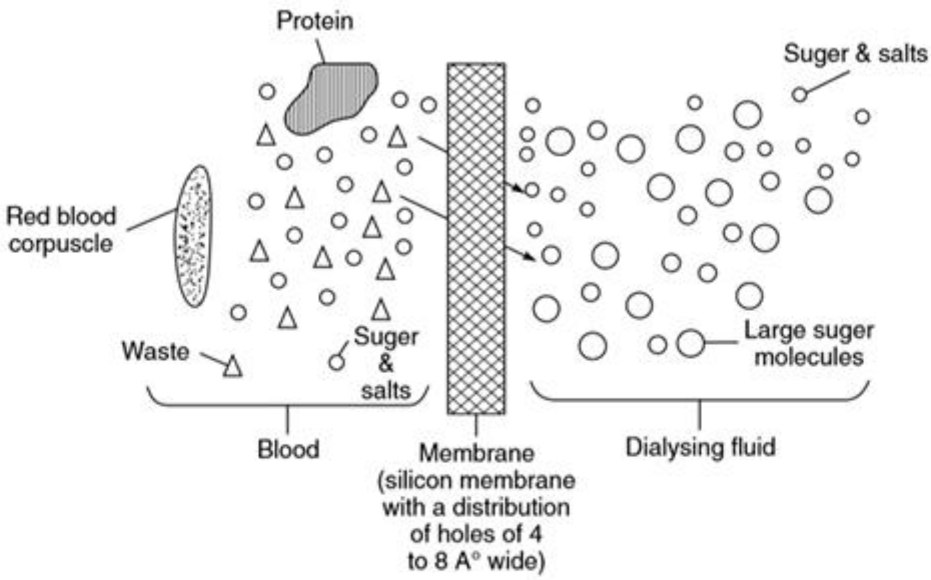
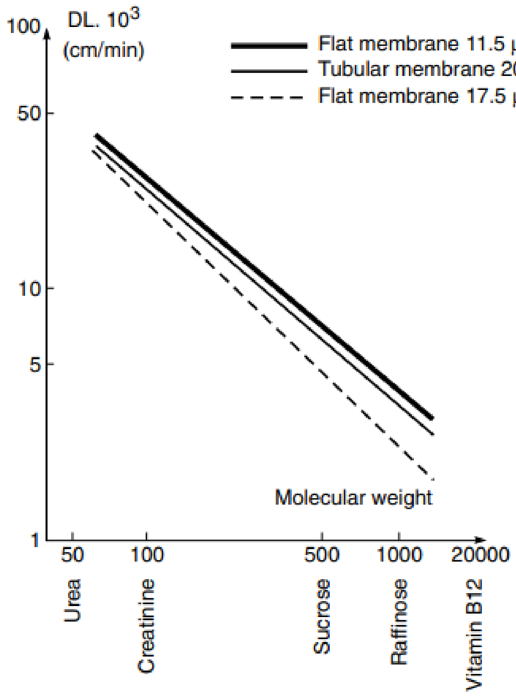


Fig. 3.1.5 Principle of dialysis in the artificial kidney

1.1.6 Membranes for Haemodialysis:

1. The efficiency of dialysis is determined by the permeability characteristics of the semi-permeable membrane. The ideal membrane should possess high permeability to water, organic metabolites and ions, and the capability of retaining plasma proteins.
2. The membrane should be of sufficient wet strength to resist tearing or bursting and non-toxic to blood and all body cells. Since a fresh membrane is required for each dialysis process.
3. It should be inexpensive to produce.
4. Virtually all artificial kidneys presently in use, employ cellulosic membranes. Such membranes operate as sieve-type membranes allowing the passage of solutes through micro-holes. Therefore, selective sieving of the blood is based upon the size, shape and density of the solute
5. Cupraphan (trademark of Enka Glanzstoff, Germany) is the commonly used membrane for haemodialysis. It is a membrane consisting of natural cellulose and is considered puncture-proof, and of high tenacity and elasticity. During haemodialysis, different substances of varying molecular weight are to be removed. The specific membrane permeability values and their dependency on substances with increasing molecular weight are shown in Figure.

6. Cupraphan is a moisture-sensitive cellulose hydrate membrane whose reaction during processing and whose functional value depends upon the water content. If it varies from the fixed standard values, consequently, it exhibits dimensional instability pertaining to a change in dimension and swelling as well as in the handling property during assembly of the dialyzer.
7. Wetting with water results in a three-dimensional change in the length of the cupraphan membranes. The increase in thickness for all types amounts to a factor of 1.9 during the transition from the normally conditioned to the wet state. Glycerine is added to the membrane as a humectant and plasticizer for smooth processing.
8. The water content of the membrane balances with the humidity level of the surroundings. It should be noted that during all phases of processing, room conditions should be around 35% relative humidity at 23°C which correspond with the equilibrium humidity of the membranes. For applications in hollow fibre dialyzers, cupraphan fibres are used.
9. With their small internal diameter, it is possible to design dialyzers with a low priming volume, making it possible to combine a large surface area with a low priming volume. The number of fibres in a dialyzer can be as high as 16,000 giving a density of fibres as 1000 per cm^2.



Relationship between permeability (DL) and molecular weight for different thicknesses of the membrane

10. Cupraphan hollow fibres are particularly suitable for the dialyses of solutes in the middle molecular weight range (500–2000). The high solute permeability in this range is not associated with an extremely high-water permeability.

****