Lecture # 7

The Kidney and Its Artificial Replacement

Introduction

The main function of the pair of kidneys in the human body is to form urine out of blood plasma, a function that basically consists of two processes:

1. Removing waste products from blood plasma

2. Regulating the composition of the blood plasma.

These activities not only lead to the excretion of nonvolatile metabolic waste products but also are responsible for the remarkable constancy of the volume, osmotic pressure, pH, and electrolyte composition of the extracellular body fluids.

The kidneys lie in the back of the abdominal cavity just below the diaphragm, one on each side of the vertebral column. Each kidney consists of about a million individual units, all similar in structure and function. These tiny units are called nephrons, whose structure is shown in Fig.1. A nephron is composed of two parts—a cluster of capillary loops called the glomerulus and a tubule. The tubule runs a tortuous course and ultimately drains via a collecting duct into the funnel-shaped expansion of the upper head of the urethra.

The kidney works only on plasma. The erythrocytes (RBC) supply oxygen to the kidneys but serve no other function in urine formation. Each substance in plasma is handled in a characteristic manner by the nephron, involving particular combinations of filtration, reabsorption, and secretion.

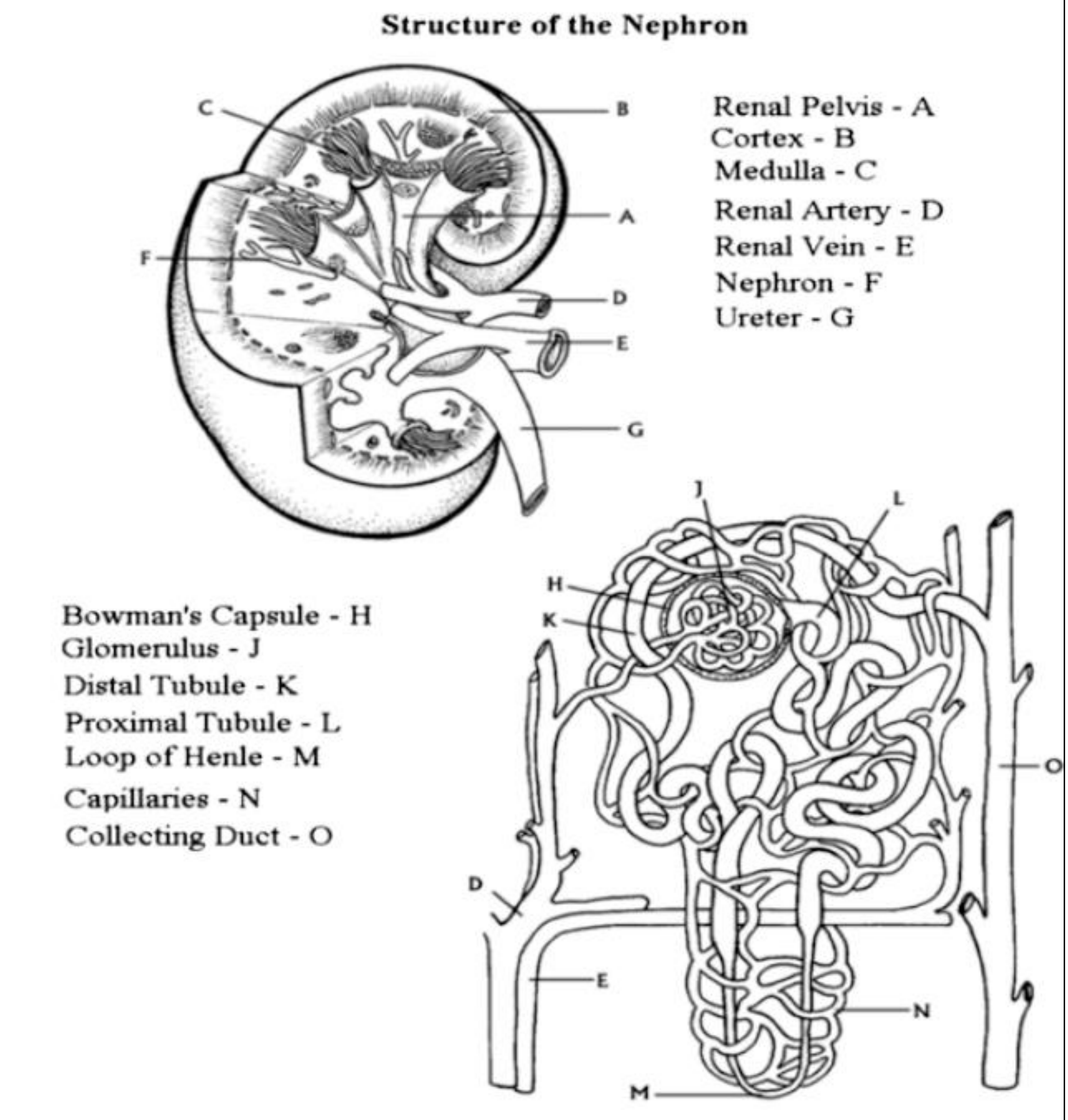

Figure 1: The schematic of a kidney, indicating its structure

The Artificial Kidney

1. **Parallel Flow Dialyzers: -**

   The parallel flow dialyzer has a low internal resistance, which allows adequate blood flow through the dialyzer with the patient's arterial blood pressure, eliminating the need for a blood pump. The dialyzing surface area of a parallel flow dialyzer is about 1 m2 at a blood flow rate of 200 ml/min and a dialyzer flow of 500 ml/min. The urea and creatinine clearance are about 80 and 64 ml/min, respectively. The rigid supports used in parallel flow dialyzers permit negative pressure to be created on the dialysate side of the membrane for ultrafiltration. The water is ultrafiltered at a rate of 9.2 ml/min, with a negative pressure of 130 mmHg. The rate is 1.8 ml/min without negative pressure. The dialysate flows continuously at 500 ml/min in a direction countercurrent to the blood, permitting exchange to take place throughout the dialyzer (Figs. 2 and 3).

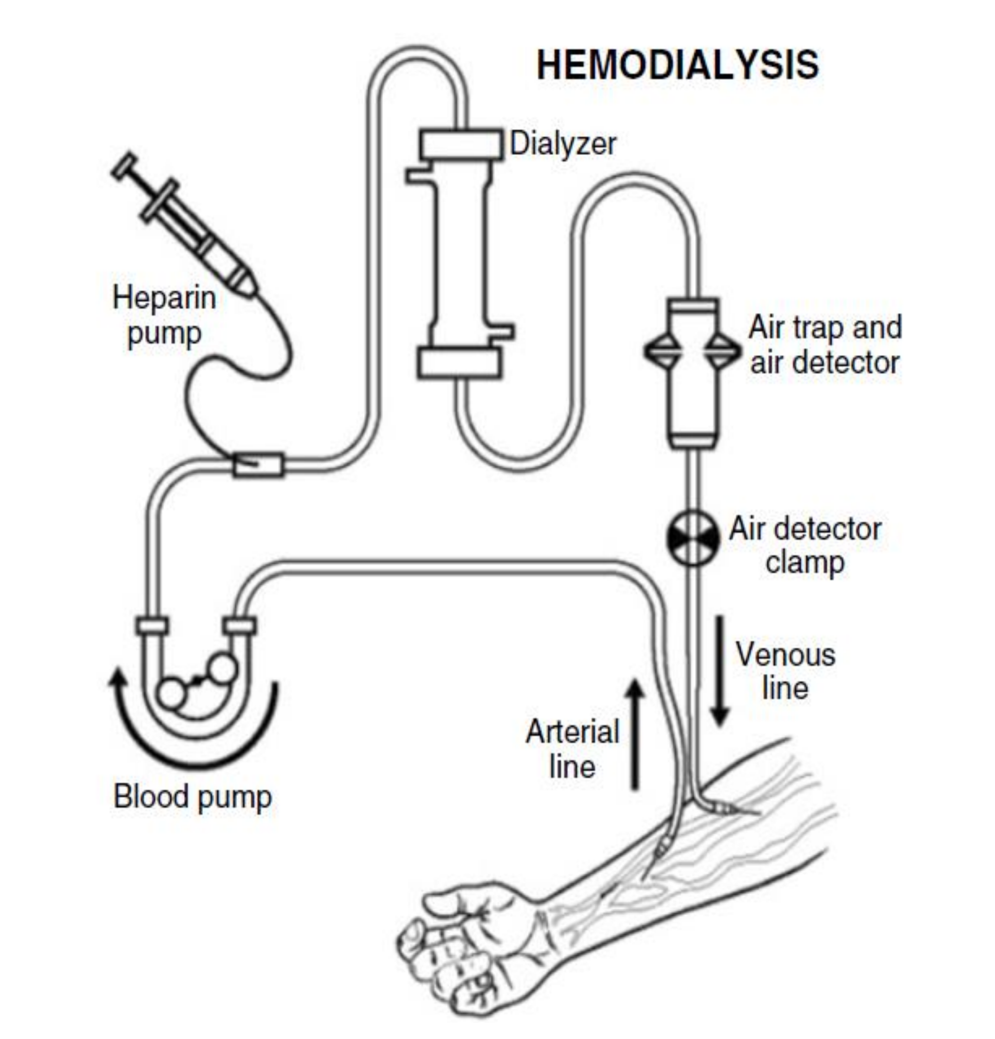

Figure 2: Schema of an artificial kidney machine

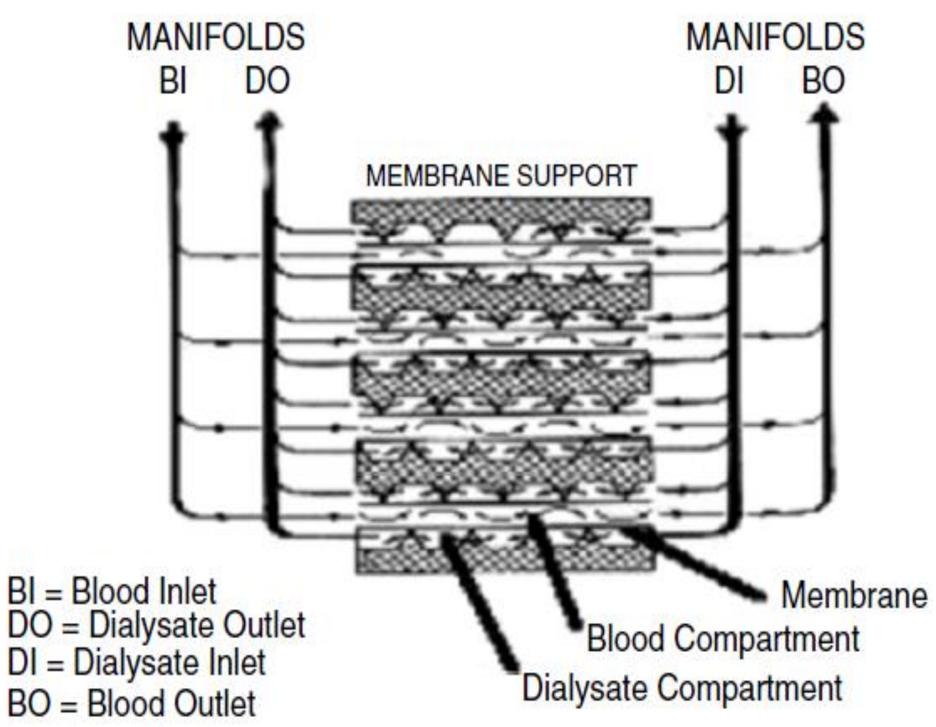

Figure 3: Schema of membrane dialyzer

2. **Coil Hemodialyzer**

A coil hemodialyzer comprises a tubular membrane placed between flexible supports wrapped around a rigid cylindrical core. The coil is immersed in a dialyzing bath. The tubular membrane can be of cellophane or cuprophane. The average wall thickness of the cellophane membrane is 20–30 μm and that of cuprophane in the range of 18–75 μm. The coil membrane support is woven screens or unwoven lattice usually. The twin coil is made with three layers of woven polyvinyl chloride-coated fiber glass screen separated by four narrow strips of the same material, which are sewn into place with cotton thread. Coil dialyzers are available with several design variations:

1. The type of membrane

2. The membrane support
3. The number of blood channels (1, 2, or 4)
4. The width of the blood channel (38–100 mm)
5. The surface area (0.7–1.9 m2).

They are characterized by high dialysis flow rates and a high resistance to blood.

3. **Hollow Fiber Hemodialyzer**

Hollow fibers are (Fig. 4) most commonly used in a hemodialyzer. A hollow fiber hemodialyzer consists of about 10,000 hollow de-acetylated cellulose dilacerate capillaries. The capillaries are jacked in a plastic cylinder 18 cm in length and 7 cm in diameter. The capillaries are seated on each end into a tube sheet with an elastometer. The capillary have 200–300-μm internal diameters and a wall thickness of 25–30 μm. The dialyzing area is approximately 9,000 cm2/unit. The primary volume with blood manifolds exclusive of tubing is approx 130 ml. The blood is introduced and removed from the hemodialyzer through manifold headers. The dialysate is drawn through the jacket under a negative pressure around the outside of the capillaries countercurrent to the blood flow. The dialyzers are disposable. Disposal dialyzers offer the advantage of reduced risk of infection and reduced operator setup time. The dialyzer sterilization procedure is also eliminated. However, the use of disposable dialyzers is an expensive procedure. This has necessitated the development of a method of cleaning dialyzer cartridges so that they may be reused. However, there are several difficulties associated with the practice of reusing dialyzers (Fig. 4).

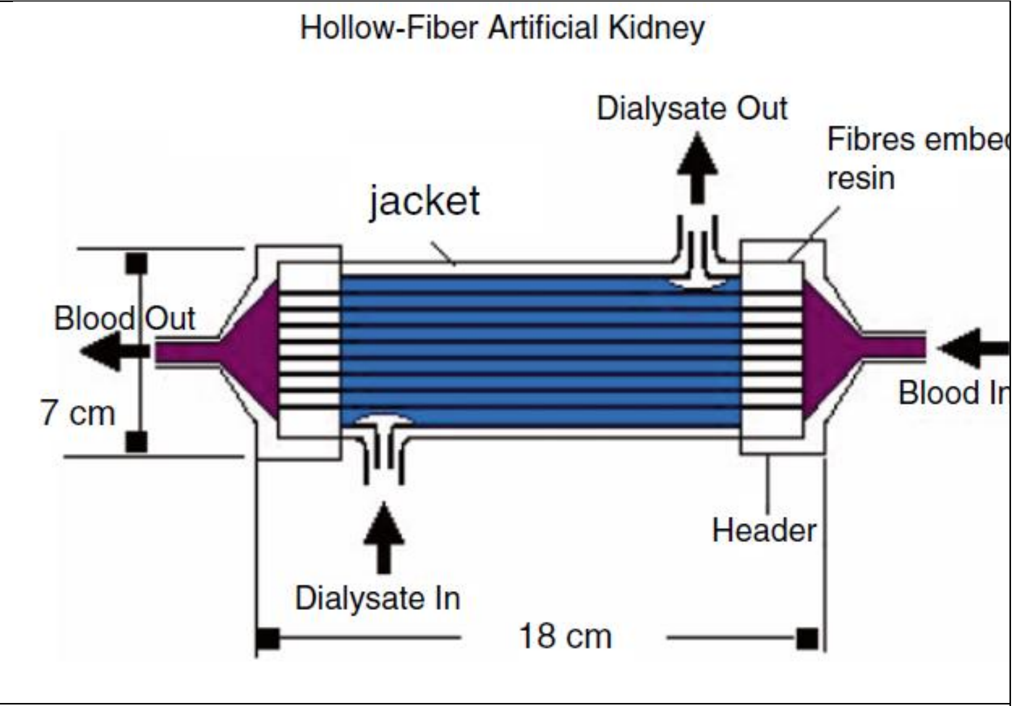

Figure 4: Schema of hollow fiber artificial kidney

4. **Performance Analysis of Dialyzers**

The dialyzers' performance can be compared in terms of their clearance of urea and creatinine, priming volume, residual blood volume, ultrafiltration rate, convenience of handling, and cost.

Clearance: The overall performance of a dialyzer is expressed as the clearance, analogous to that of a natural kidney. It represents the part of the total blood flow rate through the dialyzer that is completely clear of solute urea and the number of toxic solutions in their blood, which are generated daily. Despite the uncertainty as to which solutes and how much should be removed, the performance of dialyzers is generally as for a spectrum of molecular weight solution. **The molecular weight of urea generally is 60, that of**

creatinine 113, that of vitamin B12 1355, and that of insulin 5200.

The clearance of urea and creatinine is measured at clinically useful blood flow rates and standard dialysis fluid addition or flow rates. It is calculated as

Clearance = blood flow rate / (A + B x blood flow rate).

A and B are constants with 95% confidence limits of the mean by least squares approximation. The blood flow rates are measured by bubble transmit time over a 2-m track using the mean of three measurements. Urea and creatinine concentrations are measured in the plasma from a 1-ml sample of heparinized blood (Fig. 5). Usually, blood flow is maintained between 75–300 ml/min and dialysate fluid flow rates at 500 ml/min.

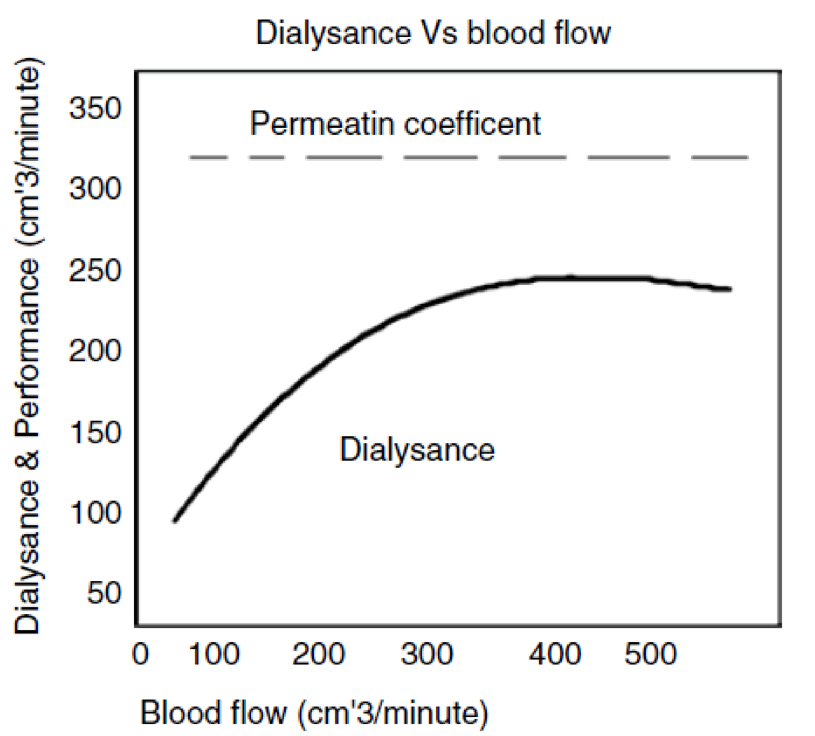

Figure 5: Dialysance vs. blood flow

The performance of the hemodialyzer is usually given by dialysance, D:

$$D = Q_b \left(C_{bi} - C_{bo}\right) / \left(C_{di} - C_{bo}\right),$$

where

Q_b = blood flow rate

C_{bi} = blood solute concentration at the dialyzer inlet

C_{bo} = blood solute concentration at the dialyzer outlet

C_{di} = dialysate solute concentration at the inlet.

The dialysance is also calculated from the clearance, by the following relationship:

Clearance = dialysance / (1+ dialysance / dialysis fluid addition rate).

It may be noted that the clearance may vary with time despite a quasi-steadystate condition. If the dialysate is recirculated, its solute concentration increases, which effectively reduces the concentration driving force. For a given blood flow rate, the clearance is greater for the smaller-molecular-size constituents. This is due to less membrane resistance and a higher liquid diffusion coefficient for smaller-molecular- weight solutes. On the other hand, the contribution of the membrane resistance value becomes greater with the increase in solute molecular weight. Keeping these facts in mind, scientists have tried to design a dialyzer with a large surface area and develop more permeability membranes.

Performance capacity = K.A = A / R,

where

A = surface area

K = permeability coefficient

R = mass-transfer resistance.

5. **Ultrafiltration Rate**

The fluid removal during dialysis takes place due to hydrostatic and osmotic transmembrane pressure gradients. The rate of fluid removal due to hydrostatic pressure effects depends upon the specification of the dialyzer in terms of mass-transfer coefficient and surface area. However, it has a linear function of the transmembrane pressure gradient.

$$\text{Mean transmembrane pressure} = 1/2\left[P_{bi} + P_{bo}\right] - 1/2\left[P_{di} + P_{do}\right]$$

where

P_{bi} = blood inlet pressure

P_{bo} = blood outlet pressure

P_{di} = dialysate inlet pressure

P_{do} = dialysate outlet pressure.

The pressure loss generated by blood and dialysate flows in their respective flow paths should be small. This ensures that the local transmembrane pressure (ΔPm) will not vary excessively from the mean pressure. High values of ΔPm can result in deformation of the membrane and possible rupture. The pressure drop ΔPm across a dialyzer is directly proportional to the length of the passage and the viscosity of the fluid and inversely proportional to the number of blood passages and some function of their cross-sectional area. The relationship of the pressure drop to blood flow is not linear at increased flow, which is accompanied by an increase in pressure that can cause a widening of the blood pressure passage and a decrease in $\Delta Pm/Qb$.

6. **Residual Blood Volume:-**

Residual blood volume measured after an 800-ml saline wash in the fluid remaining in the dialyzer and flow lines is circulated through a 1l bottle of 0.04% ammonium solution for 10 min. The residual blood volume is calculated from the formula

Residual blood volume = U (1,000 + volume of dialyzer and lines in ml) / 200S

where

U = the hemoglobin concentration of the recirculated fluid

S = the hemoglobin concentration of a sample of arterial blood taken at the end of dialysis and diluted 1:200 with 0.04% ammonia.

Residual blood volumes of hemoglobin of 1.8–6.3 ml are quoted in the literature depending upon the dialyzer type and wash-back volume. Here line means flow lines through dialyzer tubings.

7. **Priming Volume**

The volume of the blood within the dialyzer is known as the priming volume. It is desirable that this should be minimal. The priming volume of a present-day dialyzer ranges between 75–200 ml, depending on the membrane area geometry and operating conditions. The requirement of a low priming volume permits the use of the patient's own blood to prime the circuit without serious hypovolemic effects. This is particularly significant in the case of long-term dialysis therapy.

Extracorporeal blood volumes become important with those dialyzers requiring priming. Priming is usually accompanied at relatively low pressures. Recent innovations have largely required the extracorporeal volume, and saline priming is frequently used.

8. Pyrogenicity

Pyrogen (body temperature riser) reactions are rare with all disposable dialyzers. However, they are known to exist with dialyzers, but at rates well lower than 1%.

9. Leakage Rate

Blood-to-dialysis fluid leak with the dialyzer is found to be 3%, but it varies with the dialyzer, the batch of membrane, and the skill of the operator. The leak rate from all curophane coils is high, however.

10. The Hemodialysis Machine and Its Parts

The artificial kidney, or dialyzer, is part of an overall hemodialysis machine. Other parts in this machine include

- A blood pump moves blood through plastic tubing to the dialyzer to be cleansed and returns it to the body.
- An inflow dialysate line delivers dialysate (the cleansing fluid) to the dialyzer.
- An outflow hose carries used dialysate away from the dialyzer to a drain.
- A heparin pump provides the right amount of heparin to keep the blood from clotting.

- Monitors are used to detect any potential problems.
  - An air bubble detector prevents air bubbles from getting into the bloodstream.
  - A blood pressure monitor makes sure the patient's blood pressure does not become too high or too low.
  - Alarms are used to alert the dialysis team of any potential problem.