Nephrogenic Diabetes Insipidus—Failure of the Kidneys to Respond to Antidiuretic Hormone. Occasionally, the renal tubules do not respond to antidiuretic hormone, causing large quantities of dilute urine to be excreted. As long as the person is supplied with plenty of water, this condition seldom causes severe difficulty. However, when adequate quantities of water are not available, the person rapidly becomes dehydrated.

Fanconi's Syndrome—A Generalized Reabsorptive Defect of the Renal Tubules. Fanconi's syndrome is usually associated with increased urinary excretion of virtually all amino acids, glucose, and phosphate. In severe cases, other manifestations are also observed, such as (1) failure to reabsorb sodium bicarbonate, which results in metabolic acidosis; (2) increased excretion of potassium and sometimes calcium; and (3) nephrogenic diabetes insipidus.

There are multiple causes of Fanconi's syndrome, which results from a generalized inability of the renal tubular cells to transport various substances. Some of these causes include (1) hereditary defects in cell transport mechanisms, (2) toxins or drugs that injure the renal tubular epithelial cells, and (3) injury to the renal tubular cells as a result of ischemia. The proximal tubular cells are especially affected in Fanconi's syndrome caused by tubular injury, because these cells reabsorb and secrete many of the drugs and toxins that can cause damage.

Treatment of Renal Failure by Dialysis with an Artificial Kidney

Severe loss of kidney function, either acutely or chronically, is a threat to life and requires removal of toxic waste products and restoration of body fluid volume and composition toward normal. This can be accomplished by dialysis with an artificial kidney. In certain types of acute renal failure, an artificial kidney may be used to tide the patient over until the kidneys resume their function. If the loss of kidney function is irreversible, it is necessary to perform dialysis chronically to maintain life. In the United States alone, nearly 300,000 people with irreversible renal failure or even total kidney removal are being maintained by dialysis with artificial kidneys. Because dialysis cannot maintain completely normal body fluid composition and cannot replace all the multiple functions performed by the kidneys, the health of patients maintained on artificial kidneys usually remains significantly impaired. A better treatment for permanent loss of kidney function is to restore functional kidney tissue by means of a kidney transplant.

Basic Principles of Dialysis. The basic principle of the artificial kidney is to pass blood through minute blood channels bounded by a thin membrane. On the other side of the membrane is a *dialyzing fluid* into which unwanted substances in the blood pass by diffusion. Figure 31–8 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
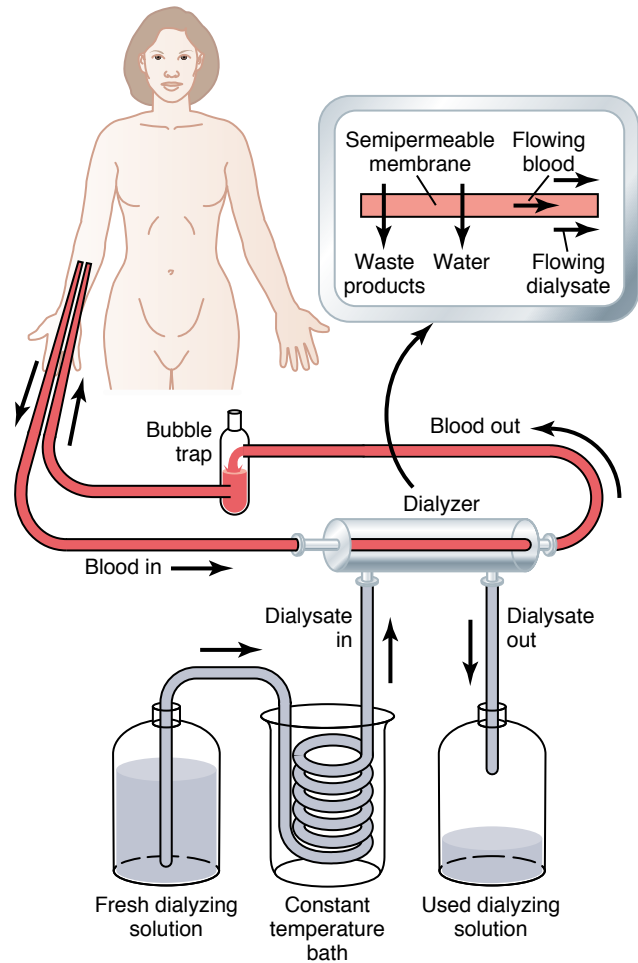

Figure 31–8

Principles of dialysis with an artificial kidney.

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.

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.

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.

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

Table 31–7

Comparison of Dialyzing Fluid with Normal and Uremic Plasma

Constituent	Normal Plasma	Dialyzing Fluid	Uremic Plasma
Electrolytes (mEq/L)			
Na^+	142	133	142
K^+	5	1.0	7
Ca^{++}	3	3.0	2
Mg^{++}	1.5	1.5	1.5
Cl^-	107	105	107
HCO_3^-	24	35.7	14
$Lactate^-$	1.2	1.2	1.2
$HPO_4^=$	3	0	9
$Urate^-$	0.3	0	2
$Sulfate^=$	0.5	0	3
Nonelectrolytes			
Glucose	100	125	100
Urea	26	0	200
Creatinine	1	0	6

the total diffusion surface area is between 0.6 and 2.5 square meters. 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*.

Dialyzing Fluid. Table 31–7 compares the constituents in a typical dialyzing fluid with those in normal plasma and uremic plasma. Note that the 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, which, as discussed in Chapter 27, 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.

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