Principles of Dialysis: Diffusion, Convection, and Dialysis Machines

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Chronic renal failure is the final common pathway of a number of kidney diseases. The choices for a patient who reaches the point where renal function is insufficient to sustain life are 1) chronic dialysis treatments (either hemodialysis or peritoneal dialysis), 2) renal transplantation, or 3) death. With renal failure of any cause, there are many physiologic derangements. Homeostasis of water and minerals (sodium, potassium, chloride, calcium, phosphorus, magnesium, sulfate), and excretion of the daily metabolic load of fixed hydrogen ions is no longer possible. Toxic end-products of nitrogen metabolism (urea, creatinine, uric acid, among others) accumulate in blood and tissue. Finally, the kidneys are no longer able to function as endocrine organs in the production of erythropoietin and 1,25-dihydroxycholecalciferol (calcitriol).

Dialysis procedures remove nitrogenous end-products of catabolism and begin the correction of the salt, water, and acid-base derangements associated with renal failure. Dialysis is an imperfect treatment for the myriad abnormalities that occur in renal failure, as it does not correct the endocrine functions of the kidney.

Indications for starting dialysis for chronic renal failure are empiric and vary among physicians. Some begin dialysis when residual glomerular filtration rate (GFR) falls below 10 mL/min /1.73 m^2 body surface area (15 mL/min/1.73 m^2 in diabetics.) Others institute treatment when the patient loses the stamina to sustain normal daily work and activity. Most agree that, in the face of symptoms (nausea, vomiting, anorexia, fatigability, diminished sensorium) and signs (pericardial friction rub, refractory pulmonary edema, metabolic acidosis, foot or wrist drop, asterixis) of uremia, dialysis treatments are urgently indicated.

CHAPTER 1

FUNCTIONS OF THE KIDNEY AND PATHOPHYSIOLOGY OF RENAL FAILURE

Function	Dysfunction
Salt, water, and acid-base balance	Salt, water, and acid-base balance
Water balance	Fluid retention and hyponatremia
Sodium balance	Edema, congestive heart failure, hypertension
Potassium balance	Hyperkalemia
Bicarbonate balance	Metabolic acidosis, osteodystrophy
Magnesium balance	Hypermagnesemia
Phosphate balance	Hyperphosphatemia, osteodystrophy
Excretion of nitrogenous end products	Excretion of nitrogenous end products
Urea Creatinine Uric acid Amines Guanidine derivatives	?Anorexia, nausea, pruritus, pericarditis, polyneuropathy, encephalopathy, thrombocytopathy
Endocrine-metabolic	Endocrine-metabolic
Conversion of vitamin D to active metabolite	Osteomalacia, osteodystrophy
Production of erythropoietin	Anemia
Renin	Hypertension

FIGURE 1-1
Functions of the kidney and pathophysiology of renal failure.

FIGURE 1-2
Statue of Thomas Graham in George Square, Glasgow, Scotland. The physicochemical basis for dialysis was first described by the Scottish chemist Thomas Graham. In his 1854 paper "On Osmotic Force" he described the movements of various solutes of differing concentrations through a membrane he had fashioned from an ox bladder. (*From* Graham [1].)

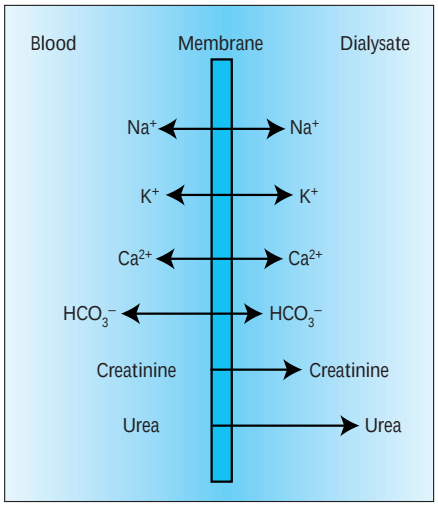

FIGURE 1-3
Membrane fluxes in dialysis. Dialysis is the process of separating elements in a solution by diffusion across a semipermeable membrane (diffusive solute transport) down a concentration gradient. This is the principal process for removing the end-products of nitrogen metabolism (urea, creatinine, uric acid), and for repletion of the bicarbonate deficit of the metabolic acidosis associated with renal failure in humans. The preponderance of diffusion as the result of gradient is shown by the displacement of the *arrow*.

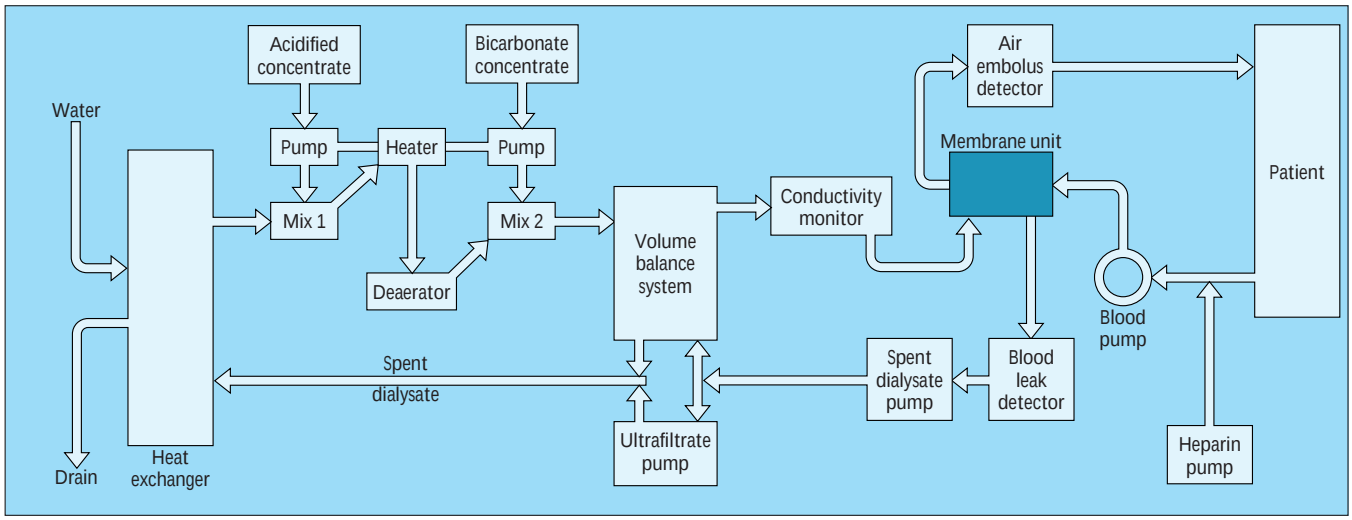

FIGURE 1-4

Simplified schematic of typical hemodialysis system. In hemodialysis, blood from the patient is circulated through a synthetic extracorporeal membrane and returned to the patient. The opposite side of that membrane is washed with an electrolyte solution (dialysate) containing the normal constituents of plasma water. The apparatus contains a blood pump to circulate the blood through the system, proportioning pumps that mix a concentrated salt solution with water purified by reverse osmosis and/or deionization to produce the dialysate, a means of removing excess fluid from the blood (mismatching dialysate inflow and outflow to the dialysate compartment), and a series of pressure, conductivity, and air embolus monitors to protect the patient. Dialysate is warmed to body temperature by a heater.

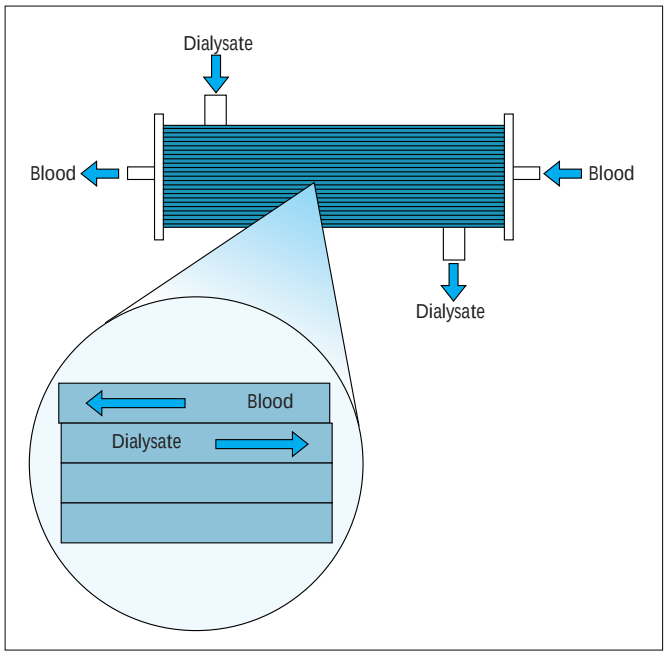

FIGURE 1-5

The hemodialysis membrane. Most membranes are derived from cellulose. (The earliest clinically useful hemodialyzers were made from cellophane sausage casing.) Other names of these materials include cupraphane, hemophan, cellulose acetate. They are usually sterilized by ethylene oxide or gamma irradiation by the manufacturer. They are relatively porous to fluid and solute but do not allow large molecules (albumin, vitamin B_{12}) to pass freely. There is some suggestion that cupraphane membranes sterilized by ethylene oxide have a high incidence of biosensitization, meaning that the patient may have a form of allergic reaction to the membrane. Polysulfone, polyacrylonitrile, and polymethylmethacrylate membranes are more biocompatible and more porous (high flux membranes). They are most often formed into hollow fibers. Blood travels down the center of these fibers, and dialysate circulates around the outside of the fibers but inside a plastic casing. Water for dialysis must meet critical chemical and bacteriologic standards. These are listed in Figures 1-6 and 1-7.

ASSOCIATION FOR THE ADVANCEMENT OF MEDICAL INSTRUMENTATION CHEMICAL STANDARD FOR WATER FOR HEMODIALYSIS

Substance	Concentration (mg/L)
Aluminum	0.01
Arsenic	0.005
Barium	0.1
Cadmium	0.001
Calcium	2.0
Chloramine	0.1
Chlorine	0.5
Chromium	0.014
Copper	0.1
Fluoride	0.2
Lead	0.005
Magnesium	4.0
Mercury	0.0002
Nitrate	2.0
Potassium	8.0
Selenium	0.009
Silver	0.005
Sodium	70
Sulfate	100
Zinc	0.1

FIGURE 1-6
Association for the Advancement of Medical Instrumentation (AAMI) chemical standards for water for hemodialysis. Before hemodialysis can be performed, water analysis is performed. Water for hemodialysis generally requires reverse osmosis treatment and a deionizer for "polishing" the water. Organic materials, chlorine, and chloramine are removed by charcoal filtration. (*From* Vlchek [2]; with permission.)

ASSOCIATION FOR THE ADVANCEMENT OF MEDICAL INSTRUMENTATION BACTERIOLOGIC STANDARDS FOR DIALYSIS WATER AND PREPARED DIALYSATE

	Colony-forming units/mL
Dialysis water	<200
Prepared dialysate	<2000

FIGURE 1-7
Association for the Advancement of Medical Instrumentation (AAMI) bacteriologic standards for dialysis water and prepared dialysate. Excess bacteria in water can lead to pyrogen reactions. Treated water supply systems are designed so that there are no dead-end connections. Because the antiseptic agents (chlorine and chloramine) have been removed in water treatment, the water is prone to develop such problems if stagnation is allowed. (*From* Bland and Favero [3]; with permission.)

$$\frac{dn}{dt} = -DA\,\frac{dc}{dx}$$

FIGURE 1-8
Factors that govern diffusion, where dn/dt = the rate of movement of molecules per unit time; D = Fick's diffusion coefficient; A = area of the boundary through which molecules move; dc = concentration gradient; and dx = distance through which molecules move. Hemodialysis depends on the process of diffusion for removal of solutes. The amount of material removed depends on the magnitude of the concentration gradient, the distance the molecule travels, and the area through which diffusion takes place. For this reason those dialyzers that have a large surface area, thin membranes, and are designed to maximize the effect of concentration gradient (countercurrent design) are most efficient at removing solutes.

$$D = \frac{kT}{6\pi\eta}\sqrt[3]{\frac{4\pi N}{3M\bar{\upsilon}}}$$

FIGURE 1-9

Fick's diffusion constant, where D = Fick's diffusion coefficient, k = Boltzman's constant; T = absolute temperature; η = viscosity; N = Avogadro's number; M = molecular weight; and υ = partial molal volume. The diffusion constant is proportional to the temperature of the solution and inversely proportional to the viscosity and the size of the molecule removed.

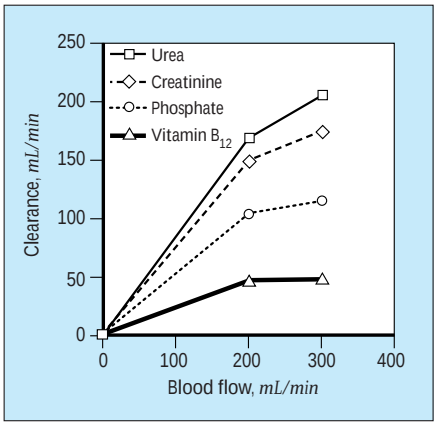

FIGURE 1-10

Effect of blood flow on clearance of various solutes, Fresenius F-5 membrane. The amount of solute cleared by a dialyzer depends on the amount delivered to the membrane. The usual blood flow is 300–400 mL/min, which is adequate to deliver the dialysis prescription. On institution of dialysis to a very uremic patient the blood flow is decreased to 160 to 180 mL/min to avoid disequilibrium syndrome. As time goes on, blood flow can be increased to standard flows as the patient adjusts to dialysis. Most patients require hemodialysis at least thrice weekly. From this graph it is also evident that small molecules such as urea (molecular weight 60 D) are cleared more easily than large molecules such as vitamin B_{12} (molecular weight 1355 D).

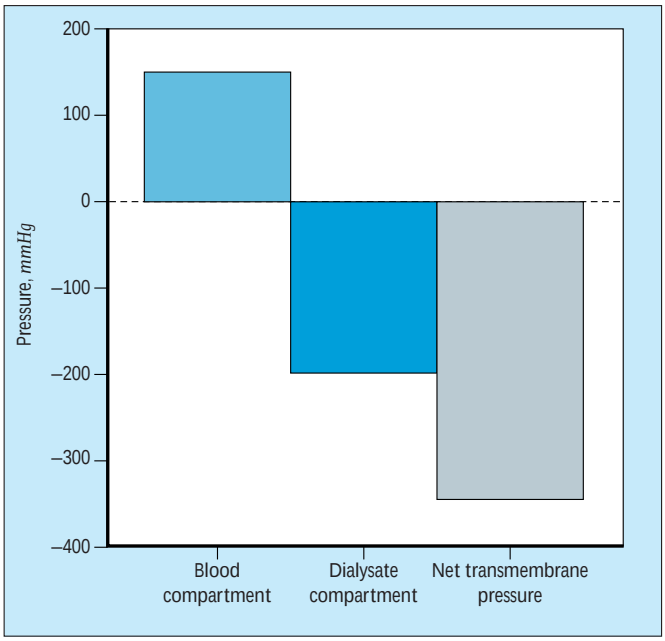

FIGURE 1-11

Hydrostatic ultrafiltration also takes place during hemodialysis. Because the spent dialysate effluent pump (see Fig. 1-4) creates negative pressure on the dialysate compartment of the membrane unit and the blood pump creates positive pressure in the blood compartment, there is a net hydrostatic pressure gradient between the compartments. This causes a flow of water and dissolved substances from blood to the dialysate compartment. The process of solute transfer associated with this flow of water is called "convective transport." In hemodialysis, the amount of low–molecular weight solute (*eg*, urea) removed by convection is negligible. In the continuous renal replacement therapies, this is a major mechanism for solute transport.

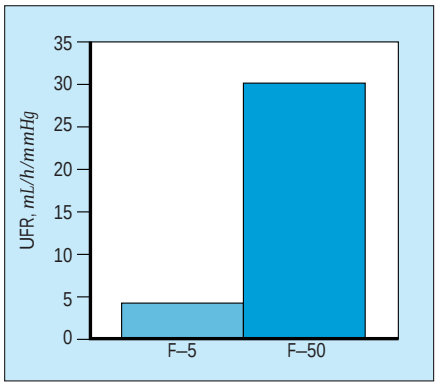

FIGURE 1-12
Dialysis membranes differ in their ability to remove fluid. Differences in ultrafiltration coefficient (UFR) are shown for two different membranes, F-5 and F-50. The F-50 is considered a high-flux membrane.

References

1. Graham T: The Bakerian lecture—on osmotic force. *Philos Trans R Soc Lond* 1854, 144:177–228.
2. Vlchek DL: Monitoring a hemodialysis water treatment system. In *AAMI Standards and Recommended Practices*, vol. 3. Arlington, VA: Association for the Advancement of Medical Instrumentation; 1993:267–277.
3. Bland LA, Favero MS: Microbiologic aspects of hemodialysis systems. In *AAMI Standards and Recommended Practices*, vol. 3. Arlington, VA: Association for the Advancement of Medical Instrumentation; 1993:257–265.
4. Daniels F, Alberty RA: *Physical Chemistry*. New York : John Wiley & Sons; 1955.