

*Current Concepts***CONTINUOUS HEMOFILTRATION IN THE TREATMENT OF ACUTE RENAL FAILURE**

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ACUTE renal failure that requires renal-replacement therapy is a relatively common condition, with an annual incidence of at least 30 cases per 1 million population.¹ Historically, the replacement of renal function in acute renal failure has involved techniques also employed in the treatment of end-stage chronic renal failure — intermittent hemodialysis and peritoneal dialysis.^{2,3} Hemofiltration was first described in 1977 as a means of removing extracellular fluid from patients with edema refractory to diuretic agents.⁴ Continuous hemofiltration, combined with the administration of an appropriate fluid, is now recognized as a form of renal-replacement therapy in acute renal failure. The technique is widely used in intensive care units for the treatment of acute renal failure, although intermittent hemodialysis continues to be used for patients with acute renal failure but without multiorgan failure.

BASIC PRINCIPLES

Hemofiltration has many superficial similarities to hemodialysis. In both techniques, access to the circulation is required and blood passes through an extracorporeal circuit that includes either a dialyzer or a hemofilter. However, the mechanisms by which the composition of the blood is modified differ markedly (Fig. 1). During dialysis (Fig. 1, upper panel), blood flows along one side of a semipermeable membrane as a solution of crystalloids is pumped along the other side of the membrane against the direction of the blood flow. Small molecules diffuse across the membrane from regions of greater concentration to regions of lesser concentration, and the composition of the dialysis fluid is designed to produce as near

normalization of the plasma as possible. Thus, the sodium concentration of the dialysis fluid is physiologic, but the potassium concentration is lower than that of normal plasma in order to establish a gradient from plasma to the fluid that promotes the removal of potassium ions from the patient's blood. The concentrations of substances that are to be removed completely (such as urea, creatinine, and phosphate) are zero in the dialysis fluid. The removal of salt and water is achieved by the creation of a transmembrane pressure gradient (with lower pressure in the dialysis-fluid compartment). According to the laws of diffusion, the larger the molecule, the slower will be its rate of transfer across the membrane. A small molecule, such as urea (60 daltons), is cleared efficiently, and a larger molecule, such as creatinine (113 daltons), less well. Phosphate ions have such low rates of clearance that hyperphosphatemia is always a problem for patients on intermittent dialysis. Dialysis has no similarity to the normal physiologic processes of the kidney, but it is effective, and many patients have lived for decades entirely dependent on intermittent hemodialysis.⁵

Hemofiltration (Fig. 1, lower panel) works in a different manner.^{6,7} In the simplest form of the procedure, blood under pressure passes down one side of a highly permeable membrane allowing both water and substances up to a molecular weight of about 20,000 to pass across the membrane by convective flow, as in glomerular filtration. During hemofiltration, in contrast to hemodialysis, urea, creatinine, and phosphate are cleared at similar rates, and profound hypophosphatemia may develop unless the patient's phosphate intake is supplemented. Larger molecules such as heparin, insulin, myoglobin, and vancomycin, which are cleared from the blood in only negligible quantities in a dialyzer, are cleared efficiently by the hemofilter.

In the kidney, the glomerular filtrate is selectively reabsorbed by the renal tubules, a process too complex to be artificially reproduced with current technology. Instead, during hemofiltration, the filtrate is discarded and the patient receives infusions (usually through the distal part of the hemofiltration circuit) of a solution in which the major crystalloid components of the plasma are at physiologic levels (the typical composition of hemofiltration replacement fluid is shown in Table 1). If there is no need for the removal of fluid from the patient, the rate at which the replacement fluid is administered is matched exactly with the rate of production of hemofiltrate. Usually, however, there is a need to remove fluid, because of either fluid overload or the clinical need to adminis-

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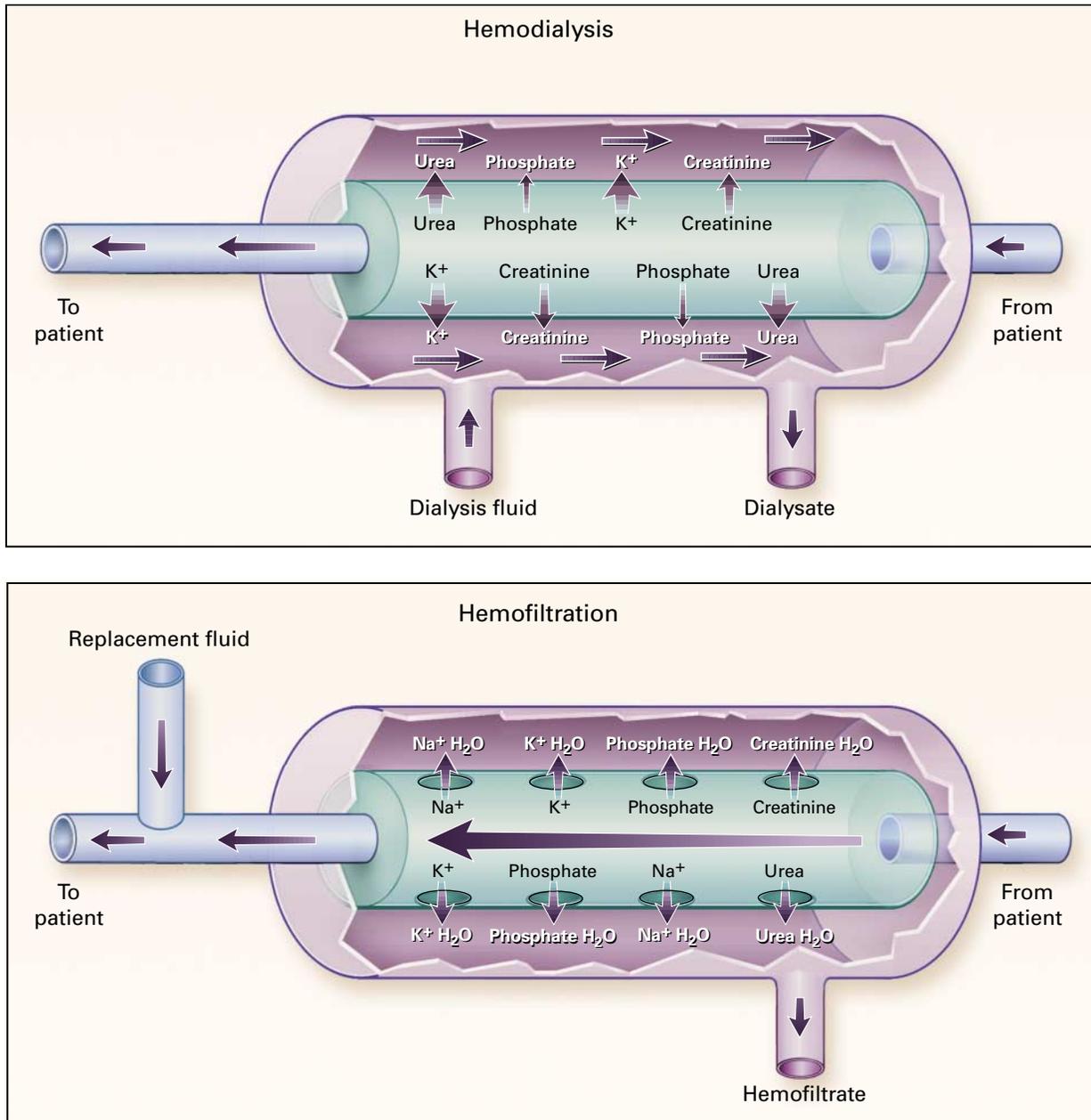


Figure 1. Hemodialysis and Hemofiltration.

The arrows that cross the membrane indicate the predominant direction of movement of each solute through the membrane; the relative size of the arrows indicates the net amounts of the solute transferred. Other arrows indicate the direction of flow.

ter fluids to a patient with oliguria. A net loss of extracellular fluid is achieved by replacing less fluid through infusion than is removed by hemofiltration.

It is important to recognize that certain physical constraints affect hemofiltration as they do glomerular filtration. In both processes, the plasma component of the blood flowing through the circuit represents the sole source of the salt and water that are

the principal constituents of the filtrate. Hemofiltration therefore inevitably leads to an increase in the concentration of both red cells and plasma protein in the blood of the extracorporeal circuit⁸; there is thus a tendency to produce viscous blood of high hematocrit and high colloid oncotic pressure at the distal end of the hemofilter. It is therefore generally unwise to induce a filtration rate that is more than

TABLE 1. TYPICAL COMPOSITION OF HEMOFILTRATION REPLACEMENT FLUID.*

COMPONENT	VALUE
	mmol/ liter
Sodium	140
Potassium	0
Calcium	1.6
Magnesium	0.75
Chloride	101
Lactate	45
Glucose	11

*The values shown are for Gambro Hemofiltrasol 22. Potassium chloride is added to the solution immediately before use in concentrations of up to 4 mmol per liter, depending on the serum potassium concentration. To convert the value for calcium to milligrams per deciliter, divide by 0.25; to convert the value for magnesium to milliequivalents per liter, divide by 0.5; and to convert the value for glucose to milligrams per deciliter, divide by 0.05551.

30 percent of the blood-flow rate. Keeping the ratio between the two rates under 25 percent minimizes the unwanted effect. An alternative approach, known as predilution, circumvents the problem by administering the replacement fluid proximal to the hemofilter. This rarely used procedure reduces the efficiency and increases the cost of hemofiltration because a proportion of the generated filtrate is actually replacement fluid.

As hemofiltration became an increasingly popular form of renal-replacement therapy in the intensive

care unit, a number of variants were developed (Table 2). These are outlined below.

CONTINUOUS ARTERIOVENOUS HEMOFILTRATION

Continuous arteriovenous hemofiltration is the original and simplest form of the technique.^{4,9} The femoral artery and vein are cannulated, and blood passes through the hemofilter under the influence of arterial pressure alone (Fig. 2). Because the pressure in the system exceeds the atmospheric pressure, there is no possibility of air being drawn into the circuit and no precautions need to be taken to prevent this from occurring. However, the simplicity of the system is offset by several disadvantages. First, a disconnection or leak in the circuit can result in rapid loss of blood. Second, the efficiency of hemofiltration depends on the arterial pressure, which is frequently low or unstable in patients with acute renal failure. The effectiveness of the system is therefore determined mainly by factors outside the direct control of the physician. Low blood flow is associated with frequent clotting of the extracorporeal circuit, and the prolonged arterial cannulation typically used carries a risk of complications at the puncture site. Continuous arteriovenous hemofiltration often results in clearance rates as low as 10 to 15 ml per minute even in normotensive patients; clearance rates may drop to below 10 ml per minute if a patient has marked hypotension.

CONTINUOUS ARTERIOVENOUS HEMODIALYSIS WITH FILTRATION

The recognition of the inadequacy of continuous arteriovenous hemofiltration when used alone led to the addition of a dialysis circuit to the hemofilter.^{10,11}

TABLE 2. TYPES OF RENAL-REPLACEMENT THERAPY FOR ACUTE RENAL FAILURE.

TYPE	COMPLEXITY	EFFICIENCY	COST	ANTI-COAGULANT THERAPY	RISK OF HEMORRHAGE	RISK OF INFECTION	EXTRA-CELLULAR-FLUID VOLUME CONTROL	USE IN HYPO-TENSION
Peritoneal dialysis	Low	Moderate	Moderate	No	Low	High	Moderate	Yes
Intermittent hemodialysis	Moderate	High	Low	Yes	Moderate	Low	Intermittent	No
Continuous arteriovenous hemofiltration	Moderate	Low and variable	Moderate	Yes	Moderate	Low	Good	No
Continuous arteriovenous hemodialysis with filtration	High	Moderate and variable	High	Yes	Moderate	Low	Good	Variable
Continuous venovenous hemofiltration	Moderate	High	Moderate	Yes	Moderate	Low	Good	Yes
Continuous venovenous hemodialysis with filtration	High	High	High	Yes	Moderate	Low	Good	Yes

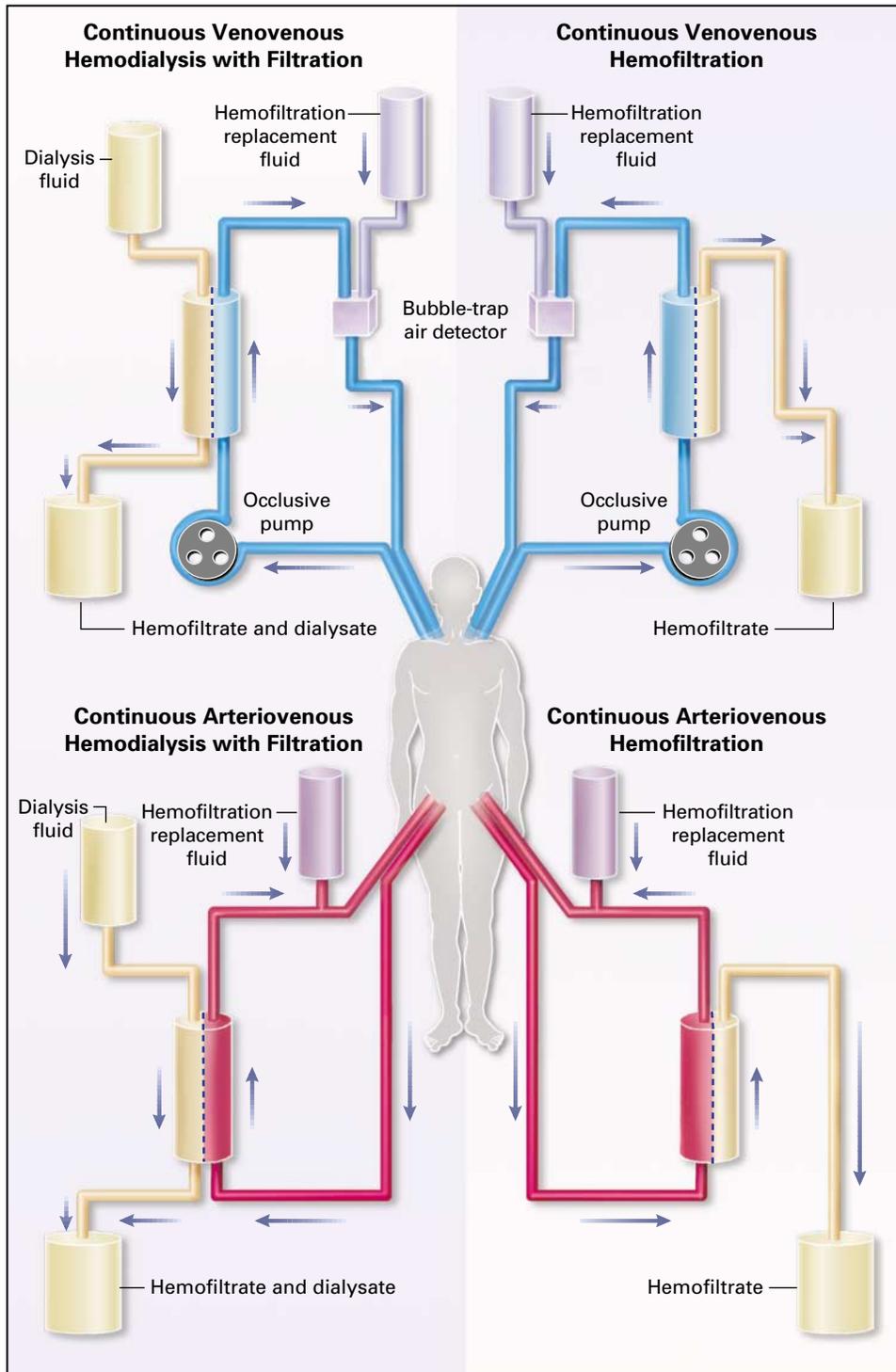


Figure 2. The Mechanisms of Hemofiltration and Hemodialysis with Filtration.

No attempt has been made in this diagram to represent the automatic control of the rates of filtration and infusion of replacement fluid.

In such a system, although a minor fraction of the circulating blood is cleared by the filter, the remainder undergoes dialysis, which results in an important improvement in the clearance of at least the smaller molecules that accumulate in renal failure. The inefficiency of arteriovenous hemofiltration alone is thus overcome at the price of a considerable increase in the complexity of the equipment, and the other disadvantages of continuous arteriovenous hemofiltration are not eliminated.

CONTINUOUS VENOVENOUS HEMOFILTRATION

The incorporation of an occlusive pump into the filtration circuit, together with the use of a femoral, subclavian, or internal jugular vein as the source of blood for the extracorporeal circuit, allows for control of the blood flow and the filtration rate without the limitations imposed by relying on the arterial pressure to move the blood.^{7,12,13} The use of a pump also averts the problems associated with cannulation of the femoral artery. This type of blood circuit, called venovenous hemofiltration, also incorporates safety devices to detect low inflow pressure and the presence of air in the circuit. Filtration rates in excess of 100 ml per minute can be achieved, though such rates are rarely required in the treatment of acute renal failure. The clear advantages of this system over simple arteriovenous hemofiltration have led to its widespread use in intensive care units.

CONTINUOUS VENOVENOUS HEMODIALYSIS WITH FILTRATION

Yet another system adds hemodialysis to venovenous hemofiltration in the same way that dialysis was added to continuous arteriovenous hemofiltration.^{14,15} There is no doubt that higher clearance rates of small solutes are achieved at any given blood flow by this modification, but it is questionable whether there are any advantages over continuous venovenous hemofiltration alone unless one wishes to shorten treatment and make it intermittent. If a continuous mode of treatment is appropriate, more than adequate clearance rates are possible with the simpler and cheaper system of continuous venovenous hemofiltration alone. With more than 6000 patient-days of treatment in our unit, we have never had a situation in which continuous venovenous hemofiltration alone was incapable of achieving metabolic control.

PRACTICAL ASPECTS OF CONTINUOUS VENOVENOUS HEMOFILTRATION

In continuous venovenous hemofiltration, vascular access is achieved by the insertion of a double-lumen catheter into a great vein. The blood pump is typically set to deliver approximately 125 ml per minute, and the most common hemofiltration rate

is 25 ml per minute; this rate is controlled by an occlusive pump on the hemofiltrate line. In automated systems, the hemofiltrate is collected in bags that are suspended on a strain gauge and weighed continuously. The bags of replacement fluid, suspended on a second strain gauge, are similarly weighed. A servomechanism drives the replacement-fluid pump at a rate computed either to balance the inflow and loss of fluid or to maintain a predetermined rate of fluid loss. Anticoagulation of the extracorporeal circuit is almost always undertaken with a heparin infusion (200 to 1600 units per hour) through the inflow side of the circuit. Although heparin-induced thrombocytopenia can develop in patients who receive continuous heparin therapy, this syndrome is not a common problem.¹⁶ If thrombocytopenia should develop or if there is excessive bleeding for any reason, it is sometimes possible to continue treatment and either withhold anticoagulation or substitute epoprostenol (prostacyclin) for heparin. Care must be taken if epoprostenol is used in critically ill patients, because of the drug's systemic effects.^{17,18} Epoprostenol is also much more expensive than heparin (approximately \$176 per 24-hour course of therapy, as compared with \$3 for heparin).

Hemofiltration removes virtually all ions from the plasma, including calcium, magnesium, and bicarbonate (Fig. 1); these must be replaced appropriately. Since it is impossible to manufacture a stable solution that contains the appropriate concentrations of these ions, a variety of anions have been substituted for bicarbonate in replacement fluid. The anion most commonly used in replacement fluid is lactate, because it is assumed that lactate will be converted to bicarbonate. This assumption is valid for most patients, although not for those with lactic acidosis. In patients with lactic acidosis, the exogenous lactate load from the replacement fluid, coupled with the continued removal of bicarbonate ions by the hemofilter, merely increases the plasma lactate concentration and reduces the arterial pH. Under such conditions, use of the hemofilter actually worsens the patient's acidosis. If hemofiltration is undertaken in these circumstances, bicarbonate ions must be provided directly. In our unit, this is done by infusing a mixture of isotonic sodium chloride and isotonic sodium bicarbonate in a ratio determined by the severity of the acidosis.^{19,20} Because of the incompatibility of calcium salts with such a replacement-fluid mixture, calcium salts are infused together with magnesium salts at a separate part of the circuit.

HEMOFILTRATION FOR ACUTE RENAL FAILURE

It is probably the continuous nature of hemofiltration, more than any other feature, that makes the technique so beneficial in the treatment of patients

with acute renal failure in intensive care units (where most such patients have multiorgan failure).²¹⁻²³ Such patients frequently receive more than 2 liters of fluid a day, much of which represents nutrition. In patients with a robust circulation, intermittent hemodialysis can correct biochemical abnormalities and remove, in a short time, the extracellular fluid accumulated over 24 hours, although there is usually a degree of hypovolemia and hypokalemia associated with the process. In the more common situation of a patient with acute renal failure and compromised circulation, hemodialysis may lead to serious hypotension or cardiac arrhythmia. This fact may limit possible treatment; restriction of the patient's fluid intake may be attempted, usually with a concomitant restriction of nutrition. With continuous hemofiltration, however, almost any quantity of fluid can easily be removed over a 24-hour period. In computing the energy needs of a patient with acute renal failure who is receiving nutritional support, due allowance should be made for the calorific value of the lactate content of regular hemofiltration replacement fluid. At a filtration rate of 25 ml per minute, the net contribution of lactate to nutrition is approximately 500 kcal per day.

It is frequently pointed out that mortality due to acute renal failure remains high despite recent improvements in treatment.²⁴ It may therefore be questioned whether continuous hemofiltration, despite its advantages, has been of any real benefit. In our experience, there has been a substantial improvement in survival coincident with the use of continuous hemofiltration among patients with similar characteristics.^{25,26} The question whether such an improvement would have resulted from other advances in intensive care had patients continued to be treated by intermittent hemodialysis alone has not been answered unambiguously. No large-scale randomized trial comparing continuous hemofiltration and intermittent hemodialysis has been reported, although data from several small series suggest that hemofiltration may be preferable.^{27,28}

COSTS OF HEMOFILTRATION

For treatment lasting an average of 9.3 days, with replacement of the extracorporeal circuit every 2.5 days, the cost of consumables (hemofilter, blood and fluid lines, and replacement fluid) for each episode of acute renal failure in our unit is \$1,614; the cost of replacement fluid (\$880) is the most important single item. The equivalent cost for treatment with intermittent hemodialysis is \$672, assuming 10 daily treatments. Labor costs are less easy to calculate because they depend to a large extent on local practice. In our intensive care unit, the supervision of hemofiltration is incorporated into the duties of the nurse responsible for the patient; the treatment entails no additional labor costs. Hemodialysis with filtration,

if undertaken so as to achieve plasma values for urea or creatinine similar to those achieved with hemofiltration alone, increases costs markedly because the combination process has a smaller effect per unit of replacement fluid consumed.

CONCLUSIONS

Continuous hemofiltration is a highly effective system for the replacement of renal function in patients with acute renal failure. The control of biochemical characteristics is constant, and the patient need never have any unwanted alterations of extracellular-fluid volume, even if large quantities of fluid are administered (for nutritional or other purposes). The use of hemofiltration has coincided with a substantial reduction in mortality. Hemofiltration does not cure acute renal failure, but it is a safe and efficient way of replacing renal function while the kidneys recover from disease or injury.

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