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END-STAGE RENAL DISEASE (ESRD) AND THE PROSPECTS FOR A MACHINE-FREE LIFE

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End-Stage Renal Disease (ESRD) is the term used by nephrologists to describe cases of renal failure that have progressed to the point where continued viability depends on a substitution for kidney function.

A generation ago ESRD was a terminal condition because there was no substitute for kidney function. Survival time depended on factors such as age and the presence of complicating diseases such as diabetes. Today, dialysis technologies are available that promise many additional years for ESRD patients. Kidney transplants have become fairly common but are preceded by some form of dialysis or followed by some form of dialysis in the event of transplant rejection. Except in unusual circumstances, the kidney transplant is not considered an option for persons past the age of fifty-seven. As a matter of fact, *any* form of treatment for ESRD is considered too expensive in some countries to be an acceptable part of nationally-financed health programs. In those countries, ESRD continues to be a terminal condition.

Such is not the case in the United States. Congress made a decision in 1972 to pay 80 percent of the cost of kidney transplants and dialysis through the Medicare program for *anyone* whose kidneys failed. According to the *Time* article "One Miracle, Many Doubts" (Friedrich, 1984), the number of patients receiving such support reached 82,000 in the following decade, up from 10,300 the first year of the program.

To the ESRD patient who normally would look forward to many more productive years, the generosity of American society is reason for a greater sense of optimism as opposed to the resignation or despair that would otherwise prevail. It is one thing to be told that one's kidneys can no longer function adequately. To be told that nothing can be done about it is quite another.

The development of the "artificial kidney" — the hemodialysis machine — was a significant technological development in medicine. Such machines have now been engineered to smaller size and have monitoring systems that enable a trained lay person such as a spouse to administer hemodialysis at home. However, most ESRD patients on hemodialysis go to a center three times a week for 4 to 6-hour sessions, attached to the machine while the total volume of the blood is circulated across a special semipermeable membrance in contact with a large volume of dialysate. Water and nitrogenous waste products diffuse across the membrance from the blood to the dialysate, reducing the waste products that build up between dialysis sessions.

The intermittent nature of hemodialysis and the long sessions required are obvious drawbacks. Surgery is required to create the proper vascular access for circulation of the blood into the machine and back. Connections to the machine are not unlike those required for blood transfusions. Between sessions on the machine, the patient experiences the fatiguing and debilitating effects of the

increasing waste products in the blood. Post-session adjustment of the body's fluid balance often causes feelings of malaise.

During the last four or five years, a machine-free form of self-administered dialysis has been made available to some ESRD patients. One form of this type of kidney-function substitute is called Continuous Ambulatory Peritoneal Dialysis or CAPD.

The peritoneum is the membrance that lines the body cavity and holds the abdominal organs in place. The membrance is an effective dialyzer and contains a rich supply of capillaries. The CAPD patient carries dialysate solution in the abdominal cavity, introduced there through a surgically-installed catheter system. In CAPD, as the name implies, dialysis is continuous; it is interrupted only to replace the dialysate three or four times a day. The replacement of spent dialysate with fresh dialysate is called an *exchange* and requires about 45 minutes. The patient is free to go about his usual activities between exchanges.

The dialysate is a sterile solution of dextrose in water. Additional small amounts of solutes regulate the pH and provide the proper concentration of electrolytes. The only function of the dextrose is to act as an osmotic agent, and the osmotic pressure gradient between the dialysate and the blood is regulated by the percentage of dextrose in the solution. The choice of dextrose concentration depends on the patient's requirements for fluid removal. The usual volume of dialysate placed in the abdominal cavity during an exchange is 2000 mL. After a "dwell" of four to six hours, the volume may increase by as much as 800 mL, depending on the amount of water removed from the blood. This large volume of water removal is achieved by using the highest concentration of dextrose (4.25 percent); the lowest concentration of dextrose (1.5 percent) removes up to 80 mL of water per exchange. An intermediate concentration (2.5 percent) removes up to 500 mL of water per exchange. All three concentrations are equally effective in removing nitrogenous waste from the blood.

Two waste products normally removed by the renal system are creatinine, a product of muscle metabolism, and urea, a waste product of protein digestion. Dialysis does not restore the blood levels of these products to normal, but the reduction is sufficient to reduce the fatiguing effects of uremia.

It has been estimated that about 15 percent of the dialysis population is on CAPD. Ages of these CAPD patients range from newborns to 90 years, with a mean of about 50 years, according to the National Association of Patients on Hemodialysis and Transplantation (*NAPHT News,* 1982).

Effective as CAPD is, it is not without side effects and risk of infection. The dialysate is an almost perfect medium for bacterial growth at body temperature, and the risk of peritonitis is ever present. Contamination of the catheter system that provides access to the peritoneal cavity can be avoided only by aseptic procedures during each exchange. The exchange involves removal of the plastic bag containing spent dialysate and replacing it with a fresh bag of dialysate. This requires the removal of the connecting device (the "spike") from the bag of spent dialysate and inserting it into the port on the fresh bag. The brief period during which the spike is exposed to air can result in contamination by air-borne bacteria. Inadvertently allowing it to contact any nonsterile surface may also result in bacterial contamination.

Because peritonitis is almost inevitable, CAPD patients are given thorough

training on the addition of special antibiotics to the dialysate. This is done by injecting the medication into a special port on the bag of dialysate under sterile conditions. The protocol is specific for the treatment of peritonitis and lasts for ten days or more under the supervision of the nephrologist and close monitoring of CAPD clinic nurses.

The osmotic agent used in CAPD is dextrose (glucose), and the body typically absorbs this sugar from the dialysate during CAPD. This can cause an increase in cholesterol and triglycerides in the blood; high levels may lead to diseases of the vascular system. For an ESRD patient with diabetes, the absorption of glucose from the dialysate can produce dangerous levels of blood sugar. For these and other reasons, CAPD patients use the lowest possible glucose concentration in the dialysate that will provide an adequate osmotic gradient for water removal and may add insulin directly to the bags of dialysate regularly.

Another side effect of CAPD is the removal of water-soluble vitamins from the blood. Every CAPD patient must take daily oral doses of multiple vitamins and folic acid to replace those removed in the dialysate.

A major effect of renal failure is the decreased production of the hormone erythropoeitin which stimulates the production of red blood cells. The resultant anemia is one of the first symptoms of renal failure. No way has been found, short of blood transfusions, to significantly raise the red blood cell count of ESRD patients. Because of the chronic problem of anemia, ESRD patients characteristically find it difficult to perform physical activities that require a good supply of oxygen in the blood. However, mild exercise programs with appropriate demands are recommended and possible. Iron supplements are part of the oral medication regime for CAPD patients, but the limit to the effectiveness of such treatment is the volume of red blood cells. It is not unusual for a CAPD patient to have less than 60 percent of the normal red blood cell volume.

Another function of the kidneys is to regulate fluid volume, which is a factor in determining blood pressure. Many ESRD patients suffer from hypertension, and it is not unusual for afflictions of the vascular system to plague those on dialysis. Fluid balance is another problem, and edema due to water retention in the tissues is common. Sodium and fluid intake have to be regulated in such cases. CAPD avoids the rapid fluctuations in blood pressure that characterize hemodialysis treatment and also affords more constant control of water retention.

From the chemical viewpoint, one interesting complication of ESRD is the effect of inadequate removal of phosphate from the blood. Phosphate is a product of protein metabolism, and too high a level of phosphate in the blood can cause calcium release from the bones, with the possible result that the bones become weak and more subject to fracture. The excess calcium and phosphate ions combine to form insoluble calcium phosphate, and minute crystals of this material deposit in the soft tissues and the skin, where it causes itching. To avoid this, when blood studies show low calcium or high phosphate, phosphate binders such as aluminum hydroxide are prescribed to tie up the dietary phosphate in its passage through the body. Calcium supplements are sometimes prescribed because kidney failure usually results in a loss of the effectiveness of vitamin D, without which calcium cannot be absorbed normally from foods.

Potassium can build up in the blood when the kidneys do not function, and dialysis does not fully correct this problem. A higher than normal level of

potassium in the blood has few obvious symptoms and the effect can be insidious, ranging from high blood pressure and irregular heart rhythm, to cardiac arrest. The best way to avoid this problem is to avoid foods that are high in potassium. Compared to hemodialysis patients, CAPD patients are less likely to have a problem with potassium level.

In spite of its many advantages, CAPD is not for everyone on dialysis. For those who have the interest and the ability to care for themselves, it affords a degree of freedom that contributes much to the sense of well-being that is essential to a happy life. It can be a machine-free existence. On the other hand, recent technology provides for intermittent peritoneal dialysis through overnight automated cycling. Available only in some locations, these cyclers afford freedom from the machine and from day-time exchanges during waking hours. Several exchanges occur while the patient is sleeping, and the removal of waste products from the blood is done effectively. Such machines take up about two square feet of floor space and stand about five feet high. Microprocessors regulate inflow, outflow, and dialysate temperature. Supply has not yet caught up with demand for these cyclers, but in time they will offer a degree of freedom during the day not afforded by CAPD, though not providing for a truly machine-free life.

A Personal Note

When I was told in the fall of 1981 that I had lost two-thirds of my kidney function, my only symptoms were fatigue and shortness of breath on exertion. The clinical detection of anemia led to further tests, particularly the measurement of creatinine and urea in my blood. These confirmed the diagnosis of chronic renal failure, and the prognosis was that my kidneys would eventually become inadequate, possibly failing altogether, necessitating some form of dialysis. That day didn't come until the fall of 1984 when the level of waste products in my blood and my increasing fatigue indicated that it was time to have the CAPD catheter surgically implanted. This decision was made jointly by me and my nephrologist, and was based on a long record of clinical measurements that showed gradual but unmistakable continued loss of kidney function. For three years, I had been gradually running down like a neglected spring-driven clock, and the gradual increase in my malaise had masked the way I really felt. After about five weeks on dialysis, I suddenly realized how much better I was feeling. I now feel that CAPD has given me a new lease on life, and even though the schedule of three or four exchanges a day is disruptive, I am thankful that I live in a country that has the resources to provide this kind of therapy.

Aside from that, I have found CAPD to be a fascinating and very personal mode of treatment, full of interesting chemistry and biology. My students have found it to be an intriguing story that adds a human dimension to their studies.

(Author's comments: Much of the content of this paper is drawn from the thorough training provided by the CAPD clinic personnel, particularly Carl J. Richards, M.D., Renal Dialysis Center, St. Francis Hospital, Waterloo, IA. Dr. Richards has reviewed the paper for its technical accuracy.)

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