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THE ARTIFICIAL KIDNEY, A DESCRIPTION AND DISCUSSION OF THE MODIFICATION OF LEONARDS AND SKEGGS

A. Waite Bohne, M.D.* and Paul J. Hettle, M.D.**

The use of the artificial kidney has been a recent development in the field of medicine and surgery, and has become a useful and life saving measure in many conditions. A description of the Leonards and Skeggs modification follows with a discussion of the principles, the indications, and some of the results.

1. Dialysis

Dialysis, the basis of all artificial kidneys in clinical use at the present time, is a process of “selective filtration.”1,2 Basically, this means that a membrane which permits substances up to a given molecular size to pass freely, is placed between the solution, e.g., blood, containing those substances for removal and another solution, the dialyzing solution, which has no such substances present or present in lesser concentrations.2 The products to be removed will pass into the dialyzing solution until equilibrium is established. If, initially, the dialyzing solution contains none of the products for removal and is changed as the concentrations of these products rise during the procedure, one can accomplish almost complete removal of the products. Able, Roundtree, and Turner in 1912 were the first investigators to utilize this principle in the extracorporeal dialysis of living animals.3,4

Within certain limitations, the efficiency of dialysis is directly proportioned to the following:

1. Concentration of the substance in the patient’s blood.5
2. Surface area of the membrane.6,7
3. Hydrostatic pressure gradient.8,7
4. Osmotic pressure gradient.
5. Thinness of the membrane.5

2. Leonards and Skeggs Dialyzer9

The dialyzing mechanism of this “kidney” is made up of twelve units connected in parallel series. Each unit consists of two rectangular sheets of cellophane, the membranes, sandwiched between two rectangular, corrugated rubber sheets. The blood of the patient is caused to flow in at one end between the sheets of cellophane and the dialyzing solution to flow in at the opposite end between the cellophane and the rubber sheet. In this manner counter-current action is obtained and the efficiency increased.8 The blood is propelled through the machine by a Beck pump, as is the dialyzing solution. A constant temperature is maintained by a thermostatic heating unit, through which the dialyzing solu-
tion passes before entering the machine. Dialyzed blood leaves at the opposite end to entry and goes into an air trap before return to the patient.

The dialyzing surface area of each unit is 840 cm$^2$ and during operation each contains approximately 45 c. cms, of blood. The total membrane area is about twice as great as the filtering surface of two normal kidneys. Under optimum conditions approximately 0.5 gram of urea nitrogen per hour can be removed from dogs with a urea level of 150 mg percent.$^{10}$

3. Specific Problems Regarding Components of the Machine and its Utilization

A. The Dialyzing Solution.

Most solutions are designed to have the same milli equivalents of electrolytes as normal plasma.$^{4,11}$ Therefore, if the patient's blood is high or low in a particular substance, there will be a tendency toward restitution of normal level. However, if the primary purpose of dialysis is the removal of one substance, e.g., K$^+$, it theoretically would be advantageous to reduce that ion in the dialyzing solution, thereby effecting a more efficient transfer of potassium from the patient's blood.$^{12,13,14}$

The pH of the solution is maintained at 7.3–7.45. If the pH varies greatly in either direction, untoward effects are noted in the patient, as would be seen clinically in acidosis or alkalosis.$^7$ Further, as a secondary change, hemolysis might be noted.$^{15}$

The osmotic force exerted by the dialyzing solution should equal or surpass that of the patient's blood in order that edema not ensue from transfer of water.$^{16,2}$
Consequently, most solutions have a hypertonicity as regards glucose. During dialysis, however, the sugar passes the membrane readily and the blood sugar of the patient rises. With this rise, the osmotic gradient away from the patient is correspondingly decreased. It is well to note that the urea, per se, in the patient's blood will affect the osmotic gradient and this factor is reduced as urea is dialyzed. By measuring the osmotic activity of the patient's serum and comparing with that of the dialyzing solution, prior to dialysis, one is able to obviate the possibility of edema during the procedure.

BLOOD PLASMA

<table>
<thead>
<tr>
<th>BASE mEq/l.</th>
<th>DISALYZING SOLUTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na 142</td>
<td>Na 142</td>
</tr>
<tr>
<td>K 5</td>
<td>K 5</td>
</tr>
<tr>
<td>Ca 5</td>
<td>Ca 5</td>
</tr>
<tr>
<td>Mg 3</td>
<td>Mg 3</td>
</tr>
<tr>
<td>155</td>
<td>155</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ACID mEq/l.</th>
<th>BASE mEq/l.</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCO₃ 27</td>
<td>HCO₃ 31</td>
</tr>
<tr>
<td>Cl 103</td>
<td>Cl 113</td>
</tr>
<tr>
<td>HPO₄ 2</td>
<td>HPO₄ 3</td>
</tr>
<tr>
<td>SO₄ 1</td>
<td>Lactate 8</td>
</tr>
<tr>
<td>Org.Acid 6</td>
<td>Protein 16</td>
</tr>
<tr>
<td>Mg 3</td>
<td>155</td>
</tr>
</tbody>
</table>

Fig. 2—Diagram of Blood Plasma and Dialyzing Solution.

B. The Dialyzing Membrane.

Ordinary, commercial cellophane is utilized as the "selective membrane." When wet and swollen, cellophane will allow substances with a molecular weight of 15,000 and less to pass. Urea, creatinine, uric acid, indoxyl, nonprotein nitrogen and all electrolytes, accordingly, dialyze readily. The membrane is impermeable to plasma proteins, viruses and bacteria.

Reports in the literature indicate that glycerin must be washed out of the cellophane, since glycerin is hemolytic even in small quantities. We have studied the effect of washed and unwashed cellophane as regards hemolysis and have been unable to demonstrate any clinically significant hemolysis due to either preparation.

4. Indications and Contraindications to Dialysis

A. Indications

The best candidate for dialysis is that patient who, if helped over a critical period, has a reasonable hope of recovery by his own physiological mechanisms.
Acute renal insufficiency, regardless of etiology and after a trial of conservative therapy, is an excellent indication for dialysis. A patient in chronic uremia may be prepared for surgery by preoperative dialysis, particularly if the surgery is directed toward correctable disease of the genito-urinary tract. The chronic uremic may be helped over an acute exacerbation of his disease and his symptoms be alleviated for months by dialyzation for a matter of hours.

Very precise indications for the use of dialysis are: (1) To relieve any acute poisoning in which the substance is not completely tissue fixed (e.g., salicylates, bromides, carbontetrachloride, and mercurials)*, (2) to restore a specific electrolyte imbalance (e.g., hyperkalemia due to renal shutdown), (3) to relieve pulmonary edema in a uremic patient, and (4) to help correct uremia and hypotension associated with hepatorenal syndrome.

B. Contraindications.

Contraindications for dialysis are: (1) Active bleeding, as it is necessary to heparinize the patient during the procedure, (2) Severe, rapidly progressing hypertension, as the patients often show a rise in blood pressure during the first hour of the procedure, (3) chemical uremia without symptoms, as these patients can usually be maintained by conservative therapy.

5. Technique of Dialysis.

The procedure that we now use is as follows:

The cellophane is placed in the machine in the dry, unwashed state. Boiling water is pumped simultaneously through the dialyzing and the blood side, thereby removing glycerin. Live steam is then passed through the blood side for thirty minutes, effecting sterilization. New rubber tubing is used on the blood side for each run of the machine. This eliminates possible pyrogenic reactions due to reused tubing. The blood side of the machine is washed with seven to ten liters of sterile, normal saline, which hastens cooling as well as preventing hemolysis due to water remaining in the machine.

Our dialyzing solution is made up from solution “A” and solution “B,” stored separately in the refrigerator. They are separate to prevent precipitation of calcium as the bicarbonate. These solutions are added to distilled water just prior to dialysis in order to give the following concentrations:

<table>
<thead>
<tr>
<th>*</th>
<th>Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na⁺</td>
<td>142. mEq.</td>
</tr>
<tr>
<td>K⁺</td>
<td>5. mEq.</td>
</tr>
<tr>
<td>Ca⁺</td>
<td>5. mEq.</td>
</tr>
<tr>
<td>Mg++</td>
<td>3. mEq.</td>
</tr>
<tr>
<td>Cl⁻</td>
<td>113. mEq.</td>
</tr>
<tr>
<td>HCO₃⁻</td>
<td>31. mEq.</td>
</tr>
<tr>
<td>PO₄³⁻</td>
<td>3. mEq.</td>
</tr>
<tr>
<td>lactate</td>
<td>8. mEq.</td>
</tr>
</tbody>
</table>

Glucose is added to give a level of 200 mg %. During eight hours of dialysis approximately forty gallons of solution is required. The dialyzing solution is pumped at a rate of 250-400 cc’s/minute and the blood is propelled at 200-250 cc’s per minute.

Large size plastic catheters are inserted into the inferior vena cava (a cut down being done on the saphenous vein and the catheter threaded up the vessel)
and into an antecubital vein. Blood is taken from the former and returned in the latter. The blood side of the dialyzer is primed with a pint of compatible bank blood that has 50 mg. of heparin added. Blood from the patient may be used if pulmonary edema is present. Dialysis is begun by joining the catheter lying in the inferior vena cava to the blood pump and then joining the antecubital catheter to the air trap.

Just preceding active dialysis, the patient’s temperature, pulse, respiration, blood pressure and subjective condition are recorded. These are checked every twenty minutes. Intake and output are recorded, an indwelling Foley catheter facilitates this. The patient’s weight, recorded before the procedure, is obtained every hour. This is especially important if the primary purpose is removal of edema fluid. An hematocrit is drawn every two hours for in this way one can follow hemolysis and exchange of fluid if they occur. Ten milligrams of heparin are given to the patient every hour in order to replace that which is lost by dialysis. If we are particularly interested in the removal of $K^+$, we make a periodic EKG to follow this ion closely.

After eight hours of dialysis, the time we have empirically set for termination of the procedure, the patient is given 150 milligrams of protamine sulphate intravenously. Blood is withdrawn via the catheters for chemistries to compare with pre-run levels. As a minimum we measure Na, K, Cl, CO$_2$ and NPN. However, the chemistries ordered will vary in individual cases, dependent upon the indication for dialysis. The catheters are removed, pressure dressings applied, and a prophylactic antibiotic administered.

6. Subjective, Objective and Chemical Alterations Due to Dialysis

A. Subjective and Objective Alterations.

The comatose patient may become conscious during or shortly after the procedure. This is especially true if the removal of a substance like bromide is accomplished. The withdrawal of edema fluid greatly improved vision and relieved intractable headache in one of our cases. Dyspnea may be decreased if pulmonary edema is present. One worker has reported extraction of approximately twenty pounds of edema fluid during an eight hour run. Twenty-four hours may pass before maximum improvement is noted, but in the chronic uremic patient forty-eight hours may elapse before clinical change is apparent. Nausea and vomiting may be reduced and conservative therapy, thereby rendered more accurate and effective. Not uncommonly diuresis may follow dialysis.

B. Chemical Alterations.

Chemical results are often very striking. Bromides may be lowered to 80% of their initial blood level. Alkalosis or acidosis may be corrected and all specific electrolytes may approach normal values. Nonprotein nitrogen may fall fifty per cent (e.g. an NPN of 200 mg. per cent was reduced to 100 mg. per cent in one of our patients during an 8 hour run). In order to evaluate the amount of urea removed, one cannot simply compare the pre-run BUN or NPN with the post-run values. It has been shown repeatedly that more urea-nitrogen can be found in the dialysate than was present by calculation in the entire body fluid of the patient. This has been found true with only a slight fall in the patient’s
BUN and NPN. Thus, urea contained in the patient’s tissue seems to replace that which is lost by dialysis. As a consequence, we now measure the urea contained in a representative sample of the used dialysate and as much as 200 grams of urea has been removed by our procedure in an 8-hour period.

An unexplained finding following dialysis is a reduction in serum protein concentration. As the patient’s weight is often unchanged, the explanation cannot be simple dilution. Whether this change in protein concentration is clinically significant is not known at this time.

7. Generalizations about Dialysis

At this time our experience is too meager to support generalizations. To date Merrill et al have had the most extensive experience with extra-corporeal dialysis in this country. From about 250 clinical trials they have arrived at the following conclusions:

(1) There is good correlation between clinical improvement and chemical changes.
(2) The polyuric, normotensive patient responds better and for a longer time than the relatively oliguric, hypertensive and uremic patient.
(3) The chronic uremic patient with a urine volume greater than 1500 cc’s per day, who has no hypertension, and who fails to respond to conservative therapy may expect a good response to dialysis.
(4) Successive dialysis tends to be less successful.
(5) Patients with acute glomerulonephritis and especially with severe hypertension, respond poorly to dialysis.

8. CONCLUSION:

From reviewing the enlarging literature on dialysis and from our experience, we believe that this procedure is a useful adjunct in the treatment of selected types of uremia, as well as specifically indicated in other conditions previously cited. We feel that the results obtained will vary directly with clinical experience and, therefore, will improve with further application. In the future we will undoubtedly see many more and varied disease states in which dialysis may be an accepted part of therapy.

BIBLIOGRAPHY


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