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Comparative efficiency in the treatment of uremia with peritoneal lavage, artificial kidney, and gastric lavage

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THE COMPARATIVE EFFICIENCY IN THE TREATMENT OF UREMIA WITH PERITONEAL LAVAGE, THE ARTIFICIAL KIDNEY, AND GASTRIC LAVAGE

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THE COMPARATIVE EFFICIENCY IN THE TREATMENT OF UREMIA WITH PERITONEAL LAVAGE, THE ARTIFICIAL KIDNEY, AND GASTRIC LAVAGE

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INTRODUCTION

Uremia has been one of the chief causes of death since the beginning of medical history. Until very recently, the therapy for uremia has been based entirely upon efforts to stimulate the kidneys to work further, or to stimulate the skin to excrete.[1] With these limitations in therapy, death was the natural end result of uremia caused by temporary kidney damage. Many times these cases terminated fatally because the uremia retarded kidney repair and caused death.[1] If the kidney could eliminate this block sufficiently to permit excretion of adequate endogenous waste products, the patient survived. It is believed by many that if this uremic period can be delayed for a matter of even a few days, in many cases of kidney damage the cells will regenerate from their basement membranes, the block will relieve itself, and the patient will regain partial or total kidney function. It is also believed that partial or total relief of the persisting uremia aids greatly in permitting damaged tissue to repair itself. Among the many conditions in which the treatment of uremia is indicated, whether by peritoneal irrigation, the artificial kidney, or by gastro-intestinal lavage, there is one cardinal principle into which the case must fit. This is simply that the kidney lesion must be repairable. It would be to no avail to sustain a patient with an incurable cancer or the contracted kidneys of a prolonged disease.

One of the conditions in which this type of treatment is warranted is the crush syndrome. Here, a combination of shock, myoglobinemia and hemoglobinemia causes a kidney block by plugging the tubules, and there is a lowering of the blood pressure. The lowered blood pressure is thought to originate because of the accumulation of toxic products due to protein breakdown caused by ischemia. This is a temporary condition, and, if the patient survives long enough, sometimes rights itself.[2] This condition carries a definite mortality rate, which may be lowered by treating the uremia present. Other conditions similar to this are transfusion reactions, heavy metal poisoning, bilateral urethral stones, precipitation of sulfa drugs in the tubules with total block of the kidneys, hypercalcemia from parathyroid tumor[3], muscle rupture, and electric shock therapy.[4]

In my opinion, it is definitely contraindicated to prolong life and suffering by these methods of treatment if the outcome is hopeless. However, I also feel that there is excessive conservatism and complacency on the part of the doctor who does not make every attempt to recognize these conditions early, and to treat them with the latest methods of therapy, such as will be discussed.

PERITONEAL LAVAGE

The principle for the use of peritoneal lavage was perhaps introduced when Rosenberg, in 1916, found that ascetic fluid withdrawn from the abdomen of a patient dying from uremia contained approximately the same urea concentration as did the blood of the patient.[5] Later, Strause reported improvement of uremia by recovery and replacement of abdominal fluid in uremic cases. Landis has shown that crystalline substances will pass in either direction through the peritoneal membrane. Putnam has shown that crystalloids will diffuse through the peritoneal membrane, whereas colloids will not.[5] In reviewing these findings, their essence is that the principle of the peritoneal membrane is much like the membrane of the glomerular filter, and that the products of metabolism should pass through this membrane much like filtration through the kidney. Klein[6], in his paper, mentioned that the peritoneal area is approximately equal to the surface area of the skin. As early as 1877, Wegner found that crystalloids in fluids were readily absorbed from the peritoneal cavity. Ganter, in 1923, studied peritoneal lavage as a therapeutic measure. He caused uremia in dogs by ligating both ureters, and then washed the abdominal cavities with normal saline . He was able to prolong life over the life expectancy of other control dogs. Rosenak and Oppenheimer, in 1926, carried out continuous peritoneal lavage with a 5 per-cent glucose solution, and had therapeutic results that were some better than any of those previously noted. Heuser and Werden, in 1927, used an isotonic Ringer's solution, and got still better results. They also came to the conclusion that successful irrigation necessitated the irrigating fluid to be as close to plasma in crystalloid content and osmotic pressure as possible, in order to gain the most beneficial results. They also noted that solutions which were not at least isotonic, or hypertonic, were markedly absorbed and caused, in many instances, pulmonary edema and general overloading with marked electrolyte unbalance. Frank, Fine, and Seligman[7] found that the speed of diffusion and removal of nitrogenous metabolic end products is proportional to their concentration in the blood stream and to the osmotic differential set up by the perfusing fluid. They also noted that very closely related to the concentrations in the blood stream was the amount of extracellular products stored in the intracellular extravascular spaces. It is also true that the index of successful treatment, as measured by the blood non-protein-nitrogen and blood urea nitrogen is somewhat false, in that it does not measure the true toxic products of uremia in the blood stream. Wear, Sisk, and Trankle[8] believe the oxyproteic acid is the most toxic element in the blood stream in uremia. They also believe that the number of polypeptids present in the blood stream are better prognostic signs than are the non-protein-n trogen and urea nitrogen levels. Hartwick and Hessel noted that dogs lived longer if their ureters were transplanted into the portal circulation than if they were transplanted into the general circulation, or merely ligated. In their opinion, it indicated that the liver plays a very major role in the de-toxification of the poisons of uremia. These workers also observed that during uremia the alkali reserve is considerably reduced, and with the kidneys not functioning, there is no means of excreting the acid metabolic waste products.[9] These men were also of the opinion that elimination of these toxic substances from the body would speed the recovery of the damaged kidney.[10] Bliss, Castler, and Nadler in 1932 kept nephrectomized dogs alive for 13 to 16 days, and were able to remove urea, creatinine, phosphates, sulfates, uric acid, and other undetermined substances from the abdomen by peritoneal lavage. This I will conclude from their experiments as meaning that all ionizable substances of a molecular size sufficient to pass through the peritoneal membrane may be removed by perfusion. Considering the fact that these men were able to keep animals alive for up to 16 days, whereas control animals in the same series would die in from three to five days, it will also indicate that some of the toxic products of uremia are also eliminated in this manner. These workers also reaffirmed the statement that lavage fluid which closely resembles plasma is much more satisfactory. They used mammalian tyrodes. They also found that perfusion with a hypotonic sodium chloride soluti n caused removal of calcium, chlorides and sugar from the blood stream, and also caused a loss of alkali reserve. They suggested that perhaps the peritoneal lavage fluid should be buffered to combat the tendency of acidosis of uremia. One of their indexes of prognosis was that of the alkali reserve of the patient. In other experiments [3,5] they found that 5% glucose injected into the peritoneum in a volume of 10% of the body weight caused marked dehydration and a loss of 20% of the total blood sodium. This disterbance in the electrolyte balance of the extracellular fluids seemed proportional to the osmotic difference between the fluid in the intracellular spaces of the peritoneal membrane, the blood stream, and that of the perfusion fluid.[1] Since the peritoneal irrigation fluid will resemble glomerular filtrate very closely, it is logical to expect that the amount of fluid lavaged through the peritoneal cavity will have to be equal to, or greater than, normal glomerular filtrate. This would be especially true if one were treating uremia and had large amounts of waste products to remove.[1,7]

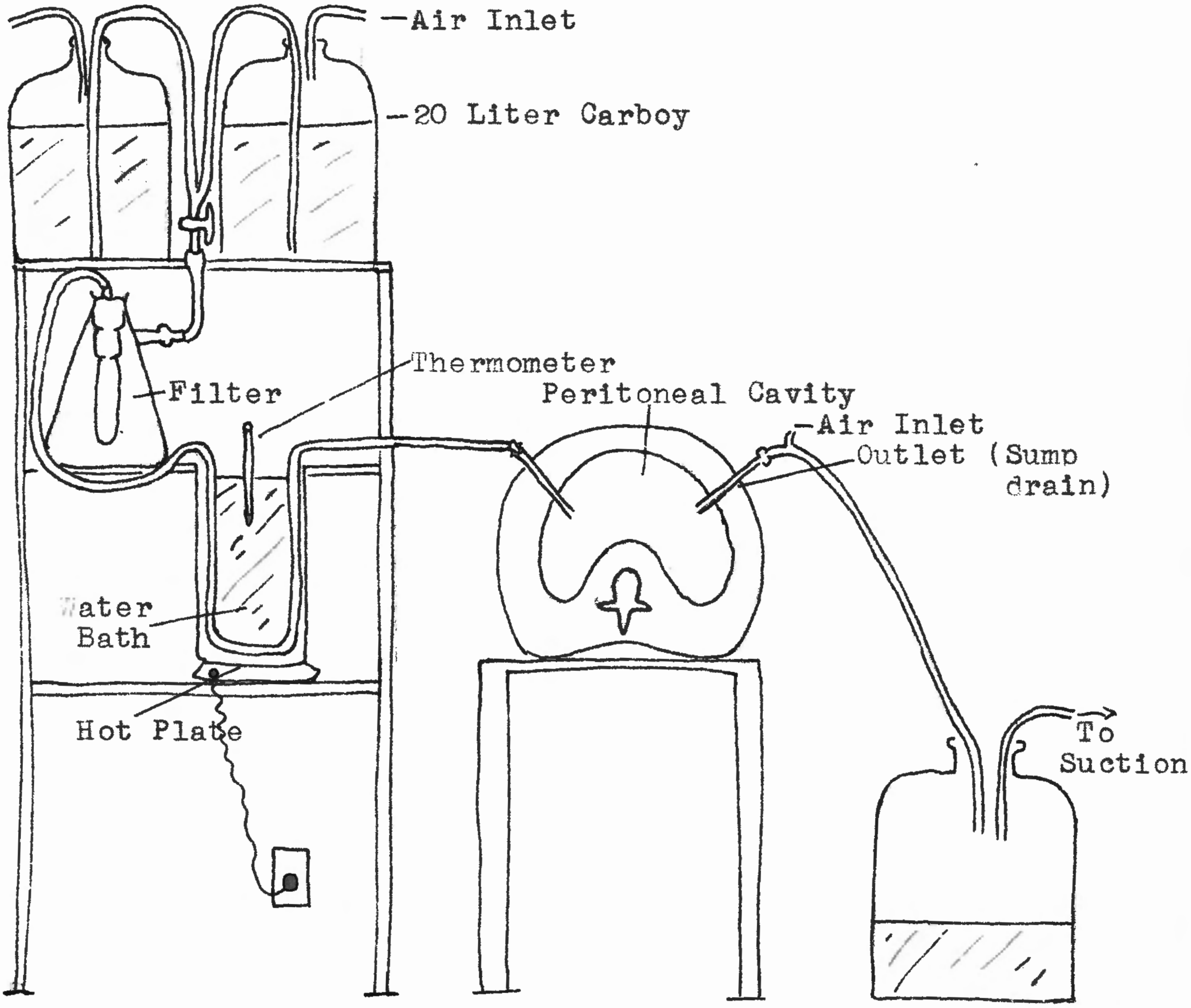
Optimum flow rates through the peritoneal cavity can very easily be established by measuring the end products removed from definite amounts of recovered fluid at known rates of flow. The rate of formation of glomerular filtrates in dogs, as measured by inulin or creatinine clearance is given as 94 ml. per sq. m. per min.[9] For instance, in a dog with 0.45 sq. m. of surface area, the glomerular filtration rate is given as 38 to 47 ml. per min. This very closely approximates the observed optimum flow rates for peritoneal irrigation in these animals, which were 30 to 50 ml. per min. At these rates of flow, the ratio of the concentration of urea in the irrigation drainage fluid is approximately one-third to one-half of the glomerular filtrate. Therefore, the efficiency of peritoneal dialysis might be expected to be about one-half to one-third that of glomerular filtration.[9,11] However, peritoneal irrigation effects a higher percentage of normal renal urea excretion than these figures would indicate. This is because glomerular excretion of urea exceeds total urinary excretion by virtue of the reabsorption of urea in the tubules. Peritoneal lavage may actually be more efficient in removing metabolic waste than are the kidneys. The principle of excretion and absorption of electrolytes from the peritoneum make it possible to judge and predict the various stages of hydration of plasma and of extracellular fluid.[5] It is not known, however, if this method offers a safe route of excretion of excess body water. It has been the experience of some, Lemphly, Creighton,[1] that this is not the case. Other workers have demonstrated with patients that, when solutions are made hypertonic with gelatin or glucose, water can so rapidly be removed from the general circulation as to cause hemoconcentration and shock. It is my opinion that it may be advisable to reduce the plasma chloride level by an attempt to substitute molar lactate buffer to combat acidosis, and sufficient glucose to help maintain nutrition and also counteract that lost in the lavage fluid. Should hemoconcentration occur, this can be combatted by an intravenous administration of fluids. This also presents an excellent means of maintaining the nutrition of the patient.

If I have made this appear simple, please let me inject that statement that it is difficult to predict the outcome of excretion and absorption across the peritoneal membrane. This will vary with the type of irrigating fluid used, and with the state of hydration of the plasma and extracellular fluids. There is evidence[5] that the peritoneal membrane will selectively absorb from the lavaging fluid many elements, irrespective of their osmotic relationship.

Technique

One of the problems in the development of peritoneal lavage as a form of therapy has been the determination of the proper lavaging fluid. As previously mentioned, it was determined by trial and error that the electrolyte content of the fluid must correspond very closely with the electrolyte content of the plasma. One of the fluids which has been efficiently used by many workers is that of mammalian tyrodes. It is composed of sodium chloride, 8 parts, potassium chloride 0.2 parts, calcium chloride, 0.1 parts, magnesium chloride 0.1 parts, sodium hypophosphate, 0.05 parts, and sodium bicarbonate, 1 part. To this fluid is very often added glucose for hypertonicity and to prevent loss of lucose from the body, penicillin and sulfa for bacterial stasis, and heparin in approximately 0.5 mg per liter to prevent fibrin clots from occluding the catheters. All of these salts can be mixed and sterilized together, with the exception of sodium bicarbonate, (which would combine with the calcium present to form an insuluable precipitate), heparin, and the antibiotics. Glucose is added in 1% to 5% strength, depending on the tonicity desired. It is interesting to note here that glucose is lost from the lavage fluid in approximately the same concentration as it is found in the blood, which is about 90 mg%.[7,12] The mammalian tyrode solution has been used in preference to Ringer's solution because it contains the sodium bicarbonate and has a high chloride content. This is desirable because uremic patients are usually in acidosis before therapy is started, and further loss of the fixed base is undesirable.[3] It has been demonstrated that any isotonic solution of sodium chloride used as a perfusion fluid causes considerable sodium retention and a resulting pulmonary edema.[13,14] Several investigators have found that Hartman's solution is also desirable.[5,15] Tracy, Jackson, and Putnam found that the lavage fluid should be slightly hypertonic in order to slightly dehydrate the patient, as prophylaxis to edema. Perhaps one of the drawbacks of hypertonic solutions are that they are usually more irritating and less comfortable to the patient and often show local reactions at the site of injection. The speed with which peritoneal irrigation lowers the blood level of retained excretory products depends on the amount stored in the vascular compartments.[16,17,18] This will in turn vary with the body weight, and with the amount of edema present, as well as the rate of flow of the irrigation fluid. By trial and error, Fine, Frank and Seligman[7] found that their most optimum rate of flow in patients was 40 to 60 ml. per minute. They estimated that 15 ml. per minute would possibly be adequate on the basis that ordinarily not more than 10% of the average normal maximum renal clearance of urea of 75 ml. per minute is necessary to prevent the accumulation of excretory products.

Diagram of Intraperitoneal Apparatus



Apparatus

The apparatus necessary for peritoneal lavage is very simple and easily assembled. It consists essentially of a reservoir containing sterile fluid of the desired quality from which may be siphoned continually and aseptically through a definite measuring device which can be regulated, and then proceed to the patient. The fluid must be sterile, and warmed to body temperature when it enters the peritoneal cavity. The fluid need not be sterilized in its storage tanks, but should be cleaned and filtered through a Berkefeld filter. It is my personal opinion that the fluid should be sterilized and that a Berkefeld filter should be used in addition, to avoid any possible contamination. There must be some arrangement whereby the perfusion fluid is circulated in a water bath for a sufficient length of time to bring it up to body temperature before its delivery into the peritoneal cavity.

The procedure to deliver this fluid into the peritoneal cavity is usually done under local anesthesia and consists of a longitudinal slit through the flank and down through the peritoneum, with the introduction of a stainless steel inflow catheter. On the opposite side, a stainless steel sump drain is introduced, and directed towards the pelvic gutter on the same side.

Suction is then applied to the apparatus. Continuous gentle suction is necessary to remove the fluid from the abdomen.

Babcock, in a recent article,[19] has pointed out that stainless steel or glass, when introduced into the peritoneal cavity, excites very little in the way of local reaction. This is certainly not the case with other foreign materials, such as plastic or rubber drains. These types have been generally very unsatisfactory and are usually very quickly occluded by the greater omentum or by a loop of bowel, because of their foreign body tissue reaction. The sump drain is indeed well adapted to draining the abdomen. It is a stainless steel multi-perforated drain, and is less easily occluded than most other types of drains. The greater omentum reacts to any foreign body in the abdomen, and has the ability to migrate and fuse around any drain introduced, thus stopping the free outflow of the lavaging fluid. The core of this sump drain can be removed, and by gently moving the drain any existing adhesions can be broken.

Fine, Frank and Seligman have been of the opinion that the patient should lie prone and flat on his back during this entire procedure. They maintain that the abdomen is better filled. In cases with respiratory difficulty, however, the patient may be more comfortable when in a reclining position, and if already embarrassed for air, it will be possible to avoid inhibition of the diaphragm by the pressure of the lavaging fluid throughout the abdomen.

With this type of therapy, questions arise as to when the lavage should be first started, and as to the contraindications. It is my opinion that peritoneal lavage should be started as soon as the blood non-protein-nitrogen and blood urea nitrogen are elevated, if the patient has the proper history and shows definite uremic symptoms. The history is usually one of drug toxicity, previous crushing injury, dehydration, or sulfa block. In conjunction with the beginning of this type of treatment for uremia, I think the patient should be receiving parenteral penicillin in an attempt to avoid any infection, such as pneumonia. Before beginning therapy, a series of studies and a complete work-up of the patient are in order, so that therapy may always have a path and a standard from which to judge its results. These preliminary studies should include non-protein-nitrogen, urea nitrogen, chlorides, sodium, and carbon dioxide combining power.

It is essential that the patient should be made comfortable during the lavage period, and that it should be continuous for as long as the blood urea nitrogen and non-protein-nitrogen remain elevated. Every effort should be made to give good care to the patient during this period. A high carbohydrate and protein diet should be given as can be tolerated, and the patient should receive parenteral vitamins, and fluid as is desired. With long periods of constant perfusion with a hypertonic perfusate, the patient should become slightly dehydrated, and will probably ask for water. The hypertonicity of the lavage fluid is also important, because it has been shown that diffusion through the peritoneum is not on the basis of pure osmosis alone, but that there is often a selective absorption towards the blood stream, and with constant perfusion may result in a state of hydremic plethoria. I believe that the results of therapy should be checked hourly until the optimum ml. per min. flow is determined. After this, daily tests should be performed on the perfusate to determine the success of treatment. These tests should be measurement of the non-protein-nitrogen and urea nitrogen. I think an even better estimation of the successful treatment is careful study of the patient as to his mental clearness, and the comparison of his comfort and symptoms with those before treatment. The patient should be carefully checked for any increase in edema, either in the lungs or systemically. In many instances, the blood non-protein-nitrogen and urea nitrogen levels will be misleading, for it is occasionally elevated over the level obtained before beginning of the lavage. This is because further waste products have been withdrawn from the interstitial spaces and from the cells themselves.

Should the patient show pulmonary edema with an increase in temperature, leading to a diagnosis of pneumonia, I do not believe that peritoneal lavage should be stopped. I maintain that the original pathology still persists and will result in the patient's death if not treated. If pneumonia is present, it may be wise to increase the hypertonicity of the lavaging fluid by increasing its glucose content, and start the patient on massive doses of penicillin intramuscularly.

It is very important that accurate records be kept of the perfusate removed, and that a measurement of the products removed should be obtained. In this way, the therapy which is being given can be compared with normal kidney function for that individual, and retention of fluid can be avoided. The urea clearance for the patient should be at least equal to that of the kidney, or, in the face of uremia, should exceed it.

Past and Present Problems

In the first attempts to use therapeutic peritoneal irrigation, one of the main problems was to determine the correct type of perfusion to use. Some workers, in their first attempts, introduced sterile water, normal saline, and other hypotonic solutions, but noted difficulty in obtaining survivals among their experimental animals. They later found that large amounts of calcium, sodium, potassium, sugar, chlorides, and others of the essential inorganic salts were found in the perfusate fluid.[19,20,21] The experimental animals showed dilitation of the heart, tetany, convulsions, and generalized edema. These problems have been largely remedied by the use of more correct fluids that contain all the essential minerals in about the same proportion as the blood, and made hypertonic.

Also among the more acute problems in the past were those of infection and nutrition. At the present time, antibiotics form a very powerful weapon for fighting infection. Nutrition is much better understood, and with vitamin therapy and high protein, sugar, and correct mineral intake the patient can be bolstered to fight his own disease.

With removal of peritoneal irrigation from the animal experimentation stage to its use on human beings, other problems have arisen. The most important is diagnosis. Many cases are not clear-cut, and present multiple possibilities. It is often difficult to find suitable cases, as is demonstrated b the generally unsuitable results that have been found by most workers. These results are, for the most part, the evidence of mis-diagnosis.

With the discovery of heparin, and the introduction of stainless steel inflow and outflow catheters, the troubles presented by adhesions have also been somewhat overcome.

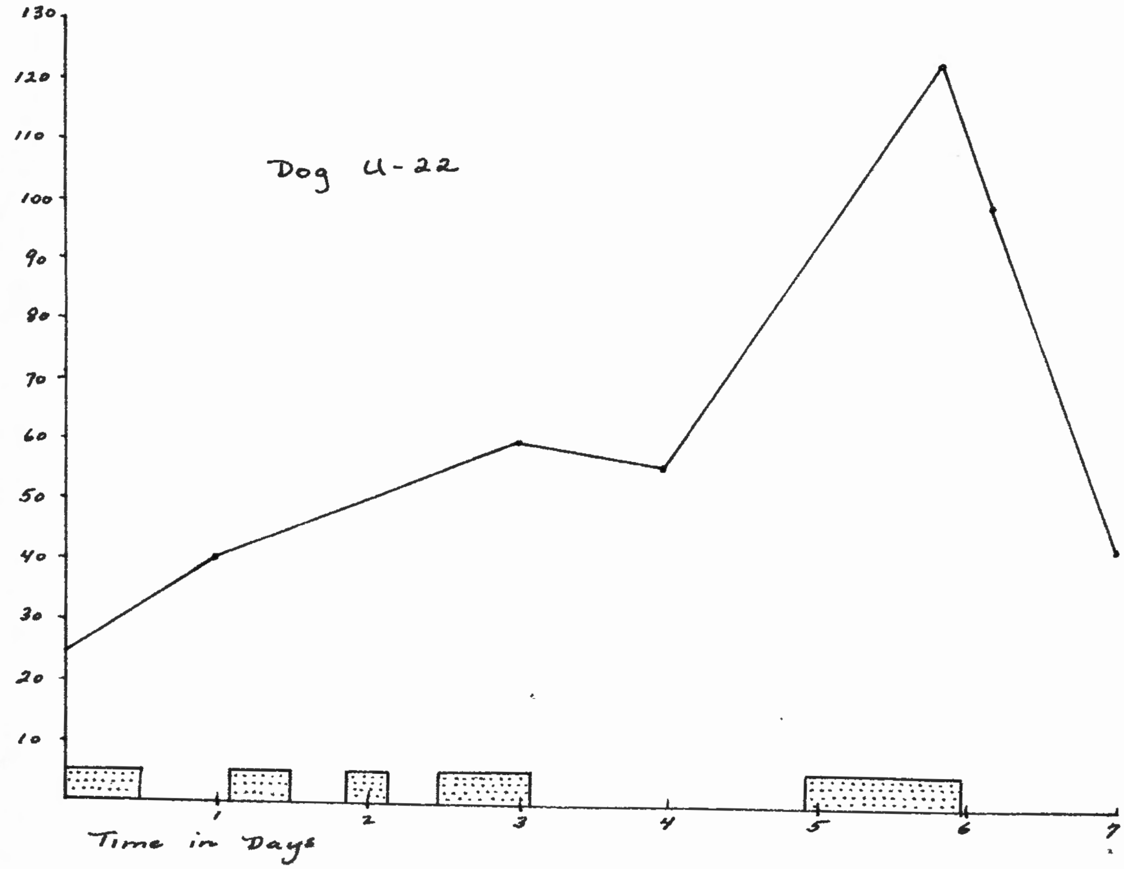
One of the truly great problems at present is the adequate analysis of the products removed. It sounds simple to say that these products should be measured. However, in actual practice[20] with quantitative measurement and combined corrlation with blood chemistry, this problem is not as easy as it sounds. Acidosis is generally present, and one of the big problems of therapy in uremia. In order to combat this, the bicarbonate ion should be increased in the lavage fluid and molar lactate should be added to the lavage fluid, in an attempt to elevate the pH of the blood.

Therapeutic Results

Experimental nephrectomized dogs were kept alive for 13 to 16 days with daily perfusion by Bliss, Kastler and Nadler, in 1932.[10] In these uremic dogs it was found that five to ten gallons of irrigation fluid, given over a period of 20 to 36 hours, was necessary to restore elevated blood levels of urea to normal. It was also found that the effectiveness of dialysis did not decrease with time.

In a group of cats, made uremic with mercury poisoning, Hamm and Fine found that 80% recovered after treatment with peritoneal lavage. In a control group of cats, only 12% recovered. These men observed that no pathology resulted from needling the peritoneal cavity.[22]

Fine, Frank and Seligman made a series of dogs anuric, and within 72 to 120 hours they showed uremic symptoms. Before treatment, the blood non-protein-nitrogen levels were 100 to 250 mg%, and the dogs were vomiting, and had muscle twitching and mental stupor. After constant irrigation, with a flow rate of 25 to 35 ml. per min., the blood non-protein-nitrogen dropped from 20 to 50 mg%, and alleviated the clinical manifestations of uremia. Before irrigation, the blood pH had been 7.4, and after irrigation it was 7.02. The blood urea dropped to normal within eight to ten hours after irrigation. These workers found that they had



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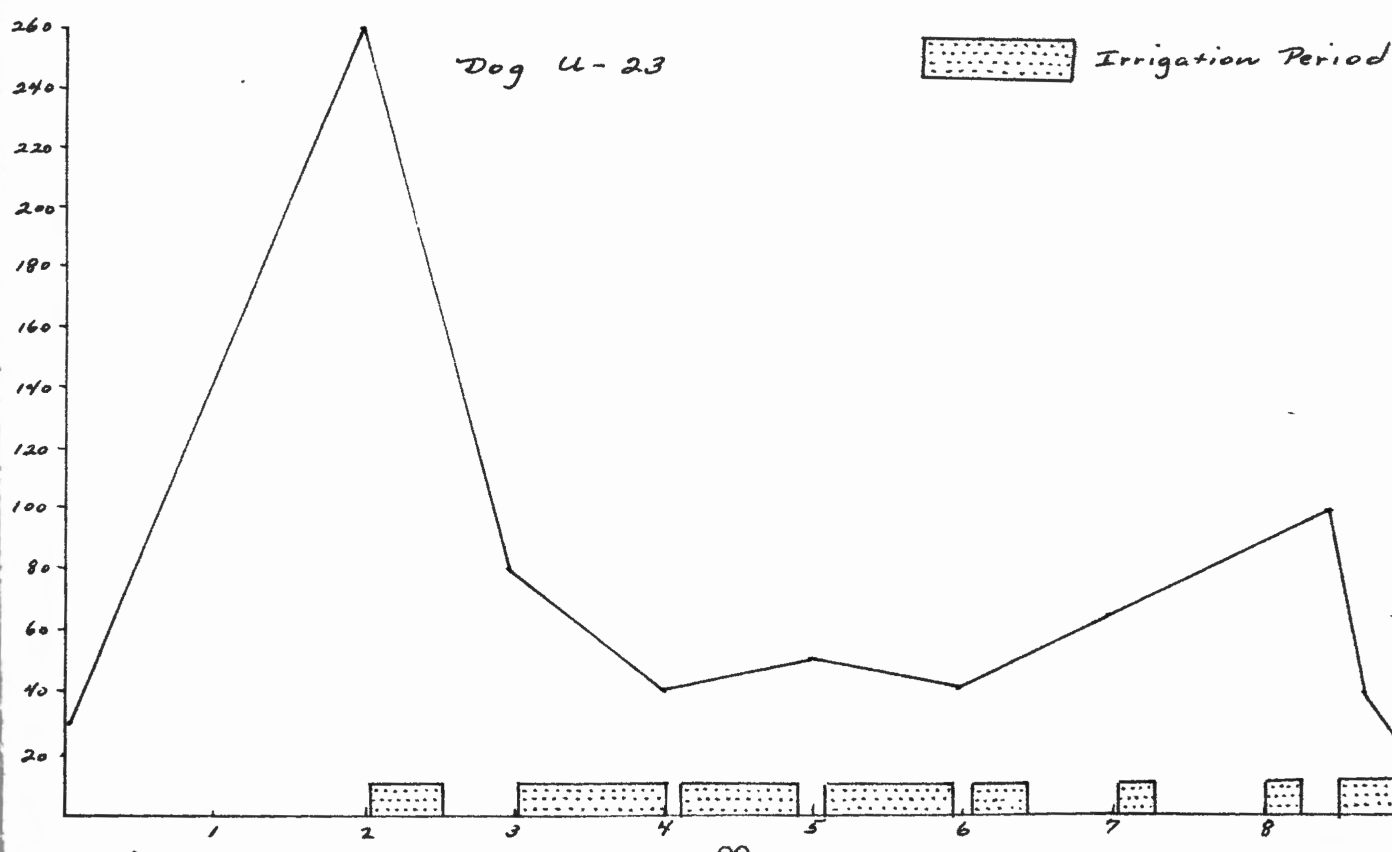


better results if they maintained the dogs in a prone position. They accounted for this on the more uniform filling of the abdominal cavity. It was found that with dogs in a supine position, peritoneal irrigation amounted to approximately 10% of normal kidney function. In prone position, it reached in some cases, up to 136% of normal, as measured by the blood non-protein-nitrogen and blood urea nitrogen. Peritoneal clearance of these dogs in prone positions was approximately 24 ml. per square meter body surface per minute, where the normal urinary flow of the dog is approximately 0.4 ml.

In presenting the above works, I am attempting to give a general survey on a small scale of the results which have been attained with animals. I have not attempted to include the entire literature, for practically all the results are comparable with those recorded above.

All work has as its ultimate goal a perfection of therapy directed towards treating the human. I will present some average case histories and results, both graphically and in story form, from a general selection of case reports by several authors.

The first case which I will present will be taken from the article published by Dr. Rhoads[23], which will introduce many of the problems involved in this procedure.

The patient, a 68 year old man, was admitted to the hospital complaining of a 5 inch carbuncle on the back. Diabetes mellitus had been discovered one week previously. Past history was irrelevent. On admission, a blood program was immediately instituted to control the diabetes, and the carbuncle was excised. Within twelve hours, it became apparent that he had a severe degree of renal failure, with a blood urea nitrogen concentration of 100 mg%. Since there was no history suggesting chronic nephritis, and there was no cardiac enlargement or hypertension, it was believed that the renal failure was secondary to the diabetic acidosis. Fluids were forced to three liters per day, sodium chloride and sodium bicarbonate were given in doses of 15 grams each per day in an effort to promote kidney function, and sodium lactate was given intravenously to combat the acidosis. The urinary output was considerably increased, but the blood urea nitrogen remained high in spite of these measures. Five days after admission the blood urea nitrogen reached 170 mg%, the patient became stuporous, and it was apparent that the customary methods of treatment had failed. Accordingly, the patient was taken to the operating room, and a cannula was introduced into the peritoneal cavity under local anesthesia. Nine liters of fluid were introduced in six installments, and a total of six and one-fourth liters were recovered.

The lavage fluid consisted of: Sodium chloride 14.5 gm/L; potassium chloride 0.4 gm/L; calcium chloride 0.2 gm/L; Lactic acid as sodium lactate 2.4 cc/L; total chlorides 256.0 m eq./L.

Samples of blood were taken immediately before and immediately after the procedure, and analyzed for serum carbon dioxide, serum chlorides, and blood urea nitrogen. The lavage fluid withdrawn from the abdomen was analyzed for urea nitrogen, chlorides and sugar. Although the procedure required two and one-half hours, it was well tolerated by the patient. The temperature was 102°F before the procedure, and 103° upon returning to the ward. The character of the patient's temperature curve was not altered by the procedure.

The pulse rate was 130 both before and after lavage, and fluctuated very little in the interval. The respiratory rate was 44 before, and 42 after lavage. The blood pressure was 130/70 before and after the procedure. The systolic pressure declined as low as 100 for a time during the lavage. The patient was completely stuperous at the start of the procedure, but towards the end he responded sufficiently to make a few intelligible complaints, and upon returning to the ward responded to a question.

The subsequent course of the patient was downward, and he expired the next day. Autopsy revealed an advanced chronic glomerulonephritis. The peritoneal surfaces were smooth and glistening, and no mark of the puncture could be found on the viscera. There was 300cc of fluid in the peritoneal cavity.

Following is a chart, showing the composition of the blood before and after peritoneal lavage:

	Urea N.	Chlorides	Glucose	CO_2	Hg (Sahli)%
Before	184	101	244	31	40
After	155	116	272	29	42

The lavage fluid recovered from the peritoneal cavity showed the urea nitrogen to be 75 mg%, Chlorides 164, and glucose 90 mg%.

The next case will be taken from Fine, Frank, and Seligman[7], who have done a vast amount of work on the subject.

A middle-aged woman entered the hospital with symptoms of nausea, vomiting and a relative anuria that had been present for the four preceeding days. At the time of her admission to the hospital, she had a generalized edema, and was treated immediately with peritoneal irrigation. This was accomplished by inserting two mushroom catheters into the peritoneal cavity through flank incisions. The peritoneal cavity at that time contained a large quantity of fluid, which was withdrawn. The blood non-protein-nitrogen content was 195 mg% at the start of irrigation. After a 24 hour period, with the flow rate averaging 45 cc. per min., 23 grams of urea was removed, and an average blood urea clearance value of 16 cc per minute was obtained. Peritoneal irrigation was kept up for another 24 hours at a flow rate of 60 cc per minute, with 246 grams of urea removed, and a blood urea nitrogen value of 23 cc per minute. After two and one half days of irrigation the blood non-protein-nitrogen was 57 mg%, the blood urea n trogen was 21 mg%, and symptoms of headache, nausea, vomiting, and anorexia were completely removed. Mental stupor and dullness completely disappeared, and urine volume increased up to 1400 cc daily. However, the urinary nitrogen content did not exceed 400 mg%, and the total daily urinary urea excretion did not exceed 10 grams. Peritoneal irrigation at this time was discontinued, due to the apparent decrease of uremia.

Flow Rate cc/min	Fluid Urea Nitrogen	Blood Urea cc/min
19	50.4	11.2
47	32.1	14.5
58	23.9	15.6
66	13.8	9.7
83	13.0	11.7
127	11.0	14.3

Although this patient showed definite improvement and seemed to be on the road to recovery, the urinary output again fell, and clinical evidence of uremia again appeared. Because at this time both peritoneal catheters were blocked and nausea and vomiting had recurred, a Miller-Abbott tube was passed and gastro-duodenal suction was introduced. The fluid removed was replaced by physiological saline solution given intravenously. When the volume of aspiration fluid was less than 500 cc. daily, the urea nitrogen content was 64 mg%. When the aspiration volume totaled 3000 cc per day, the urea nitrogen was 15 mg%. In all, one gram of urea in 24 hours by gastro-duodenal aspiration was removed. The uremic state was not improved. In a further attempt towards therapy, under spinal anesthesia, a twelve inch loop of ileum with both ends exteriorized was accomplished in order to determine the effect of intestinal irrigation. At this time, carcinoma metastasis was found on the peritoneum. Irrigation of this intestinal loop at varying rates of flow produced the following results:

Flow Rate cc/min	Fluid Urea Nitrogen	Urea Clearance (GI tract) cc/min	Urea Clearance Irrigation of Intestinal loop
7.8	7	0.6	0.5
14.6	3.3	0.54	0
15.5	2.9	0.48	0.04
15.8	3.0	0.52	0

Chart continued:

Flow Rate	Fluid Urea N.	Urea Clear. GI tract	Urea Clear. Irrigation
32.6	1.4	0.52	0
46	0.2	0.36	0.03
63	0.5	0.34	0
166	0.2	0.3	0

Irrigation of this intestinal loop for short periods of time at various rates of speed showed such poor clearance of blood urea as to indicate that perfusion of a 200 inch loop of gastro-intestinal tract would be required to achieve a blood urea concentration of 10 cc per minute, which is the minimum necessary to avoid uremia. The average achieved with this twelve inch loop during a 24 hour period was 0.56 cc per minute. The total urea removed in a 24 hour period was 0.1 gram. Fifty percent magnesium sulfate did nothing to increase this, and caused marked nausea and vomiting.

Peritoneal irrigation was again resumed, and within 24 hours 38,000 cc of fluid was lavaged through. Within the next thirty hours, thirty liters of fluid was lavaged. The blood urea concentration value was 13 cc per minute, 35 grams of urea nitrogen was removed, and the non-protein nitrogen was proportionally decreased. Uremia disappeared and the urinary flow increased. The patient lived without recurrance of this condition until carcinoma resulted in her death. A note here is that the entire procedure was carried out without dis-comfort to the patient.

The next case is taken from Abbott and Shea[9]. A fourteen year old girl entered the hospital with active rheumatic fever. In the course of therapy, she was given a transfusion with incompatable blood. Within a few hours, she showed a hemoglobinemia and hemoglobinuria, elevation of temperature, and a relative anuria of 30 cc per day. The carbon dioxide combining power was 30 vol%. The patient developed bilateral pneumonia. She became edematous and stuporous. The hemoglobin was 36%, red blood count 2,450,000, blood urea nitrogen 80 mg%, and the girl had a fast ulse and elevated temperature. In view of the complicating pneumonia, the problem of uremia was not considered as the primary problem, and so treatment by peritoneal irrigation was deferred for 36 hours. She was given penicillin therapy in conjunction with sodium sulfadiazine, and given 1000 cc of compatable blood. Peritoneal irrigation was then begun, with the following results:

		Peritoneal Fluid		
Days	Volume cc's	Flow Rate cc/min	Urea Nitrogen mg%	Total Urea grams
1	9250	6.0	61	11.3
2	9250	6.0	61	11.3
3	9000	12.5	38	6.8
4	2000	11.0	56	2.2
5	3000	8.0	76	4.6
6	9000	16.6	77	13.9

Days	Volume	Flow Rate	Urea Nitrogen	Total Urea
7	18,000	12.5	39	14.0
8	18,000	12.5	39	14.0
9	24,000	16.6	50	24.0
10	12,000	16.6	50	12.0
11	18,000	12.5	37	13.3
12	18,000	12.5	37	13.3
13	36,000	40.0	32	23.0

Urine

Days	Volume cc's	Flow Rate cc/min	Urea Nitrogen mg%	Total Urea grams
1	0			
2	108	.08	20	0.04
3	64	.05	15	0.02
4	109	.08	60	0.13
5	60	.04	40	0.05
6	74	.05	74	0.11
7	184	.13	40	0.15
8	210	.15	109	0.46
9	260	.18	89	0.46
10	305	.21	122	0.75
11	610	.43	78	0.95
12	610	.43	260	3.00
13	1300	.88	118	3.10

Blood

Days	Urea Nitrogen mg%	Blood Urea Clearance cc/min Peritoneal	Renal
1	68	5.4	-
2	55	6.7	-
3	35	13.5	-
4	60	10.3	-
5	70	8.7	-
6	82	15.6	-
7	68	7.2	0.25
8	63	7.7	0.27
9	60	13.8	0.43
10	60	13.8	0.54
11	62	7.5	2.01
12	55	8.4	2.10
13	45	28.5	-

Abbott and Shea[9] have also presented the case of a 51 year old white male, with anuria of five days due to sulfathiazole therapy. His treatment in the hospital consisted of excessive parenteral fluid, which produced generalized edema. Extreme uremic intoxication ensued after five more days, and the patient seemed moribund.

Peritoneal irrigation was started at this time, in spite of a severe ileus and pulmonary edema and acidosis. Within four days of continuous peritoneal irrigation therapy, the azotenia was reduced to normal values, this being fourteen days after complete anuria. The urine began to flow at this time. Output increased steadily, until the urinary urea reached a level capable of preventing uremia on the seventh day of irrigation. At this time, irrigation was stopped. Progressive improvement of renal function cont nued thereafter. One week later, the patient left the hospital. At that time his urea clearance was 33% of normal, and phenolsulfaphthalein test was normal. The urea clearance later increased to 50% of normal.

At about the third day of irrigation, pulmonary edema had become distressing, and parenteral fluids were omitted. Glucose was added to the peritoneal fluid in an attempt to correct the starvation acidosis, and a

Levine tube was used to apply suction to the ileus. This yielded 6000 cc of fluid. On the fourth day of irrigation, E. coli appeared in the outflow fluid, and persisted until irrigation was stopped. However, there was no clinical evidence of peritonitis. One million units of streptomycen per 1000 cc of fluid was injected into the peritoneal cavity, although the patient clinically did not seem to require it.

This is one example of a patient, almost moribund at the time of treatment, to whom cure seems to have been entirely brought about by this type of treatment.

Ronald W. Reid[24] is of the opinion that intermittant injection and withdrawal is a safer procedure than continuous perfusion. His theory is that with continuous perfusion, vast quantities of sterile fluid are required, and the exchange goes on so rapidly that dangerous changes may occur before the laboratory examinations would indicate their presence. Intermittant injection and withdrawal would give the operator time to re-evaluate the clinical position of the patient before starting perfusion again. Also, in continuous perfusion the fluid may possibly follow one tract, which may be soon enclosed by adhesions of bowel and omentum. This author has not had the same success with peritoneal irrigation as the other authors I have mentioned. A case history will be presented to demonstrate clinical results from this contrasting method of treatment.

The patient was admitted to the hospital suffering from anuria, as a result of sulfadiazine block. Initial therapy consisted of large quantities of alkaline fluids given by mouth, but with no results. A cystoscopy was performed, and crystals and a clot were found to be protruding from the edematous uretheral orifice. The blood urea at this time was 117 mg%, and the clinical condition was rapidly deteriorating. Throughout the day the patient showed signs of edema of the lungs. Another cystoscopy was performed, but catheters would not pass up the ureters.

It was decided that a one-sided nephrostomy should be done. The kidney was exposed, and a clear rush of urine followed incision of the pelvis. A Cabot's nephrostomy was performed, and a plastic tube introduced into the recto-vesicle pouch. A bronchoscopy was performed at the same time, and the bronchial tree cleaned out. Biopsy of the kidney showed the presence of sulfadiazine crystals in the tubules.

On returning the patient to the ward, 2000 cc of 5% glucose in normal saline was run rapidly into the peritoneal cavity. Hourly samples were taken for analysis. The fluid was suctioned out three hours later, and 1650 cc were recovered. Dialysis was later repeated with the same solution, but the patient complained of such severe pain that the tube had to be withdrawn. A trochar was passed through the peritoneal cavity into the right iliac fossa, and this tube drained 1600 cc of fluid. The patient showed a marked increase in pulmonary edema. One day later, the blood urea was still 117 mg%, but the cl nical condition seemed improved. Within a short time, the patient began to pass urine, and recovered. Only four grams of urea had been recovered as a result of dialysis.

It seems to me that the injection of glucose in normal saline in such small quantities, and with such slight recovery of the fluid, would be a very dangerous procedure when the patient is already suffering from pulmonary edema. If any procedure were to be effective, large amounts of lavaging fluid should be used, and the fluid should be sufficiently hypertonic to prevent absorption. Only by somewhat matching the amount of fluid which goes into the kidneys could one hope to combat uremia.

ARTIFICIAL KIDNEY

The principle of the artificial kidney is one of pure physical diffusion of crystalloids through a semipermeable, artificial membrane. It is successful because the products of uremia seem to be ionizable sufficiently, and of small enough molecular size, to pass through this membrane. In any given case, the blood is seperated from a bathing fluid, which is osmotically equal in all the inorganic salts to that of blood, but in which there is an osmotic potential between the nitrogenous metabolic products of the blood. It is obvious, of course, that the bathing fluid must contain all of the constituents that you do not wish to seperate from the blood. The end products of metabolism will, under these conditions, diffuse into the lavaging fluid, where they can be measured and eliminated. Therefore the name, artificial kidney. [25]

Technical Plan

Although the principle of the artificial kidney is simple, it is quite another thing to make the apparatus work. The apparatus[19,26,27] involves a length of 1/2 to 1/4 inch viscing tubing tubing immersed in a bathing solution, with a source of the patient's blood, from an artery or a vein, flowing into the tubing, through it, and back into the patient.

In order to accomplish this, the patient must be thoroughly heparinized to prevent clotting. Also, heparin, in a dilute solution, must be introduced into the tubing. There are two machines now in use, the Murray[20] and the Kolff[25].

In the Murray apparatus, the iliac vein is cannalized with a catheter. With a small, low-powered pump, the blood is pumped through this catheter to the cellophane coil through which it is to be dialyzed. At the entrance of the coil, there is a soft rubber valve, which serves to prevent crushing of the blood cells as they pass, and also to prevent regurgitation back into the system. With the pressure provided by the pump, the blood is circulated in the system, which has been immersed in a bathing fluid. The bathing fluid consists of sodium chloride, calcium chloride, magnesium chloride, sodium hypophosphate, dextrose, potassium chloride, and sodium bicarbonate in approximately the same proportions as found in the lood stream, with enough glucose added to make he fluid slightly hypertonic. The blood is returned to the patient through a similar soft rubber valve through the femoral vein, which is similarly catheterized through the greater saphenous.[20]

The Kolff machine differs in only a few small ways from the Murray apparatus. Dr. Kolff canalizes the radial artery and permits blood to flow through the series of coils by systolic pressure. The blood is later returned to the body by means of a canalized vein, usually in the same arm.

The blood circulates through a 1/2 inch cellophane membrane, 120 to 140 feet long, which has been wound around a large cylinder. As the cylinder revolves, the blood flows purely by gravity, and then is returned to the body, through a bubble-catcher, by means of a small pump. The bathing fluid used is not sterile, but is clean. The fluid does not contain calcium, for fear of calcium precipitation with sodium bicarbonate. Calcium glucinate is given intravenously to the patient to counteract any calcium loss through dialysis. Glucose is added to the fluid in a 1% quantity to counteract hemolysis of the red blood cells. If pulmonary edema is present, glucose is added in a higher percentage. If the patient is anemic at the time of treatment, blood transfusion is given at the same time to avoid harming the patient by removal of blood and also because of its therapeutic value. On the other hand, if the patient has pulmonary edema, it is often therapeutic to remove some of the circulating blood.

Dr. Darmady[27] has done some work on a newer type of machine in which cellophane tubing is wound through a series of thin plates about 1/16 inch apart, with a large dialyzing surface thus achieved. The flow of the dialyzing fluid is arranged by means of a number of small tubes in the plates, which allow the dialyzing fluid to flow from the center outward in either direction. This machine at present has not produced as satisfactory dialysis as does the rotary machine of Kolff.

Problems of Application

Although they are decreasing, problems with the application of the artificial kidney still are formidable. The first anti-coagulants used were generally very toxic to the experimental animals, and not satisfactory for use with humans. Hirudin was the generally used anti-coggulant. The present availability of heparin has overcome this difficulty, making the procedure routinely feasable.

The electrolyte composition of the lavaging fluid is still a problem, as it concerns minute quantities of essential minerals removed which are not easily measured. It has been found that the blood plasma closely approximates the lavaging fluid in electrolyte composition if the patient has been treated with the artificial kidney for any length of time.

An early problem, which has been satisfactorily solved at present, was that of a satisfactory dialyzing membrane. nimal casings were among the first used, and were not satisfactory because of their lack of uniformity and the difficulty in their preparation. At present, with the advent of modern cellophane tubing, a cheap suitable filter is provided, through which crystalloids are permeable, while colloids and bacteria are not. This type of tubing is also available in the desired size and quantity.

Infection is not a problem because the washing fluid does not need to be sterile. If the proper aseptic conditions are used in the cut-downs, no infection is anticipated.

In spite of adequate heparinization, the problem of coagulation still exists. In one case at the University of Indiana with which I am personally acquainted, the patient was very adequately heparinized. However, the blood clotted almost immediately after it filled the tubing. This necessitated change of the tubing and further heparinization of the patient. In some ways, this is a disadvantage. The heparinization cannot be done if the patient is post-operative, or an accident case with any wounds, for the danger of bleeding is always present. The laboratory estimation of the prothrombin time is not likely to always be truly accurate. If this procedure must be carried on many times in order to save the patient, there is the chance of venous thrombosis from the introduction of a cannula or catheter.

The same problem of diagnosis of cases suitable for this form of therapy still exists. Also, the size of the apparatus is also an inconvenience, for it is not readily transportable to wherever it could be used.

Another problem is pooling of the blood in the system. The blood should return to the patient at the same rate it is withdrawn. This is handled by means of synchronized inflow and outflow pumps, which eliminate the danger of shock to the patient. The rotating drum seems to be very satisfactory because it allows a thin spread of blood over the dialyzing surface, and produces agitation. Agitation is helpful because it insures a fresh sample of blood being constantly brought to the dialyzing surface.

The problem of osmosis is seemingly combatted by the use of isotonic salt solutions made hypertonic with glucose. This is actually not the case in many instances, or at least it presents something of a problem in maintaining osmotic balance. It was found by Darmady that, when starting with twenty liters of hypertonic bathing fluid, only seventeen liters remained at the end of two hours, with only one liter accountable for by evaporation. This mechanism is a rappid diffusion of water from the blood into the lavaging fluid, forming a hypotonic solution, which is then absorbed. It would seem that to counteract this effect, a material should be used in the fluid which is non-dialyzable. The plasma osmotic pressure in patients with uremia is frequently raised, probably due to vomiting or diarrheic loss of fluid. This should be taken into account when figuring the osmosis of the lavage fluid.

Success with Animals

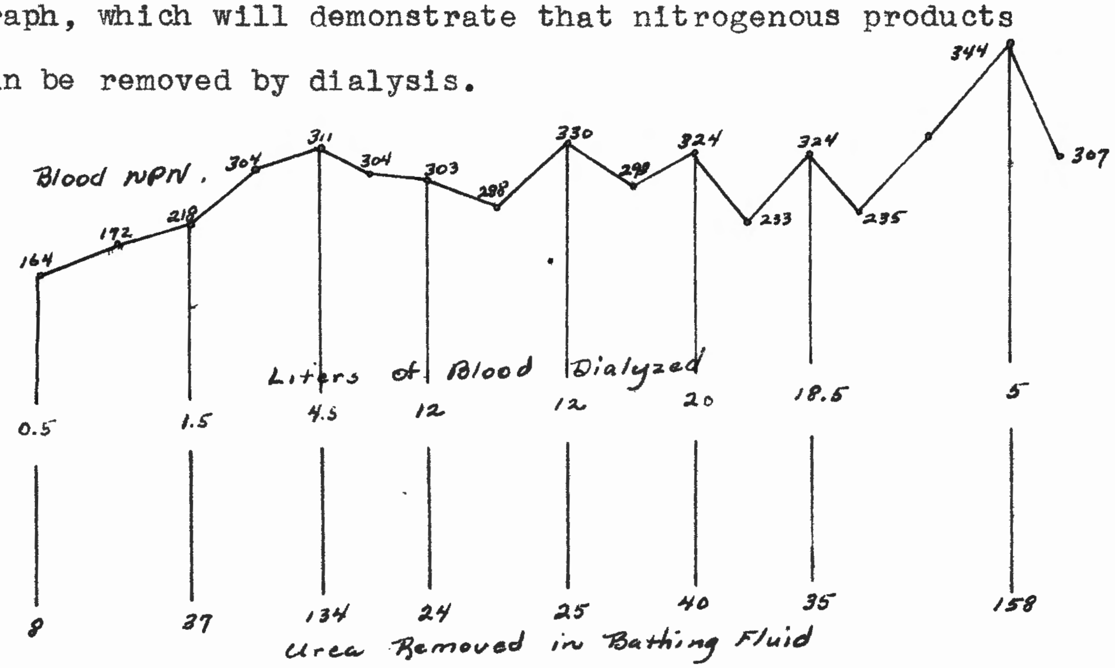
Abel, Rowntree, and Turner[21] in 1912 were able to remove retention products from nephrectomized dogs by cannelizing an artery, sending blood through a series of colloidian tubes surrounded by a normal saline wash fluid, and returning the blood to the body of the animal by means of a vein. These animals did not long survive after dialysis, and died with symptoms suggesting an electrolytic unbalance.

Thalhimer[19] worked on dogs also by cannelizing an artery, running the blood through cellophane tubing immersed in physiological saline, and then returning to the vein of the dog. In three to five hours of this dialysis, 200 to 700 mg of urea nitrogen were removed, depending on the degree of uremia prior to dialysis.

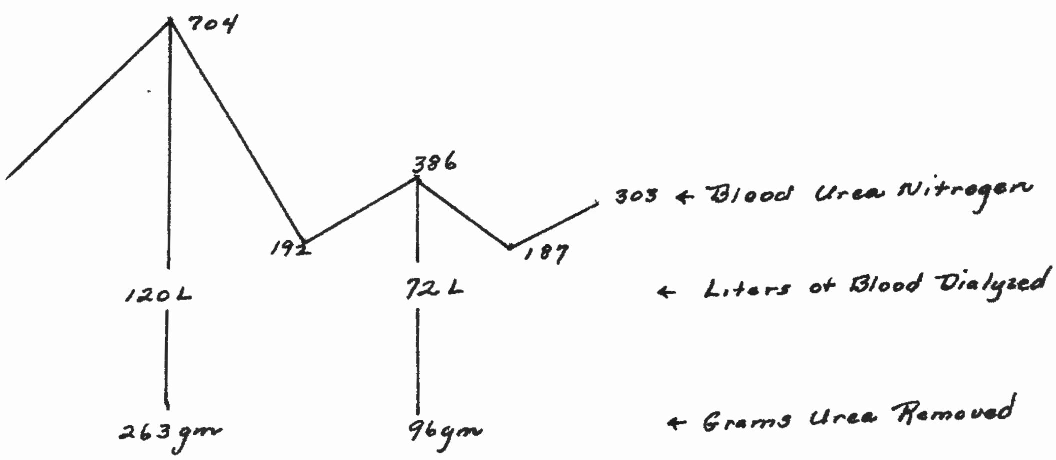
Application to Humans

In presenting the results with humans, case histories will be used to some extent. In the first sixteen patients lavaged by Dr. Kolff[25], fifteen died, and the one remaining probably would have survived without lavaging. The only conclusion it was possible for him to derive was that survival after lavaging was possible. Of ten that died, nine were found at autopsy to have chronic renal disease as the cause of their death.

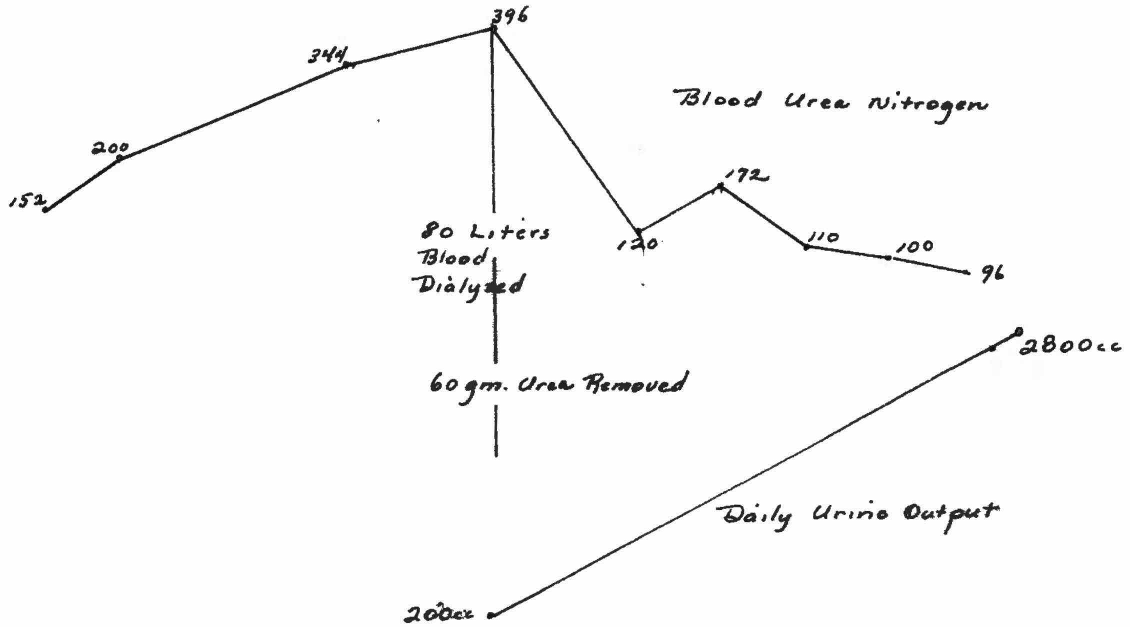
The first case will be illustrated by a graph, which will demonstrate that nitrogenous products can be removed by dialysis.



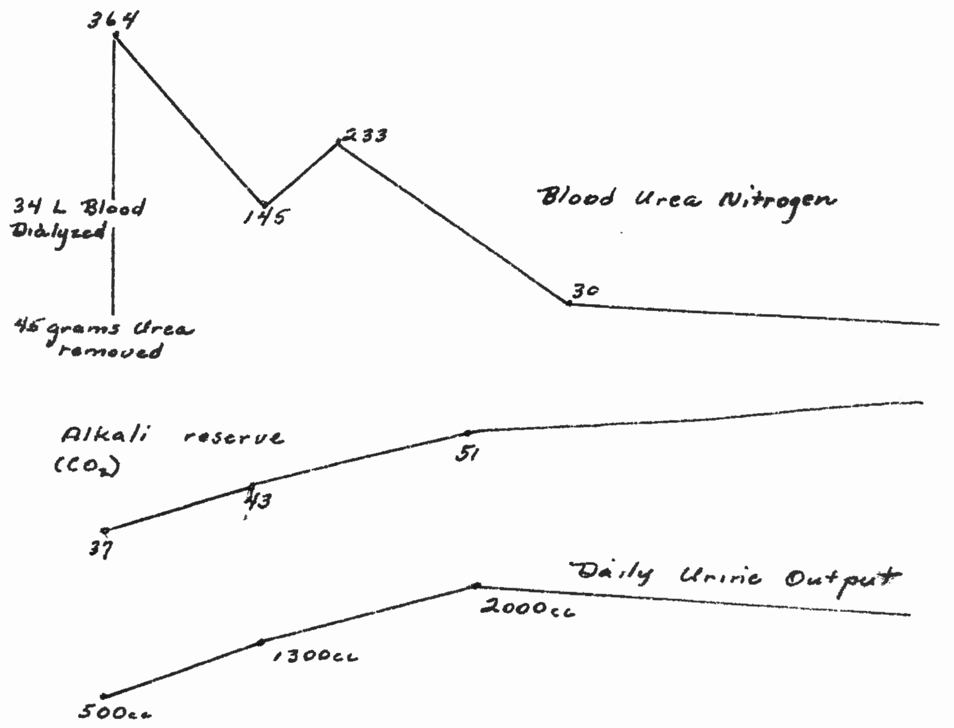
A 220 pound man entered the hospital with acute glomerulonephritis. Upon admission to the hospital, his blood urea nitrogen was 700 mg%. Dialysis of 120 liters of blood removed 263 grams of urea. The blood urea nitrogen fell to 192 mg% following dialysis. The patient died of pulmonary symptoms. Products such as creatinine, uric acid, indoxyl, non-protein-nitrogen, phosphates and potassium were measured in the lavage fluid.



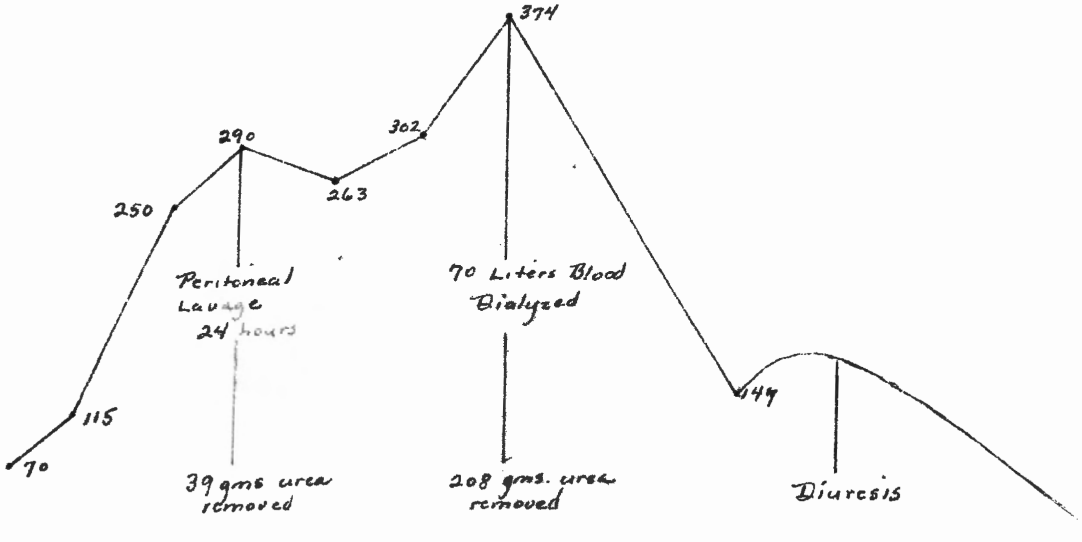
An elderly lady was suffering with anuria from a hepato-renal syndrome. The following graph is self-explanatory. It is interesting to note that after the fall of the blood level to 120 mg%, the patient became mentally clear, and talked and planned for the future, while shortly before she had been stuperous.



A thirteen year old girl suffering from acute glomerulonephritis, uremia and pneumonia was treated with the artificial kidney. The following graph will indicate the clinical course, and the success achieved with this treatment.



In a case of mercury poisoning, a 23 year old man had anuria due to toxic break-down of protein. Treatment with the artificial kidney led to recovery.



The following is a list of the cases dialyzed by a Kolff machine under the direction of Dr. Bywaters:[26]

Diagnosis	Hours of Dialysis	Bld. Flow ml/min	Fall in B.U.N. mg%	Grams Urea Removed	Survival Days
Bilateral hydronephrosis	1.0	10	470 -?	-	3.0
Cortical necrosis post-partum	3.3	75	316-223	27.0	0.3
Post-traumatic anuria	4.1	86	390-211	32.1	-
Hemoglobin nephrosis	7.5	58	460-209	92.0	0.5
Acute glomerulo-nephritis	3.0	80	504-428	29.0	0.4
Chronic nephritis	1.0	72	750-?	-	0
Bilateral hydro-nephrosis	4.4	51	440-292	44.1	1.6
Post-operative anuria	4.1	76	424-264	33.1	-
Aspirin suicide	3.0	58	105-59	7.5	5.0
Acute glomerulo-nephritis	2.3	50	428-307	21.0	0.4
Chronic nephritis	3.7	70	400-238	65.0	0.4
Bilateral hydro-nephrosis	3.3	80	360-178	28.7	14.0

At the Midwest Clinic, Dr. Murray reviewed one case in which a patient suffering from uremia caused by toxemia of pregnancy was admitted to the hospital in a coma, and having convulsions. The artificial kidney was used as a means of therapy, and the patient recovered. All symptoms entirely disappeared, and there was no recurrance.

GASTRIC LAVAGE

The principle of gastric lavage is essentially similar to the artificial kidney. A certain proportion of all the electrolytes in the body are found in the production of any of its internal secretions, including the gastric juice and intestinal secretions. If these can be removed and replaced with fluid not containing these products, there will be an osmotic potential established between the lumen with its fluid and the blood vessels in the mucosa of the lumen. If this fluid is continually replaced as the body eliminates its by-products into it, a certain proportion of its waste can be removed. I realize that this sounds simple, but it is misleading.

Recent work by Goudsmit[28] on intestinal excretion has shown that perhaps simple osmosis is not the entire picture. He is of the opinion that the intestinal hyperemia influences intestinal secretion, as a result of the lavage fluid, and that phvsical factors and vasomotor reactions regulate the transfer of fluid through the gut mucosa in either direction. On the basis of his findings, Goudsmit perfused dog stomachs with hypertonic sodium sulfate, with good results in decreasing the azotemia level.

In 1932, West and Pendleton[29] demonstrated that when saline was introduced into an isolated loop of small bowel, its urea content quickly equaled or exceeded that of the blood. From his experiments, it was concluded that the intestine acts as a semi-permeable membrane, permitting passage both ways.

Fine, Frank, and Seligman[4] measured urea clearance from various parts of the gastro-intestinal tract. They found that the jejunum was the most effectice region to lavage. They also concluded that the urea clearance was so low that perfusion of the bowel could only be used as an adjunct to kidney function, and could not adequately substitute for kidney function. They also found that the semi-permeable bowel has the ability to absorb even hypertonic fluids. This is one of the major problems with lavage, because it upsets the body's chemical equilibrium by absorption.

Methods of Use

Lavage of the gastro-intestinal system can be divided into two parts. One part consists of gastro-duodenal suction, and the other consists of lavaging an intestinal fistula.

Gastro-intestinal lavage is carried out by the introduction of a tube into the stomach, and permitting it to pass down into the duodenum. Usually a modified Levine tube is used, with a mercury bulb on the end, and an inflatable balloon near the tip. When the tube is in place, the balloon is inflated, causing an obstruction, and fluid can be injected and withdrawn above the obstruction. This obstruction is necessary to prevent the rapid passage and absorption of fluid into the body. A refinement to this method is the introduc ion of a tube beyond the obstructing balloon, and using it as a feeding tube. In this manner, a patient can be maintained indefinitely while the lavage is being carried out. A hypertonic fluid is used as a lavaging agent. Several different types have been used, as sodium sulphate solution, hypertonic saline, glucose, and a combination of saline and glucose. None of these solutions have been wholly satisfactory. I would like to sug est that in further experiments, if mammalian tyrodes or Ringer's solution made hypertonic by the addition of glucose, were used, perhaps bett r results would be obtain d.

The other type of gastro-intestinal lavage is accomplished through a fistula, made of a loop of bowel. To accomplish this, a portion of bowel is sectioned and its blood supply left intact. It is brought to the surface, forming a fistula on the body wall, with both of its ends opened to the surface so that fluid may be perfused through the loop. This is, in many ways, adventagous, because of the ease of perfusion and ease of regulating the amount of perfusion. There are also great disadvantages to this system. In order to satisfactorily use this method, at least one meter of bowel must be isolated. The process is but an adjunct to kidney function, for its power of eliminating nitrogenous waste products has been proven very limited. The patient must wait for the fistula to heal before it can be used therapeut cally. There is also the matter of trauma of bowel resection, and the danger of doing an end to end anastamosis of bowel in a very sick patient. The trauma of the operation itself could well push a uremic patient past his limit of tolerance. If the method is used, either ileum or jejunum may be used, and a fistula catheter inserted into either end to facilitate perfusion.

Success with Application

There are difficulties with gastro-intestinal lavage which alter the success of treatment to a large extent. Recovery of the lavaging fluid is difficult. Diarrhea may occur from excess absorption of hypertonic fluids, in addition to generalized reflex irritation of the entire gastro-intestinal system. The passage of the tube is very irritating to some patients, and it is occasionally impossible to pass it, or to keep it down. The presence of the tube in the mouth or nasal passages is very irritating to the sick patient.

White and Harkins[30] experimented with dogs by forming a 20 to 40 inch fistula of jejunum and ileum on the body wall. Within 11 to 20 days, the fistulae healed, and then a bilateral nephrectomy was performed. Irrigation was then started. A Foley catheter was placed in each end of the fistula, and wash fluid was permitted to drip through the fistula. The wash fluid consisted of 6.1 grams sodium chloride per liter, 0.23 grams of calcium chloride, .076 gram calcium biphosphate, 10.0 grams sodium sulphate, 0.35 gram potassium chloride, 2.2 grams sodium bicarbonate, 30 grams sodium bisulphate, and 10 grams glucose. The irrigation was intermittant, lasting two and one half to ten and one half hours, with regular fluid and food given. Five control dogs survived 73 hours, and had blood urea nitrogen levels averaging 193 mg%, with a rate of rise of 2.5 mg% per hour before death. Uremic symptoms occurred within 36 to 48 hours after the nephrectomy. Six irrigated dogs survived an average of eight hours longer than the control dogs. Their survival time was from 66 to 99 hours. The blood urea nitrogen at death averaged 144 mg%, being 49 mg% on the average lower than the control. The average rate of rise was 1.6 mg% per hour. The blood urea nitrogen level was lowered one to nine mg% during irrigation in 44.5% of the dogs lavaged. In 55% of the dogs, it rose during this period from 1 to 25 mg%. The maximum efficiency of urea removal was 14 mg% of urea per inch of intestine, per hour of irrigation. The poorest result was found in the dog in which the wash fluid was re-used. Here 1.3 mg% urea, per inch of intestine lavaged, per hour, was removed. It was found that better results were obtained when using hypertonic fluids. The hematocrit rose with most animals, showing that there was absorption even with hypertonic fluid. Some of the animals that had been in good condition at the beginning of irrigation were unable to stand or walk, and were disoriented by the time of its completion.

Large intravenous doses of calcium glucinate gave only partial relief. There was only moderate recovery after an overnight rest period. In the cases where the wash fluid was re-used throughout the survival time, this symptom complex was less apparant.

Application to Humans

Rodgers, Sellers and Gornell[31], working with this problem from the possibility of perfusing the intestine in situ, and rendering surgical innervention unnecessary, recorded the following results: In using 12 to 18 liters of perfusing fluid over a six hour period, in one case they were able to reduce the blood azotemia level from 198 to 126 mg%. In another case it was lowered from 198 to 112 mg%, and in another instance from 231 to 145 mg%. The rinse fluid contained 4.3 to 5.4 grams urea with each lavage.

Fine, Frank, and Seligman[4] perfused a short segment of bowel in one of their patients, and estimated that it would require ten feet of bowel to give ten percent of the maximum normal renal clearance.

Goudsmit[28] placed a modified Levine tube with a balloon attachment into the duodenum, and perfused the patient with hypertonic magnesium sulphate. The average volume of fluid removed was between 399 and 655 cc per hour. The average concentration of urea in the withdrawal fluid was 93% to 95% that in the blood of controls. In a 7 hour 40 minute lavage period, 3300 cc of fluid were withdrawn which contained ten grams of urea. A second patient with a normal blood urea nitrogen was perfused in the same manner, and four grams of urea were removed in the same length of time. Dr. Goudsmit is of the opinion that this is a worth-while supplementary agent to kidney function.

Gordon and Oppenheimer[32] worked with a 39 year old anuric negro patient who had a persistant blood urea nitrogen of between 90 and 110 mg% due to hydronephrosis. The patient had a marked anemia. He was given blood and his electrolyte balance carefully checked. His acidosis was corrected by the use of a 1/6 molar sodium lactate solution. Then gastric lavage was started.

Day	B.U.N.	CO_2
10th	107 mg%	16 vol%
12th	80 "	52 "
15th (5 hr. lavage period)	83 "	48 "
16th (12 hr. lavage period)	50 "	-
17th (18 hr. lavage period)	46 "	-

The patient died, and no autopsy was performed.

CONCLUSION

All of these methods will require a great deal more work and study before they are clinically entirely acceptable. In my opinion, the most promising method for the general surgeon or general practicioner, with limited experience and ability, is by far peritoneal lavage. For men skilled and experienced in using the artificial kidney, with the necessary equipment available, I believe it can be used more effectively. Although it now is beyond the reach of the average doctor, I believe that the artificial kidney holds the greatest promise of an effective means for combatting azotemia in the future. Gastric lavage, either by means of a gastro-duodenal tube or an intestinal fistula, I consider absolutely uncalled for, and not practical in relieving a patient of azotemia. I believe that gastric lavage is possibly more disturbing than helpful, because the blood chemistry is so markedly altered.

Perhaps one of the largest problems in the future will be to convince the doctor that he can help his patient by using one of these means of therapy early, when he suspects that his patient will be uremic within a short tim .

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