Staff Meeting Bulletin
Hospitals of the » » »
University of Minnesota

Temporary Renal Insufficiency

Volume XVIII Friday, January 24, 1947 No. 12

STAFF MEETING BULLETIN
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INDEX

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I.

UNIVERSITY OF MINNESOTA MEDICAL SCHOOL
CALENDAR OF EVENTS

January 25 - January 31, 1947

No. 142

Saturday, January 25

7:45 - 8:50 Orthopedics Conference; Wallace H. Cole and Staff; Station 21, U. H.

9:00 - 9:50 Surgery-Roentgenology Conference; O. H. Wangensteen, L. G. Rigler, and Staff; Todd Amphitheater, U. H.

9:00 - 9:50 Medicine Case Presentation; C J. Watson and Staff; M-515, U. H.

10:00 - 12:00 Medicine Ward Rounds; C. J. Watson and Staff; E-221, U. H.

10:00 - 12:50 Obstetrics and Gynecology Grand Rounds; J. L. McKelvey and Staff; Station 44, U. H.

11:00 - Anatomy Seminar; Contributions to Neuroanatomy during 1946; A. T. Rasmussen: and Studies in the Etiology of "Chokes"; Richard A. Miller; 226 I. A.

Monday, January 27

9:00 - 9:50 Roentgenology-Medicine Conference; L. G. Rigler, C. J. Watson and Staff; Todd Amphitheater, U. H.

9:00 - 10:50 Obstetrics and Gynecology Conference; J. L. McKelvey and Staff; Interns' Quarters, U. H.

11:00 - Roentgenology-Medicine Conference; Veterans' Hospital.

11:00 - 12:00 Physical Medicine Conference; Physical Therapy in Other Parts of the World; Christian Terrier; W-200 U. H.

12:15 - 1:15 Obstetrics and Gynecology Journal Club; M-435, U. H.

12:30 - 1:20 Pathology Seminar; Effects of urethane on mouse myelogenous leukemia; Ruby Engstrom; 104 I. A.

12:15 - 1:30 Pediatrics Seminar; Irvine McQuarrie and Staff; 6th Floor Seminar Room; Eustis, U. H.

12:00 - 1:00 Physiology Seminar; Experimental Convulsions; Ernst Gellhorn; 214 M.H.

4:00 - School of Public Health Seminar.

Tuesday, January 28

9:00 - 9:50 Roentgenology-Pediatrics Conference; L. G. Rigler, I. McQuarrie and Staff; Eustis Amphitheater, U. H.

10:30 - Surgery Seminar; John R. Paine; Small Conference Room, Bldg. I, Veterans' Hospital.

12:30 - 1:20 Pathology Conference; Autopsies; Pathology Staff; 102 I. A.

2:00 - 2:50 Dermatology and Syphilology; H. E Michelson and Staff; Veterans' Hospital, Bldg. III.

3:15 - 4:15 Gynecology Chart Conference; J. L. McKelvey and Staff; Station 54, U.H.

3:30 - Clinical Pathological Conference; Veterans Hospital.

3:45 - 5:00 Pediatrics Staff Rounds; I. McQuarrie and Staff; W-205, U. H.

4:00 - 4:50 Surgery-Physiology Conference; Heat Exchange in the Anesthetized Patient; Allan Hemingway and Ralph T. Knight; Eustis Amphitheater,U.H.

5:00 - 5:50 Roentgenology Diagnosis Conference; M-515 U. H.

Wednesday, January 29

8:00 - 8:50 Surgery Journal Club; O. H. Wangensteen and Staff; M-515 U. H.

8:30 - 10:00 Psychiatry and Neurology Seminar; Staff; Station 60 L unge, U. H.

11:00 - 11:50 Pathology-Medicine-Surgery Conference; Multiple Myeloma; E. T. Bell, C. J. Watson, O. H. Wangensteen and Staff; Todd Amphitheater, U. H.

12:00 - 1:00 Physiological Chemistry Journal Club; Staff; 116 M. H.

4:00 - 6:00 Medicine and Pediatrics Infectious Disease Rounds; W-205, U. H.

Thursday, January 30

8:30 - Surgery Grand Rounds; John R. Paine and Staff; Veterans' Hospital.

9:00 - 9:50 Medicine Case Presentation; C. J. Watson and Staff; Todd Amphitheater, U. H.

10:00 - 12:00 Medicine Ward Rounds; C. J. Watson and Staff; E-221, U. H.

10:30 - Roentgenology-Surgery Conference; Veterans' Hospital.

12:00 - 1:00 Physiological Chemistry Seminar; Biological Assay of Hormones; Elizabeth G. Frame; 214 M. H.

4:30 - 5:20 Ophthalmology Ward Rounds; Erling Hansen and Staff; E-534, U. H.

4:30 - 5:20 Bacteriology Seminar; 214 M. H.

5:00 - 5:50 Roentgenology Seminar; Review of Radiological Society of North America Meeting; Walter H. Ude, J. Richards Aurelius, and W. K. Stenstrom; M-515 U. H.

Friday, January 31

9:00 - 9:50 Medicine Grand Rounds; C. J. Watson and Staff; Todd Amphitheater, U.H.

9:00 - 10:00 Pediatric Grand Rounds; I. McQuarrie and Staff; Eustis Amphitheater.

10:00 - 11:50 Medicine Ward Rounds; C. J. Watson and Staff; E-221, U. H.

10:30 - Medicine Grand Rounds; Veterans' Hospital.

10:30 - 12:20 Otolaryngology Case Studies; L. R. Boies and Staff; Out-Patient Otolaryngology Department; U. H.

11:30 - 1:00 University of Minnesota Hospitals General Staff Meeting; To be announced; New Powell Hall Amphitheater.

1:00 - 2:00 Dermatology and Syphilology; Presentation of Selected Cases of the Week; H. E. Michelson and Staff; W-312, U. H.

1:00 - Roentgenology-Neurosurgery Conference; H. O. Peterson, W. T. Peyton and Staff; Todd Amphitheater, U. H.

II. THE TREATMENT FOR TEMPORARY RENAL INSUFFICIENCY

B. A. Smith
G. B. Eaves

Many of the cases of acute renal failure where the lesion in the kidneys is reversible, need not be fatal if a means can be found to eliminate the toxic products by some extra-renal route during the period of depressed renal function. Examples of the types of lesions amenable to this method of therapy are: (1) tubular injury or occlusion, due to in ravascular hemolysis, (2) renal injury produced by drugs or toxins, (3) acute renal failure due to prolonged shock or obstruction such as that produced by urinary calculi and prostatism.

Diseases or accidents associated with intravascular hemolysis are: incompatible transfusion reactions, intravascular hemolysis following transurethral resections, hemolysis due to drugs such as the sulfonamides, hemolytic reactions associated with diseases such as black water fever, favism, etc. Group two is well represented by the toxic nephrosis following sulfonamide administration, or the ingestion of bichloride of mercury. Group three can be represented by the reflex anuria following occasionally after bilateral retrograde pyelograms, following manipulation of an ureteral stone, and the acute uremia associated frequently with prostatism.

M thods that have been used in the past for the extra-renal elimination of the toxic produces are:

1. Attempted elimination of these products by sweating, the production of diarrhea, and gastro-duodenal aspiration.

2. The reciprocal transfusion method suggested by Thalhimer.[10]

3. Plasmapheresis.

4. Elimination of the toxic products by dialysis:

   a. External dialysis, or as it is frequently called, vividiffusion.

   b. Internal dialysis, or the use of the peritoneum or pleura as a dialyzing membrane.

Sweating the patient, or the production of diarrhea is ineffective in eliminating significant amounts of urea and other waste products. In addition it is exhausting to the patient, causes a serious depletion of water and salt, and in the case of sweating, causes a disturbance in the heat regulating mechanism of the body.

The reciprocal transfusion method suggested by Thalhimer[10] has definite limitations when experimentally applied, and it may actually be dangerous to the healthy donor when used clinically, Thalhimer, using hirudin as an anticoagulant in the dog made uremic by bilateral nephrectomy, was able to lower the blood urea nitrogen from 75 mgm. per cent to 54 mgm. per cent, or approximately one-third, by the exchange of forty 200 cc. transfusions. Clinically, if one uses but a single donor, the limit of the amount of blood that can be transferred by repeated reciprocal transfusions is an exchange of 50% of the blood volume, and this requires an infinite number of transfusions. Using 500 cc. volumes of blood, one can in six transfusions exchange one-third of the donor's blood for the recipient's. It is impractical to go beyond this with the same donor, since it requires an infinite number of transfusions to increase the blood volume transferred from one-third to one-half.

In Plasmapheresis blood is drawn from uremic animals, centrifuged and separated from the plasma, and the washed corpuscles are returned to the animal in Locke's solution. This method produced serious depletion of the plasma proteins with reduction of the osmotic pressure of the blood with resultant edema due to a redistribution of body water.

Abel, Rowntree and Turner[5] were the first to use external dialysis. They constructed an apparatus consisting of a closed container enclosing branched celloidin tubes as a dialyzing membrane.

In order to fill the tubes it required about one-half of the animal's blood volume. These celloidin tubes were bathed in normal saline solution, using hirudin as an anticoagulant. They showed that urea and glucose could be recovered in the dialysate. They had considerable difficulty with shock in their experimental animals since the apparatus required such a large volume of blood to fill it. Sterilization of the apparatus was difficult. Thalhimer[10] used a similar apparatus in experimental uremia in animals, made uremic by bilateral nephrectomy, with temporary benefit.

Haas[16,17] also used a similar apparatus both experimentally and clinically with temporary benefit. He used 5% glucose as a dialyzing solution and was able to lower the blood urea nitrogen, however, the animals died, and death was attributed to chloride depletion. More recently the problem of external dialysis has been taken up by Kolff and Berk.[11] Added impetus to the investigation of the possibilities of external dialysis ensued from the development of a better anticoagulant, namely heparin.

Before discussing the use of the peritoneum as a dialyzing membrane, a discussion of the principles of dialysis and a comparison of the peritoneum to a perfect dialyzing membrane is in order. A perfect dialyzing membrane is a semi-permeable membrane, that is to say, permeable to molecules of small size but impermeable to molecules of large size. If the perfect dialyz ing membrane separates two solutions of equi-molecular concentration, one solution containing salt and the other sugar, both of which are diffusible, these will ultimately diffuse across the membrane so that at the end of the procedure they will be in equal concentration in both solutions. If a semi-permeable membrane separates two solutions of unequal molecular concentration, but containing diffusible ions only, these diffusible ions will ultimately reach identical concentration in both solutions but there will be a shift in water in the direction of the more concentrated side, proportional in amount to the increased osmotic pressure which the more concentrated solution had originally. If a non-diffusible substance such as the protein molecule is added on one, side of the membrane, the ultimate concentration of the diffusible ions will still be the same on both sides of the membrane at the end of the diffusion. However, the shift in water will again be towards the side where the protein molecule was added, since this increases the osmotic pressure of the solution on that side. The rapidity with which solutions diffuse across the membranes is dependent upon the size of their molecules. The smaller the molecule, the more rapid the diffusion. Sodium or chloride ions will diffuse across the membrane and reach equi-molecular concentration on both sides of a dialyzing membrane more rapidly than will glucose which has a larger molecule.

Some of the more significant research concerning the peritoneum as a dialyzing membrane should be examined before using the peritoneum for that purpose.

Von Recklinghausen[19] and Wegner[21] found that particulate matter such as red blood cells, milk, and India ink were absorbed from the peritoneal cavity of their experimental animals, dogs and cats.

Orlow[4] showed that homologous serum injected into the peritoneal cavity was progressively absorbed. He also demonstrated by his experiments that isotonic solutions of salt and sugar were progressively absorbed from the peritoneal cavity and that hypertonic salt solutions were absorbed from the peritoneal cavity without increasing the flow of lymph. H cannulated the thoracic duct following the inection of a 5% salt solution into the peritoneal cavity and measured the concentration of the salt and the rate of flow in the thoracic duct lymph. Neither the rate of flow nor the concentration were increased above the normal. He also showed that the intravenous injections of hypertonic solutions hastened the absorption of solutions introduced into the peritoneal cavity.

Von Koranyi[12] showed that there was an increase in the osmotic pressure of the serum of animals in uremia. This

increase in osmotic pressure took place as little as four hours after bilateral nephrectomy. He measured the electroconductivity of the serum and found it did not show a corresponding increase. He concluded that non-electrolytes were responsible for the increase in osmotic pressure.

Melzer and Salant[18] noted that there was an increased rate of absorption in nephrectomized animals. They concluded that this increased rate was due to the increased osmotic pressure of the blood.

Fleischer and Loeb[9] performed an extensive series of experiments concerning the absorption of 0.85% sodium chloride solution from the peritoneal cavity. They found that anything which increased the osmotic pressure of the blood such as adrenalin solution injected subcutaneously or ligation of the renal artery increased the rate of absorption from the peritoneal cavity. In three of their experimental animals, peritonitis developed following abdominal incision. In these animals there was a transudation of fluid into the peritoneal cavity rather than absorption. They injected 120 cc. of 0.85% salt solution into the peritoneal cavity and in the animals that had peritonitis, at the end of two and a half hours the volume had increased to 133 cc. In animals without peritonitis, the average volume recoverable at the end of two and one-half hours was 70 cc.

Clark[7] showed that warm solutions were absorbed more rapidly than cold solutions from the peritoneal cavity. The mechanism operating to increase the rate of absorption with warm solutions is probably a dilatation of the blood vessels increasing the dialyzing surface. He also found that no difference in the rate of absorption was created by alterating the pH of the solution. Acid, neutral, or alkaline solutions were made by mixing various proportions of acid and alkaline sodium phosphate to vary the pH. There was no difference in the rate of absorption. He also showed that when solutions of glucose are injected intraperitoneally, the volume at the end of one hour is usually greater than the injected volume, even though isotonic solutions of glucose are used. This increase in volume is accompanied by an increase in the osmotic pressure above that of the injected fluid. He explains this on the basis that salt is more readily diffusible than glucose. Salt diffuses into the peritoneal cavity from the plasma at a faster rate than glucose diffuses into the blood. The increase in the osmotic pressure of the peritoneal fluid causes a fluid shift in the direction of the peritoneum.

Darrow and Yannet[8] investigated the changes produced in the plasma following the intraperitoneal injection of a 5% glucose solution and a 1.8% sodium chloride solution. Neither solution changed much in volume during the period of observation which was three to six hours. The change in volume of peritoneal fluid amounted to less than 10% increase or decrease in the original volume. However, with a 5% glucose solution there was a reduction of plasma volume as evidenced by a concentration of the plasma proteins. There was also a reduction in plasma chlorides and sodium, equivalent to 20% of the total sodium of the body. There was a reduction of the protein concentration in the erythrocytes with very little change in the total body water. This is to say, there was a shift of water from the plasma or extracellular fluid space into the intracellular space which was produced by loss of plasma salt into the peritoneal cavity. The opposite effect was noted when 1.8% sodium chloride solution was injected intraperitoneally. There was an increased plasma volume accompanied by a decreased plasma protein, and an increased concentration of protein in the erythrocytes. In other words, there was a shift of the water from the intracellular compartment to the extracellular compartment.

Putnam[6] has shown that solutions, regardless of their osmotic pressure, ultimately are completely absorbed by the intact animal from the peritoneal cavity. Solutions with an osmotic pressure equal to or less than the osmotic pressure of a 1% sodium chloride solution show a progressive absorption, whereas solutions with an osmotic pressure greater than that of a 1.5% salt solution show a temporary increase in

volume and yet are ultimately totally absorbed. Urea appears in the solutions as does proteins. He also showed that markedly hypertonic solutions, i.e., 5% salt solution, injected intraperitoneally were poorly borne by the experimental animals.

Putnam[6] epitomized the quality of the peritoneum as a dialyzing membrane when he stated that in essence the living peritoneum resembles a dialyzing membrane with holes punched in it which permit a seepage of larger molecules than would diffuse through a perfect dialyzing membrane, and that the diffusion of smaller molecules through the peritoneum occurs more rapidly then with ordinary dialyzing membranes. This seepage occurs more readily in the direction of the blood plasma than in the direction of the peritoneal fluids. If one adds to this epitome the experience of Fleischer and Loeb that peritonitis alters the direction of flow by introducing the complicating factor of transudation or exudation, plus the fact that uremia is accompanied by an increased osmotic pressure of the blood which hastens absorption from the peritoneal cavity, one has a fairly comprehensive picture of the peritoneum as a dialyzing membrane.

The early investigators[14,15,16,17] who used the peritoneum as a dialyzing membrane failed both experimentally and clinically in the treatment of uremia principally because of a poor choice of solutions. There has recently been a rebirth of interest in this method of treating uremia due to temporary renal impairment both by the physiologists and clinicians.

Abbott and Shea[20] produced uremia in dogs by bilateral nephrectomy. Using intermittent peritoneal lavage, they investigated the changes produced using the four solutions listed in Figure 1. 5% glucose, Ringer's Solution, Hartman's solution, and Solution A.

Tyrode's solution which has been used clinically and experimentally by Frank, Fine, and Seligman[1,2,3] is qualitatively identical with Solution A and varies only slightly quantitatively.

Figure I

SOLUTIONS EMPLOYED FOR PERITONEAL LAVAGE

Cms.% Comp.	5 % Glucose	Ringer's	Hartman's	Solution A
NaCl		.900	.600	.610
KCl		.030	.040	.035
CaCl		.025	.020	.023
NaH_2PO_4				.007
$MgCl_2$				.005
$NaHCO_3$				.220
Lactic Acid (in cc.)			.240	
Dextrose	5.0			Variable 1.0 - 2.0
Total Grams	5.0	.955	.900	.900

The results obtained by Abbott and Shea are given in Figure II.

Figure II
AVERAGE CHANGE IN THE CONSTITUENTS OF THE BLOOD AND PLASMA AFTER FOUR HOURS FOR EACH SOLUTION EMPLOYED.

Blood and Plasma

Solution	% Change in Hematocrit	Plasma Protein	Chloride Conc.	CO_2 of Plasma
5% Dextrose	+43.1	+67.1	-21.3	
Ringer's	- 7.4	-10.4	+ 5.5	-9.7
Hartman's	- 7.4	- 2.2	+ 2.7	-4.9
Solution A	- 4.0	- 4.3	+ 1.3	-1.2

N te that the 5% dextrose solution produced a hemo-concentration and a depletion of plasma chlorides. Ringer's solution produced a moderate hemodilution and since it contains chloride in excess it increased the plasma chlorides. Hartman's solution and Solution A produced the least change in body

water distribution, and also the least change in the elctrolyte composition of the plasma. They examined the lavage fluid chemically and you will note from Figure JII that all four solutions investigated were about equally efficient in removing urea from the plasma.

Figure III

AVERAGE CHANGE IN THE CONSTITUENTS OF THE LAVAGE FLUID AFTER FOUR HOURS FOR EACH SOLUTION EMPLOYED

	Lavage Fluid		
Solution	Increase in Urea Nitrogen Conc. Mg.%	Miliequivalent per Liter Change in Chloride Conc.	Volume % Change in CO_2 Content
5% Dextrose	+10.6	+67.6	+23.6
Ringer's	+ 9.3	-29.3	+35.5
Hartman's	+ 7.2	+ 8.8	
Solution A	+10.4	+ 4.7	+ 8.1

Hartman's solution and Solution A showed very little change in the chloride concentration of the lavage fluid, whereas Ringer's solution which contained chlorides in excess showed a decrease and the glucose solution showed a remarkable increase in chloride concentration. Solution A produced very little depletion of the available base of the plasma as evidenced by the smallest change in the CO_2 combining power of the lavage fluid. Ringer's solution and 5% dextrose showed a rather marked increase in the CO_2 combining power of the lavage fluid, consequently these were depleting the body of available base.

One of the best methods of measuring the efficiency of peritoneal lavage in its ability to remove diffusible substances from the blood is to express this rate of removal in terms of urea clearance according to the method suggested by Van Slyke.[13] The formula for maximum urea clearance and standard urea clearance is given below, where U stands for the concentration of urea in the urine, B stands for the concentration of urea in the blood, and V stands for the minute volume of urine.

$$C\ \text{Maximum} = \frac{U}{B} V = 75 \text{ cc. average}$$

$$C\ \text{Standard} = \frac{U}{B} V\frac{}{V} = 54 \text{ cc. average}$$

Maximum clearance is obtained when the minute volume of the urine is 2cc. or more. When the minute volume of the urine drops below 2 cc., the excretion of urea varies as the square root of the urine volume.

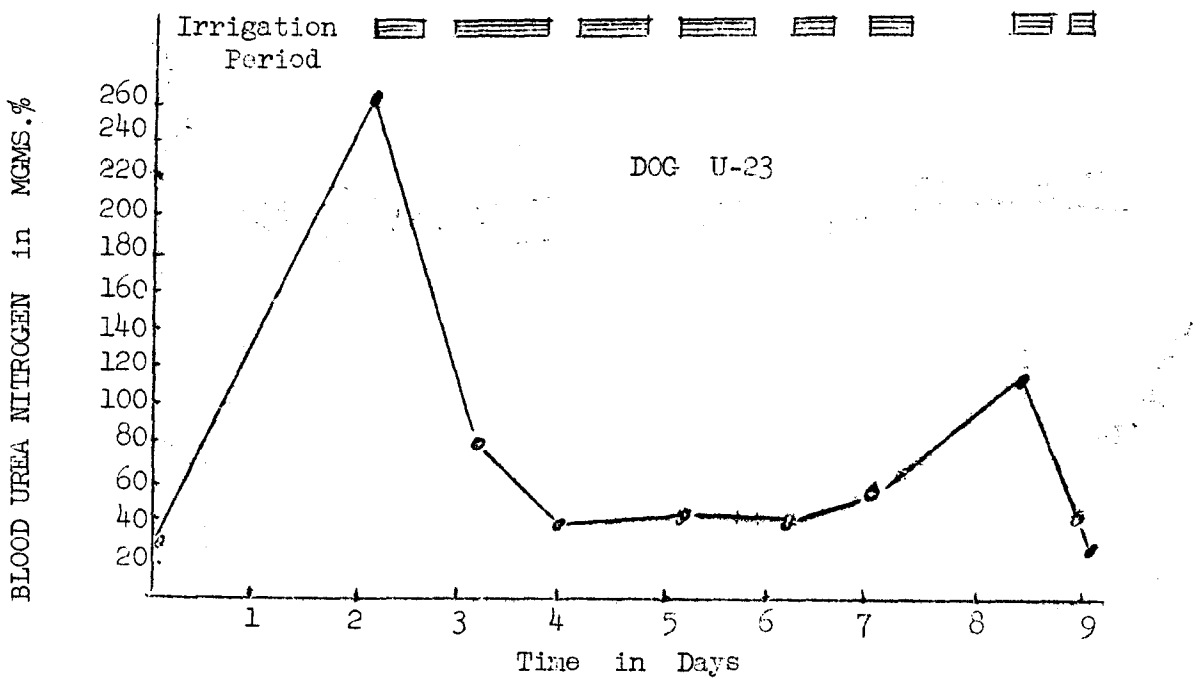
The average maximal clearance equals 75 cc. and the average standard clearance equals 54 cc. That is to say, 75 or 54 cc. of blood are totally cleared of their urea content in one minute's time. Both of these urea clearance rates are considerably in excess of the amount needed to maintain a normal non-protein or blood urea nitrogen. Usually waste produces as evidenced by an increase in the blood urea nitrogen, do not accumulate in the body until the urea clearance rate drops below 10 cc. a minute.

Frank, Fine, and Seligman[1] attacked the problem experimentally in dogs made uremic by bilateral nephrectomy. At the time of nephrectomy they also performed omentectomy. As an irrigating fluid they used modified Tyrode's solution. They modified it by the addition of glucose, penicillin, sodium sulfadiazine,

and heparin. They measured the efficiency of various rates of flow and found that the optimum rate of flow for Tyrode's solution was between 30 and 50 mil. per minute. At 30 mil. per minute this represents approximately 43 liters in twenty-four hours. In uremic dogs, 20 to 40 liters of irrigating solution given over a period of twenty out of thirty-six hours was necessary to restore blood levels of urea to near normal. Somewhat less fluid was required to maintain the normal level. A graphic representation of one of their experiments is given below.

Figure 4

BLOOD UREA CONCENTRATIONS OF DOG FOLLOWING BILATERAL NEPHRECTOMY AND TREATED WITH INTERMITTENT PERITONEAL IRRIGATION



Specimens were taken just before irrigation was started and therefore the points represent highest levels reached between irrigation periods.

In this experiment the irrigation lasted twenty hours daily for the first two days and from eight to twelve hours daily thereafter. Most of the experiments were terminated by accidental death or by bacterial contamination of the peritoneum. At postmortem examination some fibrinous adhesions were seen between the loops of bowel but no effective chaneling of the irrigating solution nor any effective isolation of the catheters was noted. They also measured the blood urea clearance rate by irrigation of isolated intestinal loop.

They lavaged ten or twelve inch isolated segments of bowel at various rates of flow. The average clearance rate per inch of bowel that they obtained is given in the table below.

Figure V

AVERAGE UREA CLEARANCE PER INCH OF GUT

Number of Cases	Segment	Urea Clearance cc./min.
1	Stomach	.01
2	Duodenum	.17
8	Jejunum	.18
3	Ileum	.12
1	Human ileum	.05
1	Pleura	2.8

The highest rate of clearance obtained from the intestinal tract in experimental animals was obtained from the jejunum. Here they obtained an average clearance rate of .18 cc. per minute per inch of bowel in the eight cases tried. In order to produce a minimal clearance rate of 10 cc. per minute, it would require approximately five feet of isolated jejunum as a dialyzing membrane. Note that they investigated the human ileum as a dialyzing membrane. Here they were able to obtain a clearance rate of .05 cc. per inch per minute. It would require approximately 17 feet of ileum to produce a minimal clearance rate of 10 cc. per minute. They also investigated the pleura as a dialyzing membrane. They lavaged one side of the pleural cavity at various rates of flow. and the maximal clearance rate they were able to obtain was 2.8 cc. per minute. This is approximately one-fourth the minimal urea clearance rate of 10 cc. per minute.

We have used the peritoneum as a dialyzing membrane in the treatment of uremia in four cases. Three patients recovered and one died. Two of the recovered cases were probably favorably influenced by peritoneal lavage and in one case it was of questionable value.

Method: The solution we used to lavage the peritoneum was modified Hartman's solution. The formula for Hartman's solution is given above, and we modified it by the addition of heparin, penicillin, glucose, and in one case streptomycin. We added heparin to lessen the danger of producing adhesions with channeling or isolation of the inflow catheter and outflow drain. The dose was from 5 to 10 mgm. per liter. Penicillin was added in the dosage range of from 5,000 to 20,000 units per liter as a prophylactic measure against peritonitis. We added glucose from 20 to 50 grams per liter to produce a hypertonic solution, and in one case we added streptomycin, 100 mgm. per liter, as a prophylactic measure against peritonitis by gram negative bacteria. Fluid was introduced into the peritoneal cavity through a 20 mushroom catheter inserted into the peritoneal cavity through a small incision in the right lower quadrant of the abdomen performed under local anesthesia. Fluid was aspirated from the peritoneal cavity by the use of a sump drain connected to a collection bottle on the floor with moderate vacuum pressure created by a Stedman pump. The sump drain was inserted into the peritoneal cavity through a small incision in the left lower quadrant made under local anesthesia. This method of peritoneal lavage was originally suggested by Frank, Fine, and Seligman, and they have subsequently improved the method by insertion of a Mandler filter between the reservoir of irrigating fluid and the inflow tube.

During the period of peritoneal lavage, we gave all four patients water soluble vitamins parenterally since these substances are probably lost by the body in the dialysate. The arbitrary daily dosage we gave was 12 mgm. of Vitamin K, 500 mgm. of ascorbic acid, 20 mgm. of thiamin hydrochloride, 10 mgm. of riboflavin, 10 mgm. of pyridoxine hydrochloride, 10 mgm. of calcium pantothenate, and 100 mgm. of niacinamide. In addition, all patients received penicillin intramuscularly during the period of peritoneal lavage. The total daily dosage varied from 160,000 to 800,000 units given in divided doses at three hour intervals.

Case 1: Miss aged 24, entered the University Hospital June 11, 1946, for a plastic operation on her breasts. Her previous health had been excellent.

Physical examination revealed a well developed, moderately obese, white female with large pendulous breasts. Heart and lungs were negative. The blood pressure was 118/64.

June 12, 1946: Day of surgery. During the operation the patient was given 500 cc. of citrated blood. During the transfusion she developed a marked cyanosis and respiratory distress, and a bronchial obstruction was suspected. The patient was bronchoscoped and a foreign body was removed from the lower trachea, however, this did not relieve the respiratory distress or the cyanosis. Blood pressure remained normal during the operative and postoperative period. After awakening from the anesthesia, the patient complained of pain in the

costovertebral angles.

June 13, 1946: First postoperative day. The patient had not voided since surgery, fifteen hours before. She was catheterized and 400 cc. of very dark urine was obtained. This urine was found to contain free hemoglobin without erythrocytes. The benzidine and guaiac reactions were both four plus and a hemolytic transfusion reaction was suspected. Examination of the patient's plasma revealed a free plasma hemoglobin level of 96 mgm. per cent with a total serum bilirubin of 1.9 mgm. per cent. The patient's hemoglobin concentration was 7 grams per cent. A recheck of the blood she had received showed it to be from an incompatible blood group. The patient was given 2000 cc. of 5% glucose in distilled water, intravenously, and her urinary output was 50 cc. for that day.

June 15, 1946: Third postoperative day. The blood urea nitrogen was 76 mgm. per cent. Urinary output was 50 cc. Her intake had averaged 2000 cc. daily, orally and parenterally. The patient had received three 500 cc. blood ytansfusions without apparent reactions. Her weight was 170 pounds. This was the first time she had been weighed since surgery. The patient was taken to the operating room and under spinal anesthesia the left kidney was exposed and decapsulated. The parenchyma of the kidney was hard to palpation and was a dark bluish-black with a streaked surface. A biopsy was taken from the lower pole, using a punch. The microscopic report on the biopsy of the kidney is as follows: The glomeruli appear normal, the tubular epithelium is intact, many of the convoluted tubules and collecting tubules contain casts which in part are homogenous and of a brownish-red color, and others are pinkish and granular. Dr. E. T. Bell reviewed the slide and stated that enough of the tubules were obstructed by casts to account for the uremia. The conclusion was obstructive tubular disease.

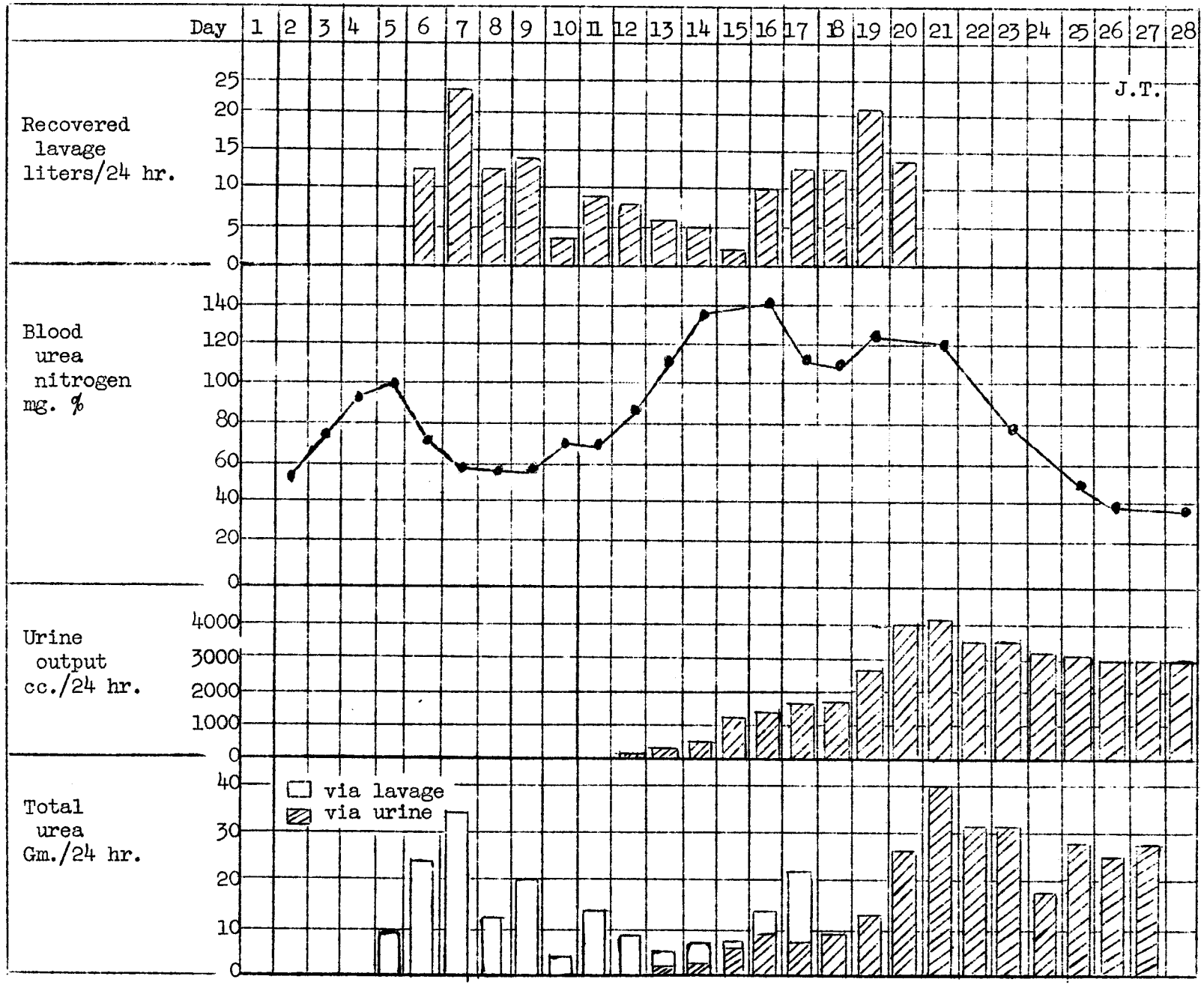
June 17, 0946: Fifth postoperative day. During the previous forty-eight hours the urinary excretion amounted to 50 cc. per twenty-four hours. Her blood urea nitrogen was 100 mgm. per cent. She had received on an average 1000 cc. of fluid orally and parenterally per twenty-four hours during this period, and her weight remained the same. Peritoneal lavage was instituted following the insertion of the mushroom catheter and sump drain under local anesthesia. A graphic representation of the results obtained is shown in Figure VI.

During the next five days we were able to lower the blood urea nitrogen to 58 mgm. per cent. We varied the rate of flow from 3 to 16 cc. per minute and found that the urea clearance rate progressively increased with the rate of flow, although we did not equal the maximum clearance obtained by Frank, Fine, and Seligman.

June 22, 1946: Tenth postoperative day. We encountered some difficulty with the outflow tube, and in spite of cleaning the tube and changing its position in the peritoneal cavity, we were unable to make it work properly. Within the next forty-eight hours no return could be obtained from the sump drain. However, we were able to run in 600 cc. of fluid through the mushroom catheter before leakage occurred around the mushroom catheter. So we lavaged the peritoneum intermittently by using the mushroom catheter as both an inflow and outflow tube. The capacity of the cavity we were lavaging progressively decreased, as did the amount of urea we were able to obtain by this method. The total twenty-four hour urea excretion via the peritoneum fell from a high of 34 grams per twenty-four hours obtained on June 20, 1946 to a low of 4 grams obtained on June 27, 1946, at which time the peritoneal pocket held only 100 cc.

June 28, 1946: The sixteenth postoperative day. We decided to reinsert the mushroom catheter and sump drain into the upper abdomen to see if we could reestablish the lavage system. The patient was transferred to the operating room and under local anesthesia, two small one inch incisions were made in the upper right and left quadrants of the abdomen. The blood urea nitrogen had risen from a previous low of 58 mgms. per cent to 140 mgms. per cent. Insertion of a finger through the small incisions in the upper abdomen disclosed filmy, fibrinous adhesions between the

Figure VI - PERITONEAL LAVAGE



outer peritoneal wall and the peritoneal contents. These could easily be broken down and were broken down as far as the fingers could reach through these small incisions. The mushroom catheter was inserted on the right and the sump drain on the left, and the patient was returned to the ward. After starting the fluid, it was found that no fluid was coming out the sump drain but there apparently was a channel between the mushroom catheter in the upper right side of the abdomen and the former site of the mushroom catheter on the lower right side of the abdomen. Consequently the sump drain was changed in position and inserted in the lower right quadrant. During the next twenty-four hours, using a slow rate of 7 cc. per minute, we were able to produce a urea clearance rate of 3.1 cc. per minute, and by doubling the rate of flow during the next twenty-four hours we were able to produce the clearance rate of 4.2 cc. per minute and for the succeeding three days the clearance rate progressively dropped, there being only a trace of urea in the peritoneal washings. The peritoneal lavage was discontinued on July 3, 1946.

A chart is given showing the average change in the blood urea nitrogen and the average change in urea clearance obtained by various rates of flow of lavage fluid and urine.

Figure VII

	PERITONEAL FLUID				URINE		
Days	Bl. Urea Nitrogen	Total Volume	Flow Rate cc./min.	Urea Clear. cc./min.	Volume	Flow Rate cc./min.	Urea Clear. cc./min.
4	87						
5	100	4670	3.2	3.6			
6	73	13420	9.3	8.0			
7	61	23750	16.5	15.2			
8	58	12700	8.8	6.7			
9	80	14100	9.8	11.4			
10	72	3970	2.8	2.3			
11	72	9400	6.6	6.3	300	0.2	1.36
12	88	7700	5.3	4.2	450	0.3	1.38
13	112	5700	3.5	1.4	1200	0.8	1.9
14	136	5500	3.8	1.2	1400	1.0	2.1
15	140	1700	1.2	3.4	1600	1.1	1.7
16	113	9550	6.6	3.1	1750	1.2	2.4
17	110	12900	8.9	4.2	2600	1.8	2.9
18	125	13400	9.3	Tr.	4050	2.8	6.9
19	124	21050	14.6	Tr.	4100	2.8	10.3
20	100	14400	10.0	Tr.	3500	2.4	10.0
21	105				3600	2.4	9.6
22	79				3200	2.2	7.3
23	68				3100	2.1	12.8
24	51				2900	2.0	16.5
25	40				3100	2.1	21.6

Discussion: Local complications: The peritoneal fluid was sterile at the time of instituting the peritoneal lavage. Cultures of the peritoneal fluid after twenty-four hours were positive for a coliform bacillus and were repeatedly positive. The only clinical sign of peritonitis the patient had was a mild ileus with some abdominal distention which was a mild ileus with some abdominal distention which was not too troublesome. However, the peritonitis that developed created a channeling and blockage, thus rendering the peritoneum ineffective as

a dialyzing membrane. Reinstituting lavage in the upper abdomen was not particularly useful since only a minimal clearance rate was obtained for forty-eight hours and the amount of urea removed in the five-day period that we used the upper abdomen was of negligible consequence.

Frank, Fine, and Seligman[3] have suggested and used an improved apparatus which should lessen this complication, namely, using a large reservoir for the fluid which obviates the necessity of frequently changing bottles of lavage solution, and the insertion of a Mandler filter between the lavage fluid and the peritoneal cavity. An additional precautionary measure against this complication should be the addition of streptomycin to the irrigating fluid since it is now commercially available.

The effects on the chemical constituents of the blood plasma: Although we used a rate of flow considerably less than the optimum, we were able to lower the blood urea nitrogen significantly with improvement in the patient's general physical condition. With Hartman's solution there was no significant loss of base by the body as evidenced by very little change in the CO_2 combining power. During the time our apparatus was not working well, the patient's CO_2 combining power fell to 35 volumes per cent and it was necessary to give the patient intravenous sodium bicarbonate solution to combat the acidosis until renal function was re-established. Chloride and calcium levels were low but showed no depletion during the time our peritoneal lavage was working satisfactorily.

Fluid balance: We decided early to follow the patient's fluid balance by daily weighing as is done on the Surgical Service. The recovered volume of solution lavaged through the peritoneum was consistently below that introduced. Part of this was due to occasional failure of our apparatus to work satisfactorily, and the dressings and bedding would become soaked with irrigating solution. This was especially true during the time we were using intermittent lavage following the blockage of our sump drain. The patient's weight prior to the introduction of peritoneal lavage was 170 pounds. After three days of lavage this was 180 pounds, and the patient had clinical signs of edema, both peripheral and pulmonary, and it was necessary to place her in an oxygen tent for the respiratory distress. Her combined oral and intravenous intake for this three day period averaged below 1000 cc. per twenty-four hours. Some of the fluid used for peritoneal lavage was obviously being absorbed. During the next three days, June 21, 1946, to June 23, 1946, with the exception of 500 cc. of blood, this patient received no parenteral fluids and her weight dropped to 168 pounds with some improvement in respiratory difficulty and a lessening of the peripheral edema. Her oral intake during this period averaged 200 cc. daily. However, the improvement in her respiratory difficulty was not sufficient to permit discontinuing the oxygen tent. From June 24, 1946 to June 30, 1946, her combined oral and intravenous fluids averaged between 2500 to 3000 cc., and most of this was given parenterally and consisted of 5% glucose in distilled water. Her weight on June 30, 1946, was 168 pounds and she was still having considerable respiratory distress, although she had a urinary output at this time of 2800 cc. At the suggestion of Dr. Smith, all intravenous fluid administration was discontinued, and the patient was encouraged to drink water by mouth. From July 1, 1946 to July 4, 1946, the patient lost 21 pounds of weight in spite of an oral intake of from 2000 to 3000 cc. of water per twenty-four hours. Her urinary output during this four-day period averaged 3500 cc. per twenty four hours. There was a remarkable improvement in her general physical condition following the cessation of intravenous fluid therapy. Within twenty-four hours the respiratory distress was considerably alleviated, and within forty-eight hours it was possible to remove her from the oxygen tent permanently.

Discussion: Although daily weighing is probably a good method of following the patient's fluid balance, two obvious errors were evidenced here. In the first place we assumed that the patient's normal weight was 170 pounds which was

her weight prior to renal decapsulation. This was taken three days after the original transfusion reaction, and the patient was probably overhydrated at this time. In addition we did not take into account the normal weight loss that would accompany a serious illness over this duration of time. Her weight at the time of discharge from the hospital was 132 pounds. Thus we were maintaining the patient in a positive fluid balance in excess of 21% of her normal weight, a practice which certainly added to the distressful condition of the patient and not without danger.

During the period of intravenous feeding from June 17, 1946 to July 1, 1946 the patient received on an average of 300 calories per day with an average salt intake of 4 grams per day during this period. It probably would have been better to increase her caloric intake by dissolving 300 or 400 grams of glucose in a much smaller volume of fluid, for example 1000 cc. It is noteworthy that a checkup renal function test performed on October 9, 1946, was 80% of normal. Her urea clearance on this day was 52.6 cc. per minute.

Case 2: [redacted], aged 68, was admitted to an outside hospital May 26, 1946. The chief complaint was symptoms of prostatism which had recurred after a transurethral resection done elsewhere in 1940. This was associated with gross hematuria. An excretory urogram showed a normal upper urinary tract. His general physical condition was excellent. On rectal examination he had a one plus benign prostatic hypertrophy. Past history was non-contributory. Laboratory examination: Hemoglobin was 87% (Sahli), leukocyte count 5,815 with 58% polymorphonuclears. Serology was negative. The blood urea nitrogen was 21 mgm. per cent. Urinalysis: Specific gravity 1.017, the albumin and sugar were negative. Microscopic examination at the time was negative.

May 28, 1946, under spinal anesthesia, supplemented with pentothal, a transurethral resection was performed. Fifty-eight grams of tissue were removed with an operative blood loss of 600 cc. The blood loss was excessive and according to the operator was due to an early perforation of the prostatic capsule with venous bleeding. In order to control the bleeding after completing the resection, it was necessary to distend the bag on the Foley catheter with 60 cc. of water with the bag in the prostatic fossa. The pathological report of the tissue removed was benign prostatic hypertrophy. Water under pressure was used during the resection as an irrigating solution. The patient received 500 cc. of commercial plasma postoperatively and no transfusions. No serious operative or postoperative drop of blood pressure was encountered.

May 29, 1946, there was an icteric discoloration of the sclera, and edema of the conjunctiva. The patient had remained stuporous since the time of his operation. Examination of his plasma showed free hemoglobin although the actual quantity was not determined; it was dark red to inspection. The patient's blood urea nitrogen was 49 mgm. per cent, and CO_2 combining power was 63 volumes per cent. Chlorides were 510 mgm. per cent, and his hemoglobin was 50% (Sahli). His urinary output for the first twenty-four hours amounted to 825 cc. The clinical impression was a hemolytic reaction caused by irrigating fluid entering the prostatic veins during the resection.

May 30, 1946: His second postoperative day. The serum was still straw-colored and there was definite clinical jaundice. The patient's blood urea nitrogen was 70 mgm. per cent, CO_2 combining power 56 volumes per cent, and his urinary output was 690 cc. He was given 1,730 cc. of 5% glucose in distilled water, and 500 cc. of citrated blood.

June 5, 1946: His eighth postoperative day. The patient's blood urea nitrogen was 109 mgm. per cent; his urinary output had varied between 350 and 500 cc. per twenty-four hours. He had been receiving 2,000 cc. of fluid daily, chiefly 5% glucose in distilled water. He had also received an additional transfusion of 500 cc. of citrated blood, with no apparent reaction. He was developing edema of the extremities and scrotum. There were no signs of pulmonary edema. Peritoneal lavage was instituted, using

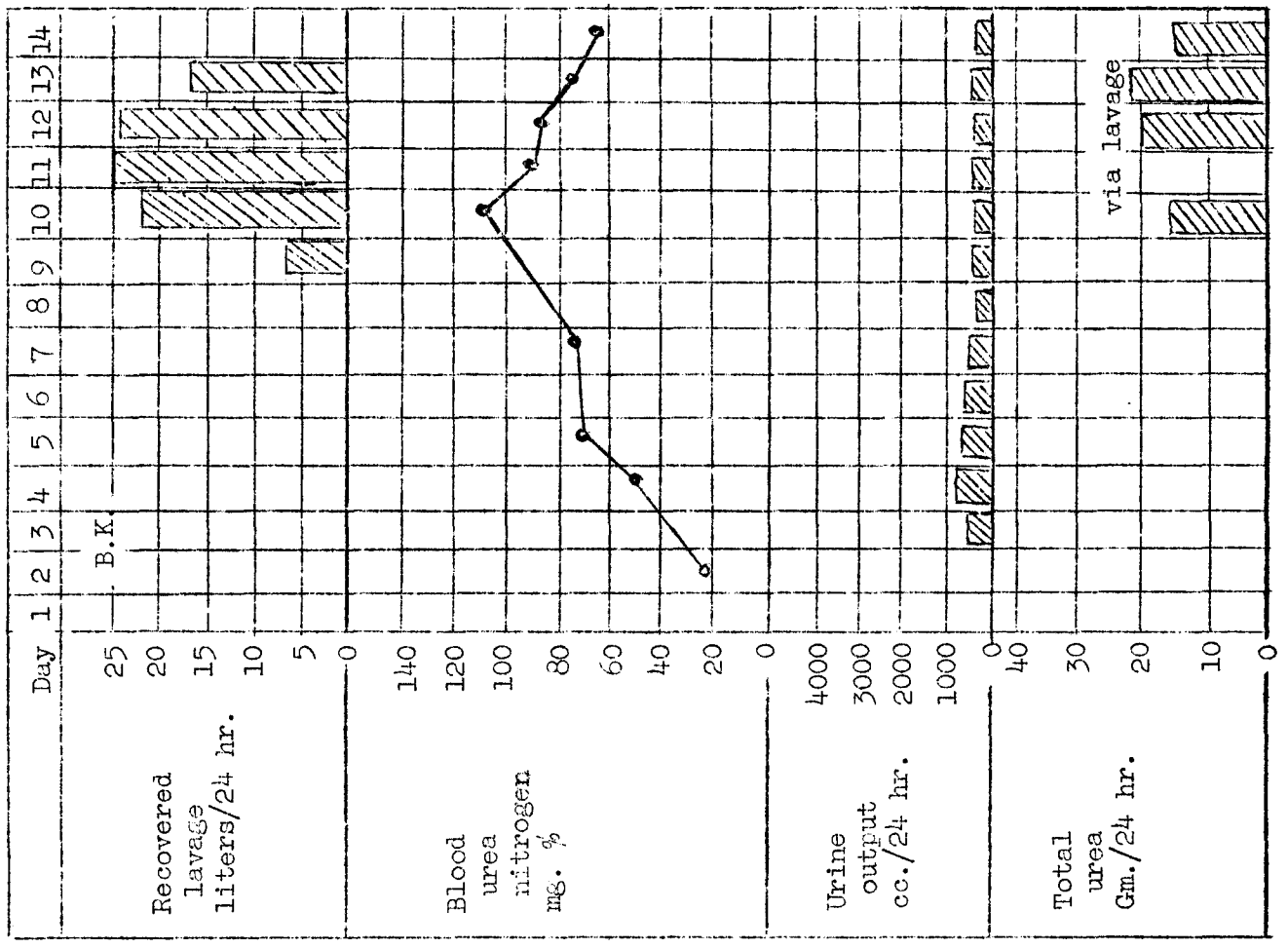


Figure VIII - PERITONEAL LAVAGE

Hartman's solution modified by the addition of penicillin, heparin, and 50 grams of glucose per liter.

Clinically the edema was increasing and there were signs of pulmonary edema. The patient was still stuporous and restless. He received 800 cc. of 5% glucose in distilled water. A graphic representation of the results obtained is given in Figure VIII.

June 6, 1946: The patient was given an additional 1000 cc. of 5% glucose in distilled water intravenously and 500 cc. of 5% sodium bicarbonate. The blood urea nitrogen was 92 mgm. per cent, CO_2 combining power 48 volumes per cent, chlorides 487. His urinary output was 450 cc. and his general condition remained about the same.

June 7, 1946: No intravenous fluids were given on this day and the urinary output was 500 cc. Blood urea nitrogen was 86 mgm. per cent, CO_2 combining power 58 volumes per cent, chlorides 500 mgm. per cent. The patient's abdominal distention and edema were increasing. Nasal suction was started.

June 8, 1946, the patient had an oral intake of 600 cc., a urinary output of 400 cc. and 500 cc. were obtained by nasal suction. The patient appeared brighter but more restless. The peripheral edema seemed less but the pulmonary edema was increasing. Nasal

suction was discontinued. In the afternoon the patient developed auricular fibrillation with a rapid ventricular rate and he was digitalized intravenously with the use of cedilanid, 8 cc. given in divided doses. Respirations were labored with marked expiratory effort. Nasal suction was reinstituted. The patient was placed in an oxygen tent, the lavage fluid was changed to alternate 2000 cc. of 5% glucose solution, and 2000 cc. of modified Hartman's solution.

June 9, 1946: The patient had no oral or intravenous intake of fluids and his urinary output was 400 cc. There was considerable reduction of peripheral edema and clinical evidence of peritonitis, consisting of marked ileus with abdominal tenderness. There was a large number of white blood cells in the peritoneal washings. The peritoneal culture was positive for Escherichia coli. The patient was given 3 grams of streptomycin in divided doses and respiratory difficulty increased, and was not relieved by oxygen. The patient expired suddenly at 6 p.m. that evening.

Autopsy: The essential findings at autopsy were a bilateral pulmonary edema, without evidence of consolidation. Kidneys were enlarged, the right weighed 215 grams, and the left 235 grams. On section the cortex and medulla were thick. The cut surfaces were dark red and homogeneous. The ureters showed no evidence of any dilatation. On microscopic examination of the kidneys, the most conspicuous finding was a large number of hemoglobin casts and hemolyzed red blood cells filling many of the distal collecting tubules. The distal tubules proximal to the casts were dilated. They were lined by a low flat epithelium. The glomeruli appeared normal. There was considerable fibrin in the peritoneal cavity but no adhesions.

Discussion: This patient was overhydrated before peritoneal lavage was begun, and this over-hydration was increased by absorption of fluid from the peritoneal cavity. Since the immediate cause of death was probably pulmonary edema, it might have been possible to alter the outcome by reducing the edema by the use of a more hypertonic irrigating solution. Over-hydration of a patient with reduced urinary output is valueless as a diuretic agent.

Case 3: , aged 57. This patient was admitted to an outside hospital on September 4, 1946. The patient developed an acute urinary retention one week prior to admission for which a physician had been catheterizing him daily. This physician prescribed sulfathiazol tablets, grams 0.5, three or four times daily, as a prophylactic measure. Three days prior to admission the patient developed a conjunctivitis associated with a maculopapular skin eruption and a decreased urinary output. He was admitted under the care of an urologist since his primary difficulty was prostatism.

On physical examination the temperature was 101.4, respirations 22. The essential physical findings were a marked conjunctivitis and a generalized maculopapular skin eruption with scattered areas of psoriasis. The pulse rate was 90 and regular. The blood pressure was 80 systolic, 40 diastolic. There was mild abdominal distention. On rectal examination the prostate was one plus enlarged and felt benign. The patient was catheterized and 1200 cc. of urine was obtained. An inlying catheter was inserted.

Laboratory examination: Urinalysis: Specific gravity was 1.012, pH 6, albumin 2 plus, and sugar negative. The microscopic report on the urine was negative with the exception of a few sulfa crystals. Culture was positive for a streptococcus. Hemoglobin was 11 grams per cent; leukocyte count was 17,300 with 84% polymorphonuclears. The blood urea nitrogen was 28 mgm. per cent. During the next twenty-four hours the patient's urinary output was only 500 cc., in spite of an adequate oral and intravenous intake.

September 5, 1936: The patient was cystoscoped and bilateral retrograde pyelograms were made. Specimens from the right kidney contained two plus granular casts, three plus red blood cells, two plus white blood cells, was negative for sulfa crystals Specimens from the

left kidney contained an occasional granular cast, three plus red blood cells, and an occasional white blood cell. It was also negative for sulfa crystals. The re-ray showed no urinary calculi and retrograde pyelograms were normal except for slight incomplete rotation of the left kidney.

The patient's average intake, orally and intravenously, over the next four-day period was 2000 cc. per twenty-four hours. His urinary output was 500 cc., 60 cc., 45 cc., and 15 cc.

September 8, 1946: The patient's conjunctivitis had improved and the skin rash had faded. The patient was moderately jaundiced. The diagnosis was toxic nephrosis due to sulfathiazol, or acute bilateral suppurative pyelonephritis associated with oliguria, uremia, and jaundice due to hepatitis. The patient's blood urea nitrogen at this time was 94 mgm. per cent. There was a mild hypostatic edema present without clinical signs of pulmonary edema. Peritoneal lavage was instituted using modified Hartman's solution containing no glucose. This was alternated with modified Hartman's solution containing 5% glucose.

September 9, 1946: The patient was more jaundiced. The total serum bilirubin was 4.9 mgm. per cent. There was considerable abdominal distention and nasal suction was instituted. The edema was increasing and there were some signs of pulmonary edema.

September 10, 1946: The patient was still more jaundiced. The peripheral edema and pulmonary edema were still present in about the same amounts as on the previous day. The lavage solution was changed to continuous irrigation with Hartman's solution containing 5% glucose, penicillin and heparin.

September 11, 1946: The patient was quite restless, and developed a marked twitching of the muscles. His calcium level was 8.3 mgm. per cent. He was given 10 cc. of calcium gluconate intravenously. The pulmonary edema and the peripheral edema, which was more noticeable over the back, sacrum, and dependent portion of the extremities, was increasing. His total proteins on that day were 5.9 grams per cent.

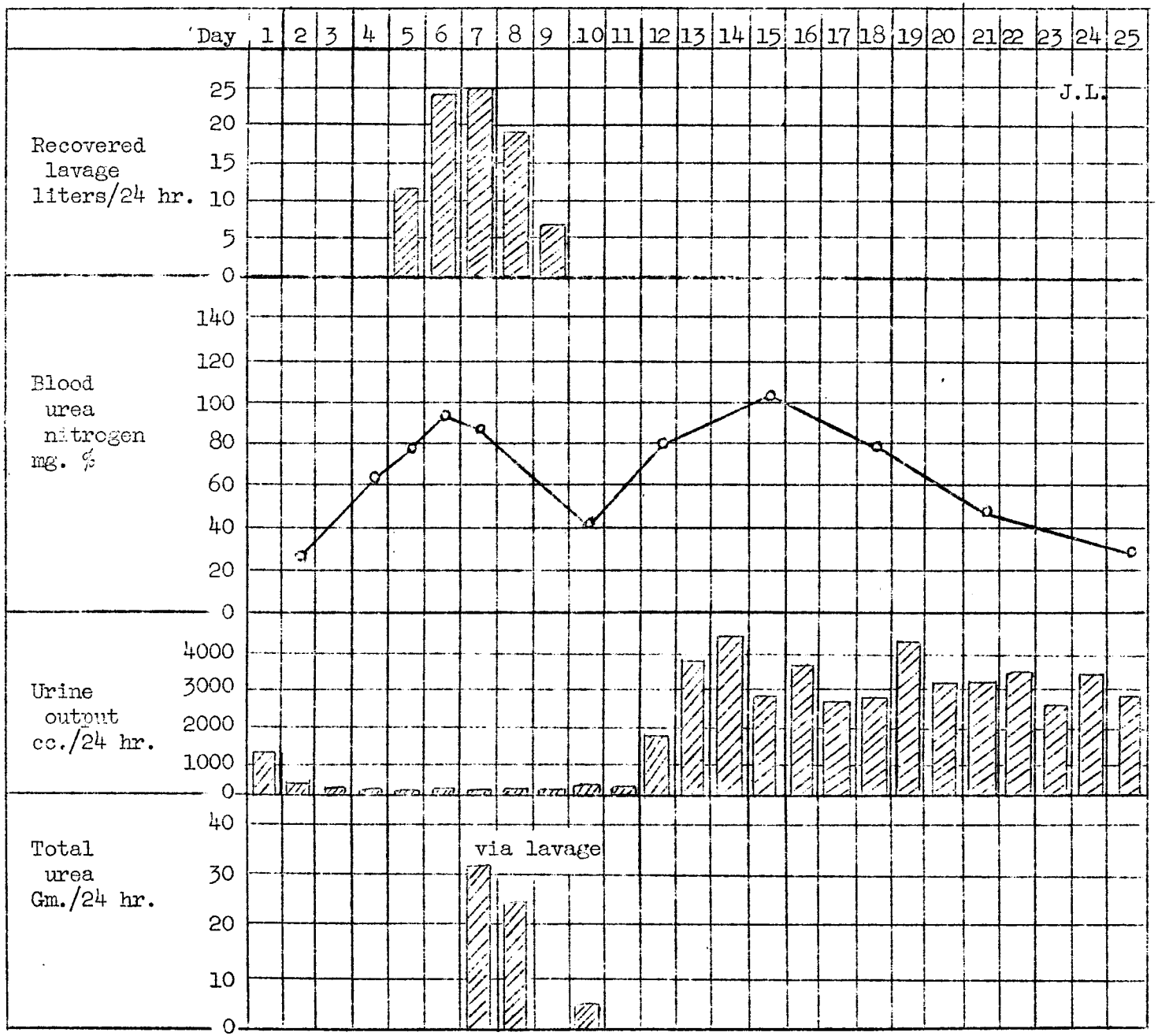
September 12, 1946: The patient developed auricular fibrillation. The dependent and pulmonary edema were more marked. The pulmonary edema was causing a moderate respiratory distress. The patient was digitalized with digifolin and the peritoneal lavage was discontinued. A graphic representation of the effect on the blood urea nitrogen is given in Figure IX.

Comment: The average oral intake of fluids during the five days of peritoneal lavage was 550 cc. per twenty-four hours. He received no intravenous fluid therapy during this time. His urinary output during this time was practically nil. In spite of this the edema increased during the five-day period and peritoneal lavage had to be discontinued because of pulmonary edema. Obviously the patient was absorbing fluid from the peritoneal cavity. As can be seen from the chart, he did not develop a significant diuresis until September 14, and on the 15th and 16th, his urinary output exceeded his intake by 2000 cc., and 3000 cc. We were able to lower his blood urea nitrogen from 94 mgm. per cent to 42 mgm. per cent, but from the subsequent rise of his blood urea nitrogen, it would have been better to maintain the peritoneal lavage for a longer period of time had we been able to obviate or reduce the amount of fluid being absorbed from the peritoneal cavity.

Case 4: , aged 60, was admitted to the University Hospitals on Nov. 21, 1946. This patient had symptoms of prostatism for four years with increased frequency and dysurea associated with a reduction in force and caliber of the urinary stream. There had been an exacerbation of the symptoms nine months prior to admission. The residual urine at the time of admission was 300 cc. The patient's past health had been excellent

Physical examination: The patient was a well developed and well nourished male with mild prostatism. Examination of the heart was negative; the blood pressure was 110 systolic, 60 diastolic.

Figure IX - PERITONEAL LAVAGE



On rectal examination the prostate was one plus enlarged, smooth, firm, and felt benign. There was a moderate tremor of both the hands and the head.

Laboratory examination: Urine specific gravity was 1.023, pH 6, albumin negative, sugar negative, and on microscopic examination contained an occasional red blood cell and an occasional white cell. Hemoglobin was 15.5 grams per cent, the white count was 10,000 with 75% polymorphonuclears. Blood urea nitrogen was 11 mgm. per cent; blood Wassermann was negative. E. coli was cultured from the urine. A diagnosis of prostatism due to benign prostatic hypertrophy was made.

November 13, 1946, under spinal anesthesia, transurethral resection was performed and 35 grams of tissue were removed with a minimal operative blood loss. Toward the end of the procedure a visible rent was made in the anterior portion of the prostatic fossa and on suprapubic palpation, irrigating fluid could be palpated in the pre-vesical space. The patient was still under spinal anesthesia and felt no pain. However, he did obtain a mild drop in systolic pressure. The pressure dropped from an operative level of 110 mm. to 70, shortly after the perforation was made. The patient was transferred to the main operating theater where a cystostomy was performed, supplementing the spinal anesthetic with intravenous pentathol and cyclopropane. On opening the pre-vesical space, free irrigating fluid was encountered. The bladder was opened and the prostatic fossa was bleeding moderately. The prostatic fossa was packed with oxycel to control the bleeding, and a 30 mushroom catheter was sutured into the bladder for cystostomy drainage. The pre-vesical space was drained and the incision was closed in layers. The first postoperative day, the patient was afebrile. He excreted 500 cc. during the first twenty-four hour period. His hemoglobin was 13.4 grams, his white count was 8,600 with 78% polymorphonuclears. The blood urea nitrogen was 37 mgm. per cent. The immediate postoperative plasma hemoglobin level was 85 mgm. per cent.

For the next seven days the patient's urinary output varied from 200 to 500 cc. in spite of the adequate intravenous and oral intake.

November 30, 1946: The patient's weight was 76 kgs. which was the same as his preoperative weight. His hemoglobin was 9.4 grams, and his white count was 8,400 with 73% polymorphonuclears. His blood urea nitrogen was 160 mgm. per cent, CO_2 combining power was 41, chlorides were 462 mgm. per cent. He had been tolerating the uremia well, maintaining a good appetite with only a few periods of disorientation. With the rapid rise of blood urea nitrogen, the CO_2 combining power had dropped to 30 volumes per cent on November 28, 1946, and he was given 500 cc. of 5% sodium bicarbonate intravenously on this day. On November 30, 1946, and December 1, 1946, the patient excreted 1000 cc. of urine per twenty-four hours. His blood urea nitrogen rose to 180 mgm. per cent. He had been transfused and his hemoglobin on December 1, 1946, was 11 grams per cent. His weight was still 76 kgs. However, he became irrational and somewhat combative with a marked anorexia and nausea, and occasional vomiting. Although the patient's urinary output was increasing, it was deemed advisable to institute peritoneal lavage because of the rising blood urea nitrogen and deterioration of his condition.

December 2, 1946: Peritoneal lavage was instituted. During the next fifteen hours we lavaged the peritoneum with 15,000 cc. of modified Hartman's solution containing 2% glucose in addition to penicillin, heparin, and streptomycin. In order to keep up his caloric intake without overhydrating the patient, we gave 1200 cc. of fluid intravenously containing 5% amigen and 300 grams of glucose. This markedly hypertonic solution was given slowly over an eight hour period.

December 3, 1946: The patient's weight was 180 pounds, a weight gain of 13 pounds over the preoperative weight. He had a moderate edema of the scrotum and sacrum, and some pulmonary edema. His blood urea nitrogen had

dropped from 180 mgm. per cent to 140 mgm. per cent. His CO_2 combining power was 37 volumes per cent; the chlorides were 466 mgm. per cent. His urinary output was 1200 cc. It was thought that the hypertonic solutions given intravenously during this period of peritoneal lavage had increased the amount of absorption and it was decided to limit his fluid intake to 500 cc. orally during the next twenty-four hours with no intravenous fluids.

December 4, 1946: During the previous twenty-four hours we lavaged the peritoneum with 25,000 cc. of modified Hartman's solution. The patient's weight increased 26 pounds over the previous day, and he was markedly edematous although having very little respiratory difficulty as a result of his pulmonary edema. The edema was chiefly of the scrotum, back, and lower extremities. His blood urea nitrogen dropped from 140 mgm. per cent to 114 mgm. per cent. His CO_2 combining power was 54 volumes per cent, and his chlorides were 517 mgm. per cent. His urinary output was 2000 cc.

Because the patient's urinary output was rapidly rising and the edema was so marked, it was considered advisable to discontinue the peritoneal lavage. The inflow and outflow tubes were clamped but left in place. During the next four days the patient received nothing but water orally. His average oral intake was 400 cc. per twenty-four hours. His urinary output averaged 3000 cc. per twenty-four hours. His weight dropped from 206 pounds to 168 pounds. His blood urea nitrogen rose from a low of 114 mgm. per cent to 126 mgm. per cent on December 7, 1946. From this day forward it showed a progressive decline and on December 27, 1946, his blood urea nitrogen was 27 mgm. per cent.

Conclusion: The problem of fluid balance was our most serious problem. In case two, the cause of death was pulmonary edema due to overhydration. In case one, the patient was markedly overhydrated with respiratory distress, the result of pulmonary edema. In cases three and four, peritoneal lavage had to be discontinued because of dangerous overhydration of the patients. The solution we were using for peritoneal lavage has an osmotic pressure slightly less than double the osmotic pressure of the normal blood plasma, but contained ions and molecules which were entirely diffusible and of relatively small size. The answer to this problem is at present unsolved. Frank, Fine, and Seligman used modified Tyrode's solution plus a 5% gelatin solution in one case they reported. They encountered considerable difficulty with this solution in that the patient went into shock during the irrigation with the fluid, and they attributed the shock to the too rapid dehydration of the patient. The answer may be using gelatin in a lesser concentration. The use of markedly hypertonic solutions intravenously has been shown experimentally to hasten absorption from the peritoneal cavity. In case four, where we gave 300 grams of glucose in a 5% amigen solution dissolved in 1200 cc. of water, the absorption from the peritoneal cavity proceeded at an alarming rate. I question the wisdom of giving hypertonic solutions intravenously even if given slowly, since we gave this over a period of eight hours. It is probably better to ignore inanition and starvation acidosis during the period of peritoneal lavage. If one regards it as necessary to feed the patient, feed by gavage in the absence of vomiting and avoid intravenous solutions. If the apparatus is working satisfactorily, there is a rapid improvement in the general condition of the patient and usually a rapid return of a good appetite.

Penicillin added to the peritoneal fluid and given parenterally was adequate in our cases to prevent peritonitis from organisms susceptible to penicillin. In case one and two there was clinical and bacteriological evidence of peritonitis caused by gram negative rods of the colon group of organisms. In case one, this seriously interfered with peritoneal lavage by isolating the sump drain and channeling the irrigating fluid. Two measures to combat this complication suggest themselves, the first being the use of the improved method of peritoneal lavage suggested by Frank, Fine, and Seligman[3]

and used by them. The second is probably the addition of streptomycin to the irrigating fluid. The use of large reservoirs for the irrigating fluid eliminates the necessity for repeated breaks in the irrigation system to replenish the fluid with the possibility of contamination. In addition the insertion of a Mandler filter between the reservoir of irrigating fluid and the peritoneal cavity lessens the danger of introducing organisms into the peritoneal cavity.

We used heparin in our irrigating solutions in far greater concentration than is reported by other investigators. We used as high as 250 mgm. per twenty-four hours and in no case did we encounter any bleeding tendencies. In case one the bleeding time on the third day of peritoneal lavage was 4 minutes and 30 seconds, and the clotting time was 6 minutes. On the sixth day of peritoneal lavage the bleeding time was 3 minutes, and the clotting time 5 minutes. In case three on the fifth day of peritoneal lavage the clotting time was 10 minutes and 25 seconds, the clotting time on admission was 6 minutes. The patient had a 2 to 1 ratio of his prothrombin time. This patient had an associated hepatitis which may have been the contributing factor in the elevation of the clotting time and the prothrombin time. Even this large twenty-four hour dosage was unsuccessful in preventing fibrinous adhesions in the two cases where there was evidence of peritonitis.

We wish to emphasize that this method is still highly experimental. There are many problems that as yet have not been solved. In addition the method has definite limitations. One would hesitate to use it following recent abdominal surgery, and the method may be supplanted by external dialysis before sufficient time has elapsed to find the solution for the unsolved problems.

References

1. Seligman, A. M., Frank, H. A., Fine, J.
   Treatment of Experimental Uremia by Peritoneal Irrigation.
   Jr. of Clinic.Invest.25:211: '46.

2. Idem:
   The Successful Treatment of Uremia following Acute Renal Failure by Peritoneal Irrigation.
   Jr. Amer.Med.Assoc., 130:703, '46.

3. Idem:
   The Treatment of Acute Renal Failure by Peritoneal Irrigation.
   Annals of Surg., 124:857, '46.

4. Orlow, W N.
   Einige Versuche uber die Resorption in der Bauchhole.Arch.f.d.ges. Physiol. 59:170, 1895.

5. Abel, J. J., Rowntree, L. G., Turner, B. B.
   On the Removal of Diffusible Substances from the Circulating Blood of Living Animals by Dialysis.
   Jr. of Pharm. & Ex.Therap. 5:275,'14.

6. Putnam, T. J.
   The Living Peritoneum as a Dialyzing Membrane.
   Amer.Jr.of Physiol.63:548, '23.

7. Clark, A. J.
   Absorption from the Peritoneal Cavity.
   Jr. of Pharm. & Ex.Therap.16:415,'21.

8. Darrow, D. C., Yannet, H.
   The Changes in the Distribution of Body Water Accompanying Increase and Decrease in Extracellular Electrolytes.
   Jr. of Clinic.Invest., 14:266, '35.

9. Fleischer, M. S., Loeb, Leo.
   Studies in Edema.
   Jr. of Ex.Med. 12:487, '10.

10. Thalheimer, W.
    Experimental Exchange Transfusions for Reducing Azotemia. Use of Artificial Kidney for This Purpose.
    Soc. for Ex.Biol. and Med. Proc., 37:641, '37-'38.

11. Kollf, W. J. and Berk, H. T. J.
    The Artificial Kidney: A Dialyzer with a Great Area.
    Acta Med. Scand. 117:221, '44.

12. Von Koranyi, A.
Physiologische und Klinische Untersuchungen uber den Osmotischen Druck Thierischer Flussigkeiten.
Ztschr. f. Klin. Med. 33:1, 1897.

13. Moller, E., McIntosh, J. F., Van Slyke, D. D.
Studies in Urea Excretion. 2) Relationship between Urine Volume and the Rate of Urea Excretion by Normal Adults.
Jr. of Clin.Invest., 6:427, '28.

14. Ganter, G.
Uber die Beseitigung Giftiger Stoffe aus dem Blute durch Dialyse.
Munchen Med. Wchnschr. 70:1478, '23.

15. Von Jeny, A.
Kann das Bauchfell bei Uramie die Rolle eines Natuerlichen Dialysator ubernehmen?
Ztschrft. f.Klin.Med. 122:294, '32.

16. Haas, G.
Versuche der Blutauswaschung am Lebendeu mit Hilfe der Dialyse.
Klin. Wchnsche.

17. Hass, G.
4 - 1; 13 - 1925.
Abderhaldens Handbuch der Biol. Arbeit. 7:717, '29.

18. Melzer, S. J., Salant, L. W.
The Influence of Nephrectomy upon Absorption.
Jr. of Med. Res., 9:33, '03.

19. Von Recklinghausen, F.
Zur Fettresorption.
Virchow's Arch., 26:172, 1863.

20. Abbott, W. E., Shea, F.
The Treatment of Temporary Renal Insufficiency by Peritoneal Lavage.
The Amer.Jr. of Med. Sc., 211:312, '46.

21. Wegner, G.
Clinugische Bemerkungen uber die Peritonealhohle, nit basonders Berucksiebtigung der Ovariotomie.
Arch.f.Klin. Clinurgie 20:51, 1877.

III. GOSSIP

With the passing of Dr. Clarence M. Jackson shortly after Dr. W. P. Larson, the number of distinguished members of this faculty who have joined the group over there has increased sharply in the last few years. For many of the newcomers, the names of departed staff members do not mean much, but to those of us who have been here for the past 25 years, we readily recall the memory of Dean E. P. Lyon, Assistant Dean Richard Olding Beard, Anatomists Thomas P. Lee and Charles F. Erdman, Pharmacologist A. D. Hirschfelder, Bacteriologist Arthur T. Henrici, Pathologist Harold E. Robertson, Obstetrician and Gynecologist John Urner, Pediatricians Chester A. Stewart, F. W. Schlutz, Surgeon Harry P. Ritchie, father of Wallace Ritchie and son of one of the early deans of the medical school, whose wife followed him this week, Neuropsychiatrist Arthur Hamilton, Radiologist R. G. Allison, Ophthalmologist William Murray, Otolaryngologist Horace Newhart, Dermatologist John Butler,, Urologists Franklin Wright and Ernest Meland, Surgeons W. A. Dennis and Alex MacLaren, and many others. As Minnesota grows older, the ranks fill in with younger men who give every indication of possessing the same high ideals and enthusiasm that our older men had.....Next week we start the section on the Osseous System at the Center for Continuation Study. The unit will close February 11 when Metabolism and Endocrinology starts. The unit on Neurology was most successful as this field presents a unique opportunity for good correlation....Dermatologist Francis W. Lynch was elected President of the Chicago Dermatological Society at their last meeting. This is an unusual honor and one which is well deserved. Carl W. Laymon has just finished his term of office as Vice President and some years ago Dr. Henry E. Michelson served as president. Doctor Lynch also has been elected to the Board of the National Society of Investigative Dermatology. The announcement that Victor Johnson is to head the Mayo Foundation upon the retirement of Donald C. Balfour this fall will come as welcome news to everyone who knows Doctor Johnson. Under Doctor Balfour's guidance, the Mayo Foundation came through the war years with a splendid record of investigation, and service to the armed forces in training medical officers. With extraordinary demands being made on the Foundation for training opportunity at the present time, future plans undoubtedly will include closer cooperation and coordination of the efforts of the Foundation and the University. The fine relations of the past years will be continued under Doctor Johnson's direction and the training program will reach new heights....Associate Professors of Public Health in Hospital Administration, James A. Hamilton and James W. Stephan who are in charge of the graduate course in Hospital Administration will conduct the course in Hospital Administration at the Center for Continuation Study, February 3 to 8. Problems to be discussed will be Rising Costs (Minneapolis General Hospital announced their costs had risen to between $9 and $10 per day per patient), shortage of nurses, construction needs, and personnel difficulties. The National Committee studying hospital needs has come out for larger institutions in small places if comprehensive service is to be rendered. This would limit the number of hospitals to be built and would exclude the smaller places which attempt to offer much major surgery. Hospital authorities fear that if something is not done to bring expenses down to reasonable limits, governmental subsidies will crowd the voluntary hospitals out of the field....I went to a neighborhood gathering in which the ladies brought our Sunday night supper. Following an excellent meal, the tables were cleared away and we tried our hand at square dancing. Our teacher had a microphone and phonograph and lots of patience and he was rewarded with a fairly good showing. There are over 50 square dance groups meeting in the Twin Cities at the present time and it is a pastime that can be indulged in by young and old.....

IV. IN MEMORIAM

CLARENCE MARTIN JACKSON

Clarence Martin Jackson, Professor Emeritus of Anatomy and former Head of the Department died January 17, 1947 at the University of Minnesota Hospitals after a long illness. He became disabled before he completed his term of service at the University and had been confined to his home for several years before being admitted to the hospitals. His death occurred in the same week in which the Phi Beta Pi fraternity had sponsored the annual lecture in his honor at which Dr. H. C. Hinshaw, Mayo Foundation, spoke on "Chemotherapy in Tuberculosis".

Doctor Jackson was 71 years old at the time of his death and had been Head of the Department of Anatomy from 1913 to 1941. He was born in Whatcheer, Iowa, which by a strange twist of fate was also the birthplace of B. J. Palmer who heads the Chiropractic Movement. Doctor Jackson received his B.S., M.S., M.D., and L.L.D. from the University of Missouri and studied in Leipzig and Berlin during 1903-1904.

After Doctor Jackson came to the University of Minnesota he developed the investigative program in the school. Under his direction and inspiration, hundreds of young men and women learned the value of careful, painstaking investigation. He pointed out that when historians judged our age, our greatest accomplishment probably would be the science of measurement. To be objective was his code and while Minnesota was still young in present day development, he stood out above the others as a teacher and investigator. He never lost the place he occupied in these early days and the Department of Anatomy continues to be one of our outstanding units.

When I was commissioned by the late President Lotus D. Coffman to explore the University for our greatest achievement in the opinions of our associates elsewhere, I found that everyone was of one mind in that Minnesota was best known for its Anatomy Department and for the group at the Agricultural School who worked on the small grains.

Anatomy at Minnesota was also our division which carried the most stars in American Men of Science. When Nutritionist Clarence M. Jackson, Embryologist Richard E. Scammon, Hematologist Hal Downey, and Neuroanatomist A. T. Rasmussen's, names were mentioned, it was difficult for others to realize that all were full professors in the same department.

Dr. Jackson was acting Dean of the Graduate School for several years during the absence of Dean Guy Stanton Ford and he was on leave from the University from 1923-24 to act as Chairman of the Medical Division of the National Research Council. He was President of the American Association of Anatomists from 1922 to 1924 and edited the Morris "Textbook of Anatomy" and a book on nutrition entitled "Effects of Nutrition and Malnutrition upon Growth and Structure".

One of Doctor Jackson's distinguished characteristics was the calm, efficient way in which he went about his work. The regularity with which he came to the University and his punctual appearance at appointments was well known. He was kind and thoughtful in his dealings with everyone, and while outwardly he may have seemed distant, actually he was one of the friendliest of men. He worked for the best interests of the school, and spent many hours in the painful period of our organization trying to reconcile differences in policies, and in the end he quietly withdrew to his department to continue its promotion after his services were no longer needed.

Doctor Jackson was the father of four daughters, who, with Mrs. Jackson, survive him. He will be missed by everyone, for even in his retirement his friends and former associates kept in touch with him and he sent messages of interest and encouragement to them.