Discussion. In the evaluation of the inhibitory action of rutin on hyaluronidase *in vivo,* the method of rutin administration must be considered. It has been demonstrated that 200 mg rutin suspended in saline, when given intraperitoneally to a rat, acted as an irritant and caused the formation of hydroperitoneum. Propylene glycol had a similar action. Rutin dissolved in propylene glycol was the most active and caused so much peritoneal fluid loss that marked hemoconcentration occurred. In the experiments of Levitan, 200 mg rutin dissolved in 1 ml propylene glycol were given intraperitoneally to rats weighing 250-400 g. Three and one-half hours later, testicular hyaluronidase and india ink were injected into the skin and the rats were sacrificed 22 hours after that. There was marked inhibition of the spread of the hyaluronidase-ink mixture, as well as a decrease in the spread of the control ink and saline. Propylene glycol alone, when given intraperitoneally, caused a smaller decrease in the spread of the hyaluronidase. Since both of these agents have been demonstrated to cause extreme hemoconcentration when given intraperitoneally, the validity of conclusions as to the efficacy of these drugs on hyaluronidase inhibition is open to extreme doubt. Duran-Reynals[10] has emphasized that "in the living animal a permeating effect on blood capillaries takes place which may contribute to the final phase of the spreading." In an animal in a condition of marked diminution of blood volume, the available fluid for the spreading reaction is greatly diminished and the conditions for spread are not optimal.

Rutin has been found to inhibit hyaluronidase *in vitro,* and this inhibition has been potentiated by Vitamin C. These studies have demonstrated that rutin, when administered orally, failed to modify the action of hyaluronidase on edema formation and elevation of hematocrit in the albino rat. Rutin in the body is presumed to decrease capillary fragility. However, the investigations performed at this laboratory have failed to produce evidence that hyaluronidase increased capillary fragility, as the edema is not accompanied by red blood cell extravasation.

Summary. 1. Hyaluronidase increased the diffusion of fluid across the capillary membrane and cause elevation of the blood hematocrit.

2. Rutin, in the amounts used in these experiments, failed to inhibit this reaction in the albino rat.

3. Rutin in propylene glycol, given intraperitoneally to the albino rat, caused the formation of hydroperitoneum and marked hemoconcentration. Propylene glycol given by the same route had a similar, although lesser, effect. When administered orally, rutin caused little elevation of the hematocrit.

The assistance of Miss Elaine Lowry is gratefully acknowledged. The author is indebted to Major Monroe E. Freeman, MSC, for the hyaluronidase preparations.

Received March 15, 1949. P.S.E.B.M., 1949, **71.**

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17064. Role of Potassium in Dialysing Fluid in Treatment with the Artificial Kidney.

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Spontaneous elevations of serum potassium levels with electrocardiographic changes similar to those found in dogs with experimental anuria[1] have been demonstrated in man during the terminal stages of uremia,[2-6] indicating that hyperpotassemia may be an important

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[1] Hoff, H. E., Smith, P. K., and Winkler, A. W., *J. Clin. Invest.,* 1941, **20,** 607.

TABLE I.
Concentration of Potassium in Patient's Serum and in the Dialysing Fluid Before and After Dialysis.

Case No.	Serum K: Before dialysis, mg %	Serum K: After dialysis, mg %	Length of treatment, hrs	K of dialysing fluid: Before treatment, mg %	K of dialysing fluid: After treatment, mg %	Amt of K removed by dialysis, g
I	26.3	23.7	6	20.1	20.9	.80
II	28.3	24.6	6	5.0	12.6	7.6
III	20.4	11.9	6*	7.76	7.56†	—

* After 4 hours 35 g of KCl was added to the dialysing fluid because of the changes in the electrocardiogram, indicating hypopotassemia. The potassium content of the dialysing fluid was hereby increased to 24.5 mg %. Treatment was then continued for another 2 hours.

† Potassium content of the dialysing fluid after the first 4 hours of treatment before the 35 g of KCl was added.

factor in the mechanism of death in uremia, especially when associated with anuria or oliguria.

This study was undertaken to estimate the use of an artificial kidney in the elimination of potassium from the body in cases of uremia in which the serum potassium levels are elevated.

Methods. Serum potassium was determined and electrocardiograms were taken in 3 patients with a severe degree of uremia, prior to, during, and after treatment with the artificial kidney. The artificial kidney and the constitution of the dialysing fluid were similar to those used by Kolff,[7] but in cases II and III no KCl was added to the dialysing fluid. The potassium in the dialysing fluid was estimated before and after treatment. Its level of 5 and 7.76 mg% in the dialysing fluid before treatment in cases II and III respectively (Table I) was probably due to potassium contaminants in the other salts and the tap water in the dialysing fluid. The other biochemical and clinical findings in these cases will be reported in detail elsewhere.[8,9]

Results. From the experimental data in Table I, it is apparent that when the potassium content of the dialysing fluid is below 20 mg% (see case II) a significant amount of potassium can be removed by artificial dialysis from the body of uremic patients with hyperpotassemia, without danger of hypopotassemia. When the potassium of the dialysing fluid is maintained at 20.1 mg% (case I) the serum potassium is lowered only slightly and an insignificant amount of potassium is actually removed from the body. In uremic patients with normal serum potassium levels, hypopotassemia can occur when the potassium of the dialysing fluid is markedly lowered (case III, Table I).

In case III, changes in the electrocardiogram indicative of some degree of hypopotassemia[10] were observed after 4 hours of dialysis and potassium was then added to the dialysing fluid and the dialysis continued for another 2 hours. Although the serum of the blood withdrawn at this time was found to contain 11.9 mg% of potassium, the patient did not show clinical symptoms associated with hypopotassemia. During the dialysis the patient voided 1,200 cc of urine. The serum potassium level 5 hours after the dialysis was 14.6 mg%.

Discussion. Kolff[7] originally omitted potassium from the dialysing fluid, but owing

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to the possible dangers of producing hypopotassemia, he and later Bywaters and Joekes,[11] both recommended that physiological amounts of potassium be included in the dialysing fluid.

From Kolff's[7] data it was apparent that hypopotassemia occurred only in a patient who had a normal serum potassium concentration to start with, very similar to that in case III, Table I.

The variable results obtained in these cases are probably due to the differences in the direction of the potassium shift. In case II, the increase of 7.6 g of potassium in the dialysing fluid during the dialysis indicated that potassium was removed from the intracellular as well as from the extracellular fluids. In cases I and III, since there was no significant increase of potassium in the dialysing fluid, the potassium shift probably occurred mainly from the extracellular to the intracellular fluids. The lowering of the serum potassium in these instances might be explained by other factors: (a) the dilution of the patient's blood with the blood added to the artificial kidney prior to its use, and by the further addition of varying amounts of blood and intravenous fluids during the treatment: (b) the fact that the glucose present in very high amount[7,11] in the blood leaving the artificial kidney to be returned to the body will, on entering the systemic circulation, be stored as glycogen, with the resultant shift of potassium from the extracellular to the intracellular spaces[10] was the main reason that Bywaters and Joekes[11] recommended that physiological amounts of potassium to be added to the dialysing fluid; and (c) potassium elimination from the blood stream by urinary excretion. This last factor may have operated in Case III where the patient voided 1,200 cc urine during the period of dialysis.

Summary. From the observations reported it would appear that the artificial kidney can serve as a safe and efficient method for removing excess potassium from the body in uremia patients with hyperpotassemia. However, further study is required to determine the amount of potassium that should be added to the dialysing fluid in each individual case. This will probably vary with the degree of hyperpotassemia present before treatment is begun.

We wish to express our thanks to Doctors G. G. Miller and J. T. MacLean for permission to study their patients. We are grateful to Dr. Martin Hoffmon for many helpful suggestions and criticisms.

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Received March 15, 1949. P.S.E.B.M., 1949, **71**.

17065. Nu 445 in the Treatment of Urinary Infections Due to Gram Negative Bacilli.*

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Introduction. Nu 445† (3,4-dimethyl-5-sulfanilamido-isoxasole) is one of the newer sulfonamides said to be highly effective for urinary tract infections due to *E. coli* and *B. proteus.*[1-6] The reported results on the therapeutic activity of this drug in man are meager

* Aided by a grant from the Patrons of Research, Beth Israel Hospital.

† Supplied through the courtesy of Hoffmann-La Roche, Inc.

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