Reduction of Hyperkalemia by Circulating Blood through a Cation Exchange Resin.* (20694)

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(Introduced by William Dock.)

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Among the procedures devised to correct potassium intoxication in anuria, the use of the artificial kidney has proven the most effective (1). The complex equipment and elaborate preparation required for hemodialysis, however, limit its general availability. Removal of potassium from the gastro-intestinal tract of anuric individuals by the oral administration of a suitable cation exchange resin has been reported to be effective in lowering extracellular potassium concentrations(2). This method is not entirely satisfactory because of delays in effect and the occurrence of adverse gastrointestinal reactions. The following report describes preliminary observations on the correction of hyperkalemia after bilateral nephrectomy in dogs by circulating the blood through a cation exchange resin.

Method. The procedure was performed on 6 mongrel dogs 72 to 96 hours after bilateral nephrectomy. Each dog was anesthetized with pentobarbital sodium (25 mg/kg). A femoral artery and vein were exposed, a No. 16 needle tied into the vein, and heparin (3 to 5 mg/kg) administered. A No. 18-T (B-D) needle was introduced into the artery. A length of plastic tubing, attached to the hub of the arterial needle, served to conduct blood, forced by arterial pressure, several feet above the level of the operating table to the top of the resin system. The latter consisted of a 125 ml separatory funnel attached to a glass column (3.5 x 30.0 cm) through an air tight rubber stopper. The flow of blood into the separatory funnel took place through a plastic adapter fitted into an air tight stopper, which served to seal the mouth of the funnel. Blood then flowed through the stem of the funnel into the glass column. The column contained approximately 180 g of the cation exchange resin, Amberlite IR-120.† The filter unit of a Plexitron R-18 administration set (Baxter Laboratories) was fitted into the bottom of the column to prevent the escape of resin particles while blood flowed from the column through a length of plastic tubing to the No. 16 needle in the fermoral vein. Thus a continuous flow of blood from artery to vein through a closed circuit containing the resin was established. *Amberlite* IR-120 (commercial preparation) is obtainable from the source in the sodium form. For use in the resin column it was washed 10 to 15 times with distilled water, 6 times with pyrogen-free saline and autoclaved. It was again washed several times with sterile saline and poured into the column. Care was taken to prevent the collection of air bubbles within the resin. One liter of saline was then allowed to flow through the column. At the end of this washing the level of saline was adjusted at approximately 1 cm above the resin and 2 cm below the stem of the separatory funnel, making it possible to view the flow of blood into the column. A heating tape was wound spirally around the column, which was then brought to body temperature. During the experiment the temperature of the column was adjusted to compensate for heat loss from the plastic tubing and thus maintain constant body temperature. The column temperature necessary to prevent loss of body heat depended largely on room temperature and in these experiments varied from 37 to 41°C. At ordinary room temperature, failure to heat the column resulted in rapid loss of body temperature and the onset of shivering.

Results. The estimated rate of flow through the resin unit ranged from 30 to 60 ml per minute. At these rates approximately 90%

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† Rohm & Haas Co., Philadelphia, Pa.

TABLE I. Plasma Electrolyte Concentrations Immediately before and after Resin Therapy in 6 Uremic Dogs.

	K conc., mEq/l		Na conc., mEq/l		Ca conc., mEq/l	
Wt, kg	Before	After	Before	After	Before	After
15	9.5	6.0	139.8	154.8		
14	11.3	7.6	146.0	156.0	4.5	3.0
25	10.8	8.0	139.2	145.8	8.0	7.5
22	8.3	5.0	148.2	159.2	7.4	3.5
20	9.1	4.7	153.8	163.8	6.4	3.9
17	9.3	7.0	137.2	141.5	4.9	3.5
8	8.0	6.1	141.0	149.4	6.0	3.8
16	10.1	4.8	146.2	162.8	6.3	4.9

of the potassium and calcium in the plasma was exchanged for an equivalent amount of sodium in one passage. Changes in plasma electrolyte concentrations which occurred as a result of 4 to 6 hours of blood circulation through the resin may be seen in Table I. In every instance there was an appreciable decrease in the plasma potassium concentration and an increase in the plasma sodium level. Decreases in plasma calcium concentration ranged from 0.5 to 3.9 mEq/l, but did not parallel decreases in the potassium levels (1.9 to 5.3 mEq/l) because of the administration of varying quantities (0 to 11.0 mEq/hr) of calcium ion during the procedure. Increases in plasma sodium concentration varied from 4.3 to 16.6 mEq/l, depending on total body potassium removed as well as the amount of calcium administered. In several instances plasma magnesium concentrations were also measured and found to decrease from 2.0 to 3.1 mEq/l.

In 4 cases platelet counts were done and there was an observed drop in the number of platelets in each case. Platelet counts never dropped below 70000 per cu mm and in none of the dogs was there any bleeding tendency after the procedure. Hematocrits and blood urea nitrogen determinations did not change as a result of treatment.

No untoward reactions were noted when the resin was prepared as described above. Gross inspection of the plasma following treatment showed no apparent hemolysis.

Discussion. The results show that elevated plasma potassium concentrations in uremic dogs may be significantly reduced by circulating their blood through a cation exchange resin. The major problem encountered with this method was the exchange of calcium and magnesium for sodium which occurred at the same time that potassium was being withdrawn. It was found that a single intramuscular injection of 25 mg per kg of magnesium sulfate was sufficient to prevent reductions in plasma magnesium levels. The control of calcium levels in the extracellular fluid is a more difficult problem. Calcium solution must be infused at a rate fast enough to prevent tetany. If it is infused too rapidly, however, an excessive amount is removed by the resin and an equally increased amount of sodium is added to the extracellular fluid. In these experiments 0 to 11.0 mEq were infused per hour, but this never was adequate to maintain the initial level. When the initial plasma sodium concentration is unduly low this may provide a safe method for raising it. When increase in the sodium concentration is not desirable, calcium replacement must be kept at a minimum.

In vitro experiments were carried out with resin which was washed with potassium-free mammalian Ringer's solution until it no longer removed calcium. The exchange capacity for potassium of 180 g of treated resin was then estimated by further washing with Ringer's solution to which potassium was added. Repeated determinations of the potassium showed that its removal from the first 2 liters of solution was virtually complete. The percentage of potassium removed from solution then progressively diminished, the total exchange capacity of 180 g of treated resin being only 20 mEq. If blood were circulated through treated resin, therefore, the capacity of the column to remove potassium would be exhausted so rapidly that frequent changing of columns would be necessary and the procedure would become impractical.

Summary. A method for removing potas-

sium from uremic dogs by continuous circulation of blood through a cation exchange resin has been described. This method has been shown to reduce the extracellular potassium concentration by as much as 50% within 4 to 6 hours. However, it is necessary to replace calcium to prevent tetany when this method is used.

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Local Action of Adrenocortical Preparations on Secondary Sexual Organs.* (20695)

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The known local effects of adrenocortical steroids include histological alteration of the skin(1), suppression of hair growth(2,3) and of wound healing(4), and alleviation of inflammation resulting from a number of causes (5-7). Local effects on the reproductive organs have not been demonstrated. Three experiments will be described in this report which are concerned with (a) the local action of adrenocortical extract (ACE) on the vaginal mucosa, (b) the effect of intravaginal application of cortisone on stimulation of the vaginal mucosa elicited by subcutaneously injected estrone, and (c) the effect of direct application of cortisone on stimulation of the chick comb elicited by subcutaneously injected testosterone propionate (TP).

Procedure. For study of the local action of ACE† on the vaginal mucosa, 0.1 ml of hog adrenal extract (equivalent to 100 μg of cortisone as determined by the liver glycogen test) or of the solvent, 25% ethanol, was introduced daily into the vagina of adult Long-Evans rats which had been ovariectomized 8-13 days previously (Table I). Daily vaginal smears were made and the vaginae prepared for histologic study at the end of the experiment. For the study of the antagonism of cortisone to estrone, 16 young adult Long-Evans rats, which had been ovariectomized 90 days previously, were primed with 14 μg of estrone, half being given subcutaneously on each of 2 successive days. Only rats which showed cornification within 48 hours were used in the subsequent study. Vaginal smears were made 10 days after the last priming injection to ensure that the estrogenic effect had subsided. On the next day the rats were divided into 4 groups and treated as follows: (a) estrone subcutaneously, cortisone intravaginally; (b) estrone subcutaneously, saline vehicle intravaginally; (c) peanut oil subcutaneously, cortisone intravaginally; and (d) peanut oil subcutaneously, saline vehicle intravaginally. One-tenth ml of estrone (3 μg) or of peanut oil was injected subcutaneously on the 12th and 13th day after priming, 6 μg of estrone being just sufficient to produce full cornification in the primed rats as determined by previous experiments. Intravaginal injections of cortisone or saline vehicle were made with a short, blunted hypodermic needle to which a shield was attached. The cortisone was prepared by suspending 80 mg in a vehicle con-

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