mammary gland growth in mice when injected with EB. Present study illustrates difference between species reactivity to these preparations, in that no significant rat mammary gland dvelopment was found after injection of larger doses of these fractions. That IE produced almost as much growth as AP indicates that mammogenic factors effective in production of lobule-alveolar growth in rats are extracted to a certain extent by methods employed in extracting ACTH, TSH, lactogen, GH, and gonadotropins(6). However, since relatively poor lobule-alveolar growth was obtained when large amounts of lactogen or GH were injected, it would appear methods employed in purification of these hormones only poorly retain mammogenic factors in the fractions being concentrated.

Since a slight increase in significance was noted when Mammogen "C" was added to 2 mg lactogen plus EB, it would appear possible that this fraction may have a synergistic effect in rats.

Summary. Using desoxyribosenucleic acid (DNA) as an index of mammary gland growth, crude and purified anterior pituitary extracts were tested for mammary gland growth promoting (mammogenic) effectiveness. Acetone dried AP powder and an initial extract of AP were shown to be effective in stimulating production of mammary gland DNA. Initial residue, Mammogen "A" and "C", shown previously to produce mammary gland growth in mice, were found to be ineffective in rats. Fractions rich in lactogen and growth hormone were found to be minimally effective in stimulating mammary gland lobule-alveolar growth.

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Sodium and Potassium Content of Rat Heart Muscle Following Nephrectomy.* (27248)

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Several investigators have reported that characteristic necrotic lesions can be found in the cardiac muscle of dogs and rats following bilateral nephrectomy(1-4). Darrow and Miller(5) produced similar lesions by injections of DOCA. These lesions were prevented by KCl, but NaCl caused uncertain effects. Selye(6) found that DOCA produced hyalinized lesions in the heart, but that 2-alpha-methyl-9-alpha chlorocortisol and certain sodium salts produced extensive myocardial necrosis. These lesions were enhanced by phosphates and sulfates, unaffected by chlorides, and inhibited by magnesium and potassium. This potassium-sodium antagonism suggested that analysis of cardiac muscle might reveal a disproportion between these 2 ions after nephrectomy.

Methods. Thirty-six male rats of a Long-Evans strain, weighing between 300 and 400 grams, were divided into 3 equal groups. The

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TABLE I. Incidence and Severity of Renal Lesions.

Severity of lesion	0	±	+1	+2	+3	+4
Control animals	8	3	1			
Nephrectomized	2		2	3	2	3
Nephrectomized-dialyzed	2	1	6	2	1	

first group of animals served as a control. The second group was nephrectomized and sacrificed 72 hours after operation. The third group was also nephrectomized; however, the animals were dialyzed 3 times during the second 36-hour post-nephrectomy period according to the technic outlined by Kolff and Page(7). The blood specimens were taken and the animals sacrificed 4 to 6 hours after the last dialysis. The animals had no food and limited access to water during the 72 hours of experiment. After sacrifice the heart was transected in such a way that comparable portions of the right and left ventricular wall and the interventricular septum were taken for analysis. Similar tissues were preserved for histological examination. The muscle for analysis was wiped free of blood and visible epicardial fat was removed by dissection. This tissue was then dried to constant weight at 112°C in a drying oven, which generally required 48 hours. The specimen was subsequently dissolved in 0.5 ml of concentrated HNO_3 and appropriately diluted. Blood was obtained from 25 animals by cardiac puncture. Serum and muscle sodium and potassium determinations were performed on a Beckman flame photometer. One of the nephrectomized-dialyzed animals failed to survive the full 72 hours and was therefore discarded without analysis, although the tissue was examined.

Results. Table I indicates the frequency of cardiac lesions, determined histologically, in 3 groups. Microscopic study showed scattered small focal areas of myocardial necrosis and cellular infiltration. These areas were predominately in the septum and the left ventricle, rarely in the right ventricle, and not encountered in the atria, although this area was not exhaustively studied. Histologically the hyaline myofiber necrosis was not different from that occurring in a number of conditions except, perhaps, for the large number of lysed fibers without a reactive cellular response. The myofibers were not vacuolated. The cellular response consisted only of neutrophilic polymorphonuclear leucocytes and a few phagocytic histocytes. The blood vessels were normal. A characteristic lesion is shown in the photomicrograph. Eight of the control hearts were histologically normal and only one had a definite, although minor, lesion. The series of nephrectomized animals showed 2 normal hearts, 2 with minimal and 8 with definite lesions. The nephrectomized and dialyzed animals also showed 2 normal hearts, one had questionable lesions, 6 had minor lesions and only 3 showed major lesions.

Table II summarizes the sodium and potassium data. After 72 hours, serum potassium had doubled in both of the groups of nephrectomized animals, although, as would be expected, serum potassium was higher in the group that had not been dialyzed. Similarly, the nephrectomized-dialyzed animals had an essentially normal serum sodium, whereas the nephrectomized animals showed a significant decrease in serum sodium con-

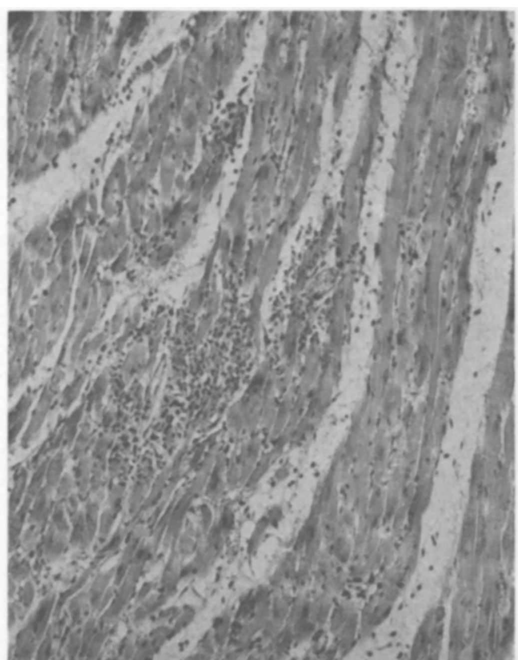

FIG. 1. Photomicrograph showing typical area of myocardial necrosis seen in nephrectomized rats.

TABLE II. Serum and Heart Muscle Electrolytes in Rats after Nephrectomy and Dialysis.

	Control			Nephrectomy			Nephrectomy dialysis		
	No.	Mean	S.D.	No.	Mean	S.D.	No.	Mean	S.D.
Serum K, meq/l	10	5.37	.26	6	*11.4	1.81	9	*9.70	.86
Serum Na, meq/l	10	150	1.87	6	*141	2.34	9	149	5.92
Heart muscle K, mg/100 mg dry wt	12	1.36	.076	12	*1.52	.140	11	*1.55	.068
Heart muscle Na, mg/100 mg dry wt	12	.552	.0465	12	*.495	.0410	11	*.482	.0490
Heart muscle, K/Na ratio	12	2.46	.164	12	*3.10	.440	11	*3.26	.366

* P value less than .01 when compared to control.

centration. The heart muscle sodium and potassium are reported in terms of milligrams per hundred milligrams of dry tissue weight. There is a significant increase in muscle potassium in both groups of nephrectomized animals, and the difference between the 2 nephrectomized groups is insignificant. The heart muscle sodium content showed a significant drop in the nephrectomized animals and again the difference between these 2 groups was insignificant. Weight loss of each group of animals, including the controls, was essentially the same for the 3 days and averaged 10%. However, previous studies(8) indicated that nephrectomy causes a significant increase in the proportion of total body water, and it must be presumed that the true body weight of the nephrectomized animals had decreased a significantly greater amount than did that of the controls.

Discussion. Trauma and surgery are known to produce a dilutional hyponatremia due to 2 opposing mechanisms(9). During the early post-stress period there is a catabolic breakdown of cells which releases potassium and water into the extracellular space. At the same time there is a relative oliguria, probably due to increased antidiuretic hormone release. In this experiment water retention is further enhanced by the nephrectomy. The net result is an expanded extracellular volume with a fixed amount of sodium in solution. Some of the potassium obviously remained in the extracellular space, but it is also probable that most of this cation reentered the intact cells with some of the released cellular water. The decrease in cardiac muscle sodium and increase in potassium in the dry tissue could be further supported if we had demonstrated that the percentage of cardiac muscle water had increased less than that of total body water. However, we have previously demonstrated(8) that voluntary muscle showed a smaller degree of overhydration than did the body as a whole after nephrectomy. With these considerations, the direction of electrolyte change should have been anticipated, although the magnitude would depend upon fluid redistribution in the heart muscle itself. The dialysis performed was relatively inefficient since only 3 exchanges, each containing 10% of the total body weight, were used. The dialysis solution contained no potassium, but was essentially normal in respect to sodium. It is possible that the extracellular sodium equilibrated with the dialysis fluid more readily than did the increased amount of intracellular potassium during the relatively short period of dialysis. These interpretations seem to be in accord with the observations.

It is of interest that the cardiac lesions in the nephrectomized animals were more marked than those in the nephrectomized and dialyzed animals, despite the fact that the electrolyte composition of the 2 groups was essentially the same except for a slightly lower serum sodium and slightly higher serum potassium in the undialyzed animals. However, the intracellular potassium and sodium in the 2 groups were essentially the same, and, if anything, the dialyzed group showed a slightly greater change. It appears that the factor producing the myocardial lesion was unrelated to sodium and potassium content, but might be related to some other material which was effectively dialyzed.

Darrow and Miller(5) reported a slight

decrease in heart muscle potassium and increase in heart muscle sodium after DOCA and after a low potassium diet. The change was more marked when both factors were combined. Grollman and Grollman(10) analyzed the heart muscle of nephrectomized dogs maintained by peritoneal dialysis and noted minimal changes in the same direction. These contradictory electrolyte shifts may have been the result of more effective dialysis than we were able to achieve in our rats; however, it is apparent from our data that potassium depletion and sodium excess were not needed to produce myocardial necroses.

Summary. Thirty-six rats were divided into 3 equal groups; control, nephrectomized and nephrectomized-dialyzed. A specific cardiac lesion was found in 8 nephrectomized animals with 2 other animals showing minimal lesions. The nephrectomized-dialyzed animals demonstrated 3 definite lesions and 6 minimal lesions, whereas control animals showed one minimal lesion. The nephrectomized-dialyzed animals had a normal serum sodium, whereas the nephrectomized animals showed a significant decrease. Both groups of animals showed a moderately elevated serum potassium and had identical increases in cardiac content of potassium and decreases in sodium per unit of dry weight. The dissociation of frequency of cardiac lesions in the 2 groups of nephrectomized animals, despite identical sodium and potassium content, suggests that electrolyte concentration is not the significant factor causing the myocardial lesion.

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Effect of Tetraethylammonium Chloride on Cardiac Muscle Fiber Responses.* (27249)

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It is well known that various compounds produce an increase in amplitude and duration of the action potentials of tissues such as crustacean muscles(1) and dorsal root ganglion cells(2). Tetraethylammonium (TEA) ion has a more powerful action than many of these compounds and is thought to affect the membrane by modifying Ca^{++} permeability(3). It is of interest to determine how tissues other than those mentioned above are affected by TEA and how the action proposed might change functions of cardiac muscle in particular.

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Methods. Trabecular muscles and Purkinje fibers were obtained from the ventricles of dogs anesthetized with nembutal (40 mg/kg). The tissues were perfused with oxygenated Tyrode solution at 37°C(4). Stimulation and recording from single cells was effected by means of a micropipette (5 Meg. Ω) penetrating the cell membrane(5). TEA was administered by perfusing the tissue with a modified Tyrode solution in which 50% of