other hand observed no change in radiosodium exchangeability in their animals, and reached a conclusion quite different from ours—namely that the decrement in bone Na was due to a change in the non-exchangeable fraction. Munro *et al.* used a 24-hour period for radiosodium equilibration whereas we employed a much shorter time.

On the basis of our data it would seem that the division of bone crystal Na into two phases—exchangeable and non-exchangeable—has a physiological justification. In the present experiments, and those of Lobeck and Forbes(5) on diabetic acidosis, it was shown that Na lost from bone came from the exchangeable fraction.

Summary. Young rats, reared on a low Na diet, manifested growth failure, and their bones contained 8-10% (depending on method of calculation) less Na than pair fed controls. Radiosodium exchangeability declined by a similar amount, and it is concluded that the change in Na content involved the exchangeable fraction.

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Effect of Low Potassium Diet on Cyclopropane-Epinephrine Ventricular Tachycardia and Arterial Plasma Potassium in Dogs.* (23972)

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Meek *et al.*(1) observed that epinephrine in doses which cause only occasional ventricular extrasystoles in unanesthetized dogs produced ventricular tachycardia during cyclopropane anesthesia. O'Brien *et al.*(2) found that the onset of arrhythmia was associated with a rapid and marked rise in arterial plasma potassium. Since liver is the primary source of potassium mobilized by epinephrine (3,4), O'Brien *et al.*(5) eliminated the hepatic circulation surgically and found a smaller rise in potassium as well as protection from arrhythmia in 17 of 18 dogs.

This study was undertaken to seek a non-surgical method for reducing the rise in arterial plasma K that normally results from an epinephrine injection and to determine whether or not any K changes that might be found could be related to the occurrence of cyclopropane-epinephrine ventricular tachycardia.

Methods. After administering cyclopropane to dogs for 30 minutes, 0.005 mg/kg epinephrine in 5 ml isotonic sodium chloride was injected intravenously at a constant rate of 1 ml per 10 seconds. Two control determinations of the occurrence and duration of ventricular tachycardia were made one week apart and with the second determination, the changes in arterial plasma potassium concentration were studied. Effects on cardiac rhythm were determined from electrocardiographic records. Blood was rapidly withdrawn from the femoral artery into heparinized syringes before and at intervals of 20, 40, 60, 80, 100, 120 and 150 seconds after the beginning of the epinephrine injection. Plasma was analyzed for potassium with the Beckman flame spectrophotometer(6). After control studies, 20 dogs were placed on a low potassium diet for 2 to 3 weeks following which the effects of epinephrine on arterial plasma potassium and cardiac rhythm were again noted.

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TABLE I. Effect of Low Potassium Diet on Cyclopropane-Epinephrine Ventricular Tachycardia and Arterial Plasma Potassium in Dogs.

	Control				After 2-3 wk on diet			
	Before Epi.	After Epi.*			Before Epi.	After Epi.*		
Dog	Plasma K conc. (mg %)	Max plasma K conc. (mg %)	Duration of VT (sec.)	% rise in K	Plasma K conc. (mg %)	Max plasma K conc. (mg %)	Duration of VT (sec.)	% rise in K
1	16.9	32.3	22	91	10.5	14.0	0	33
2	13.4	23.7	47	77	11.7	16.6	5	42
3	14.6	28.0	50	92	12.3	18.6	7	51
4	15.7	30.6	90	95	10.9	19.7	0	81
7	13.7	25.4	42	85	10.9	13.1	0	20
9	15.4	23.1	63	50	12.0	18.3	0	53
10	16.6	26.9	54	62	15.7	22.9	0	46
11	15.4	26.9	37	75	12.0	19.7	0	64
15	17.1	25.7	54	50	10.9	22.3	0	105
16	18.3	40.0	68	119	12.9	22.0	0	71
20	13.7	27.4	61	100	10.6	14.3	0	35
Avg	15.5	28.2		82	11.9	18.3		54
5	14.3	26.9	73	88	12.3	18.9	73	54
6	15.7	37.1	67	136	10.9	26.3	43	141
8	13.1	32.9	73	151	11.7	27.4	50	134
12	16.3	26.3	57	61	11.7	16.9	25	44
13	14.9	30.9	63	107	11.1	24.9	40	124
14	14.6	29.1	61	99	8.6	16.6	53	93
17	15.1	34.3	90	127	10.6	18.6	50	75
18	16.3	35.1	60	115	16.6	31.1	40	87
19	17.4	33.4	51	92	16.0	41.5	44	159
Avg	15.3	31.8		108	12.2	24.7		102

* Epi. = .005 mg/kg epinephrine. VT = ventricular tachycardia.

Results. On the 2 control determinations for the occurrence and duration of ventricular tachycardia, arrhythmias were observed on both tests in all animals. In all but 2 dogs (No. 10 and 18) the resting level of plasma potassium was lowered by the low potassium diet and in all cases but No. 19, the maximum plasma K level following epinephrine injection was also reduced. Results arranged according to the effect of low potassium diet on cyclopropane-epinephrine ventricular tachycardia are shown in Table I. Eleven had a marked reduction or absence of cyclopropane-epinephrine ventricular tachycardia and the average increase in potassium above resting level in these animals after injection of epinephrine was only 6.4 mg% (or 54%) compared with 12.7 mg% (or 82%) on their control. Nine dogs continued to show irregularities when tested after 2 to 3 weeks on the low potassium diet. The average increase in potassium in these 9 dogs after injection of epinephrine was 12.5 mg% (or 102%) above their resting level compared to 16.5 mg% (or 108%) on their control.

Discussion. Eleven of the dogs on a low K diet were in some way protected from ventricular tachycardia after injection of epinephrine during cyclopropane anesthesia and 9 were not. The question is whether these results are related to the K changes in the respective groups. In the 11 protected dogs it may be noted that not one reached a maximum K level after injection of epinephrine equal to that obtained when it was used as a control and showed ventricular tachycardia. This group of 11 on control studies showed an average K increase of 82% after epinephrine injection while after being on a low potassium diet the same injection of epinephrine resulted in an average increase of only 54%. The data on this group indicate that an increased plasma K level could be of importance in sensitizing the heart to epinephrine during cyclopropane anesthesia.

Of the 9 dogs on the low K diet that continued to show ventricular tachycardia after injection of epinephrine, the plasma K level in 4 failed to rise above that of the protected group. Therefore, according to our thinking,

these should have been protected; although this was not the case there was considerable reduction in duration of ventricular tachycardia in 2 animals (No. 12 and 17). In the remaining 5 the maximum K level was significantly above that of the protected group when ventricular tachycardia occurred. Although the reason for these variations is not clear, the fact that ventricular tachycardia was seen in 5 cases when the maximum K level was near that of their respective controls is at least some evidence for an increase in cardiac irritability being associated with an increase in plasma K.

In recent studies Dresel and Nickerson(7) have noted that some "factor" brought to the heart by the venous blood is probably involved in epinephrine induced arrhythmias during pentobarbital anesthesia. However, they doubted that the rise in arterial plasma potassium caused the arrhythmias. There does, however, seem to be justification for the idea that at least during cyclopropane anesthesia, regardless of what other factors might be involved, the rapid increase in potassium may contribute in part to the production of arrhythmias since protection from these arrhythmias was afforded by elimination of hepatic circulation which also markedly reduced potassium mobilization(5). The present studies tend to confirm this idea with the further indication that the relative increase in potassium may also be of some importance. Whatever the "factor" referred to by Dresel and Nickerson might be, it is possible that it may be associated with the release of potassium from the liver in a large proportion of animals.

Summary. The effect of a low potassium diet of 2 to 3 weeks duration on cyclopropane-epinephrine ventricular tachycardia and arterial plasma potassium has been studied in 20 dogs. Eleven dogs were protected from the arrhythmias while on the diet and 9 were not. In the protected group the K mobilized by epinephrine was considerably reduced. In the non-protected group the per cent rise in K was on the average approximately the same as in control. It is concluded that these studies confirm the view that an actual or relative increase in plasma potassium contributes, at least in part, to the increased cardiac sensitivity to epinephrine during cyclopropane anesthesia.

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Mediation of Progestational Action of Amphenone by the Rabbit Adrenal. (23973)

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Progestational proliferation of rabbit endometrium after parenteral treatment with amphenone* has been described(1). With the exception of certain steroids of gonadal, adrenal or synthetic origin, amphenone is the only compound known to exert progestational activity in the rabbit. This unique action of a non-steroid raises the question whether amphenone exerts a direct effect on the rabbit

* The structural formula for amphenone according to recent revision(2,3) is 3,3-bis(p-aminophenyl)-2-butanone. We have used the dihydrochloride.