The results of *in vitro* calcification studies were the same as of above, the control group calcified at Ca X P of 60 while the strontium treated rats failed to heal.

Ten animals were used for strontium rickets and 10 for the control rickets. Six animals of each group were examined at the end of 21 days, 4 animals of each group at the end of 30 days. The strontium group received 300 Steenbock units of vitamin D while the controls examined did not.

Conclusions. The substitution of strontium for calcium in the rickets-producing diet produces a form of rickets which fails to respond to the very large amounts of vitamin D. The endochondral cartilage of strontium-fed animals both treated and untreated fails to calcify when incubated in artificial serum solution even with a Ca X P product of 60 which produces marked calcification in the endochondral cartilage of control rachitic rats. These observations strongly suggest an injurious effect of strontium upon the "local factor" in the hypertrophic cartilage of the provisional zone of calcification which brings about calcification at this area when conditions in the serum are favorable. The ability of vitamin D to cause an increase of the Ca X P even when healing does not take place, implies that this raising of the product is the function of the antirachitic vitamin in the cure of rickets.

7354 C

Effect of Ascorbic Acid on Thyroid and Suprarenals of Guinea Pigs.*

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In previous publications from this laboratory[1-5] it has been shown that fresh plant and fruit juices contain an antigoitrous agent when

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1 Marine, D., Baumann, E. J., Webster, B., and Cipra, A., PROC. SOC. EXP. BIOL. AND MED., 1930, **27**, 1025.

2 Marine, D., Baumann, E. J., and Webster, B., PROC. SOC. EXP. BIOL. AND MED., 1930, **27**, 1029.

3 Marine, D., *Ann. Int. Med.*, 1930, **4**, 423.

4 Webster, B., Marine, D., and Cipra, A., *J. Exp. Med.*, 1931, **53**, 81.

5 Marine, D., Baumann, E. J., Webster, B., and Cipra, A., *J. Exp. Med.*, 1933, **57**, 121.

tested on immature rabbits maintained on a goitrogenic diet of alfalfa hay and oats. (The goitrogenic effect of this diet is greatly enhanced by cyanide.) It was shown that this antigoitrous effect was in general inversely proportional to the iodine reducing capacity and that treating the fresh juice with copper salts destroyed or lessened this antigoitrous effect. Our data further indicated that the antigoitrous agent was probably identical with ascorbic acid but because of the lack of crystalline ascorbic acid on the one hand and the presence of iodine (also an antigoitrous agent), on the other, in all these extracts we were unable to prove it.

About 2 years ago one of us[6] simplified Szent-Györgyi's and Waugh and King's method of extracting ascorbic acid and by utilizing iris leaves, which are extremely rich in ascorbic acid, has prepared sufficient quantities of this hormone in crystalline form for these experiments, which were carried out as follows: Young guinea pigs weighing between 150 and 250 gm. were placed on a diet of alfalfa hay and rolled oats. (This diet produces scurvy in from 15 to 20 days. Pigs maintained on this diet when injected with the thyrotropic factor develop more marked exophthalmos and thyroid hyperplasia and more quickly than when given greens daily in addition.) They were injected with ½ to 2 cc. of ox anterior pituitary extract prepared after Loeb and Bassett's method and given 25 to 100 mg. of crystalline ascorbic acid by mouth daily. The pigs were sacrificed at various intervals and the principal data of 22 are given in Table I.

The thyroids of those given ascorbic acid and the thyrotropic factor average about 30% smaller than their litter mates given the thyrotropic factor alone. It also prevented or greatly lessened the hypertrophy of the suprarenal cortex which normally occurs in scurvy or following the administration of this preparation of the thyrotropic factor. Histologically there was less and in some cases no hyperplasia of the thyroid in those treated with ascorbic acid, although the presence or absence of hyperplasia depends on the proportion of ascorbic acid and the thyrotropic factor given as well as on the duration of the experiment. The guinea pig thyroid reacts quickly to the thyrotropic factor, while ascorbic acid acts more slowly so that in 4 days there may be a marked hypertrophy, while by the 8th day it may have disappeared completely if the proper doses of ascorbic acid and the thyrotropic factor have been given. Our data indicate that ascorbic acid directly or indirectly counteracts

[6] Baumann, E. J., and Metzger, N., PROC. SOC. EXP. BIOL. AND MED., 1933, **30**, 1268.

TABLE I.

G. P. No. Series Sex	Wt. at beginning	Wt. at end	Duration of Exper.	Thyrotropic Factor Daily dose	Thyrotropic Factor No. days	Ascorbic Acid Daily dose	Ascorbic Acid No. days	Wt. of Thyroid	Wt. of Adrenals	Wt. of Pituitary	Scurvy	Thyroid Histology
	gm.	gm.	days	cc.		mg.		mg.	mg.	mg.		
Series 239												
23 F	215	253	20	2	12	25	8	65	155	9		Colloid
24 F	210	275	20	2	12			127	187	9	?	Sl. hypertrophy
25 M	187	229	20	2	12	25	8	90	130			Colloid
26 F	220	234	20	2	12	25	8	49	159	7		"
27 M	234	264	20	2	12			71	114	9	+	"
28 F	217	220	20	2	12			104	165	9	+	Sl. hypertrophy
Series 274												
121 F	169	169	6	1	6	100	6	55	99	5		Early "
122 F	211	212	7	1	7	100	7	70	141	5		Mod. mkd. "
123 M	197	232	13	1	7	100	12	40	105	8		Colloid
				0.5	5							
124 F	211	242	13	1	7			64	167	8		Mod. hypertrophy
				0.5	5							
125 F	209	213	7	1	7			59	149	5		Mkd. "
126 M	166	165	6	1	6			95	109	6		Mod. mkd. "
Series 275												
127 F	199	216	8	0.5	8	100	8	32	118	8		Colloid
128 M	244	303	14	0.5	13	100	13	42	133	8		"
129 M	166	181	20	0.5	19	100	19	26	163	8		"
130 M	173	205	20	0.5	19			34	148	7	+	"
131 M	237	263	14	0.5	13			59	148	8	?	Mod. mkd. "
132 F	188	196	8	0.5	8			46	125	5		Mod. mkd. "
Series 278												
137 M	193	216	4	0.5	4			47	81	5		Early mod. "
138 F	194	201	8	0.5	8			44	125	8		Mod. "
141 F	168	200	8	0.5	8	50	8	39	108	7		Early mod. "
142 M	205	229	4	0.5	4	50	4	47	75	7		" " "

the thyrotropic factor. This protective action of ascorbic acid against thyroid hypertrophy can be correlated with earlier work[7, 8] on (a) the production of a transient Graves' disease-like syndrome in rabbits and cats by sufficient but sublethal injury of the suprarenals; (b) with the sharp increase in the heat production of infants beginning on the 8th day after birth and associated with involution of the suprarenal cortex[9]; (c) with the beneficial effects of suprarenal cortex emulsion in the treatment of Graves' disease[10]; (d) with the metabolism lowering effect of fresh glycerol emulsions of suprarenal cortex emulsions in rabbits; and (e) with the association of Graves' disease with prolonged deep X-ray therapy to the suprarenal region in man.[11]

7355 P

Susceptibility of Heart to Electric Shock in Different Phases of the Cardiac Cycle.

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In connection with an extended series of experiments on the effects of electric shock, the fact has been brought to light that shocks whose duration is a small fraction of the cardiac cycle have a marked difference in their tendency to cause ventricular fibrillation, depending upon the phase of the cycle in which they occur. The shocks were tripped off by amplified cardiac currents after a controlled delay from a reference point in the electrocardiac cycle. The electrocardiogram together with the shock current and voltage were photographically recorded in time relation on a continuously moving film, which enabled checks to be made on the placement of the shocks in the cardiac cycle. Nearly 800 shocks with 60-cycle current of .03 and .1 second durations were administered to 92 anesthetized sheep in different parts of the cardiac cycle, with currents ranging from 1 to 17 amperes, through the pathway between

[7] Marine, D., and Baumann, E. J., *Am. J. Physiol.*, 1921, **57**, 135.

[8] Scott, W. J. M., *J. Exp. Med.*, 1922, **36**, 199.

[9] Marine, D., Lowe, B., and Cipra, A., *J. Metabol. Res.*, 1922, **2**, 329.

[10] Shapiro, S., and Marine, D., *Endocrinology*, 1921, **5**, 699.

[11] Marine, D., *Am. J. Med. Sci.*, 1930, **180**, 767.