In the experiments of Table II the diastolic volume was maintained nearly constant by adjustment of the venous inflow. In both experiments the injection of calcium was followed by a definite rise in total energy liberation measured as oxygen consumption, as well as a marked increase in efficiency. It appears from the observations of Starling and Visscher[2] that the increase in rate cannot account for more than a 10% increase in oxygen consumption in these experiments. There is therefore a definite increase in oxygen usage which is independent of the rate.

Summary. At a given initial fiber length the mechanical energy of contraction of the heart is increased under the influence of calcium. This is due not only to an increase in the fraction of the total energy liberated which is converted into useful work but also to an increased total energy liberation. The increase in efficiency occurring with administration of small doses of calcium salts indicates that the effect is a beneficial one, and might be of importance in contributing to the therapeutic effect of calcium in cardiac disease.

7642 P

Bromide Control of Experimental Convulsions.

BENJAMIN BOSHES. (Introduced by L. J. Pollock.)

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Since Locock[1] reported the successful use of bromides in several cases of epilepsy, this drug has been used extensively in the treatment of this disease. When these patients have been so treated, it has been noted that the concentration of the bromide ion in the blood is not always related to the amount of the drug administered; or is this concentration parallel to the clinical course, either in regard to the control of the convulsions or to the development of bromide intoxication.

Since the amount of bromide in the blood necessary to prevent epileptic convulsions in man varies, a determination of the concentration necessary to prevent experimentally produced convulsions in rabbits was made. The convulsions were induced by the intravenous injection of 2% thujone in 6% gum acacia, using 0.15 cc. per pound body weight. Seizures always followed such a dose, providing the

[1] Locock, Sir C., *London Lancet*, 1857, **1**, 528.

TABLE I.
Relation of Blood Bromide Levels to Thujone Convulsions.

No.	Date	Total Halide as mg. of NaCl per 100 cc. of blood	Bromide as mg. of NaBr per 100 cc. of blood	Convulsion
64	12-13	466	0	Moderate
	12-22	473	60	Severe
	12-27	455	150	None
	12-30	460	140	"
63	12-30	476	90	Moderate
29	10-12	480	140	Severe
12	12-9	468	225	" but brief
31	10-16	475	240	None
3	7-19	446	300*	"

*38% chloride replacement. This was calculated by multiplying the bromide concentation by 0.568 (the factor necessary to convert bromide values to equivalent chloride values) and dividing the figure so obtained by the total halide concentration considered as NaCl.

injections were not repeated within one week. Rabbits were fed 5 grains of sodium bromide daily by stomach tube. When a blood bromide level of 240 mg. per 100 cc. of blood as measured by the Wuth[2] method was reached, injection of the thujone no longer produced a convulsion. In some animals a lower concentration sufficed to prevent induced seizures. (Table I.)

The total blood halide remained unchanged even when there was a 38% replacement (Table I) of the chlorides by the bromide; one may readily conclude that bromide replaces chloride, ion for ion.

To determine the site of action of the bromide, the amount in the brain was compared to that in the blood. The Berglund[3] method of analysis was used. The chloride content of the brain varied in rabbits, but the average was 166 mg. per 100 gm. of brain. The brain bromide content in animals fed 5 grains of sodium bromide over different periods of time varied from 7.5 to 95 mg. per 100 gm. of brain while the respective blood bromide ranged from 40 to 300

TABLE II.
Comparative Bromide-Chloride Levels in Brain and Blood.

No.	Blood Halide as mg. NaCl per 100 cc. blood	Blood Bromide as mg. NaBr per 100 cc. blood	Brain Halide as mg. NaCl per 100 gm. brain	Brain Bromide as mg. NaBr per 100 gm. brain	Convulsion	Blood Chloride replacement %	Brain Chloride replacement %	Ratio Brain Bromide to Blood Bromide
8	390	136	167	50	Moderate	19.8	17	1:2.7
12	431	206	112	14	Strong	27.1	7.1	1:14.7
13	393	46.4	156	7.5	Mild	6.7	2.7	1:6.2
19	427	193	183	53	"	25.7	16.4	1:3.6

[2] Wuth, O., *J. Am. Med. Assn.*, 1927, **88**, 2013.

[3] Berglund, Emil, *Z. f. Analytische Chem.*, 1885, **24**, 184.

mg. per 100 cc. of blood. (Table II.) There was no definite relationship between the bromide concentration in the brain and that of the blood. The ratio of brain bromide to brain chloride bore no constant relation to the ratio of blood bromide to blood chloride. The bromide content of the brain seemed closely related to the amount of blood left in the brain after the heparinized animal had been bled from the carotid arteries. The presence of so little bromide in a well exsanguinated brain, when there was a high concentration of bromide in the blood, suggested that the action of bromide was effected in some manner other than by combining with nervous tissue as postulated by Bernoulli.[4]

The question of whether the bromide acted by lowering the chloride level of the body was next studied. Attempts to lower the blood chloride by feeding large doses of potassium citrate as suggested by von Bunge[5] were unsuccessful. Perfusion of the peritoneal cavity with warm distilled water produced a marked hypochloremia (Curtis[6]) in rabbits. Such animals were even more susceptible to the convulsant, usually dying in *status epilepticus*. Finally, a study was made to determine whether the chloride ion increased the susceptibility to convulsions. Large doses of sodium chloride were fed to bromized animals, and normal rabbits were given combined sodium bromide and sodium chloride feedings. In both instances, the studies indicated that the chloride acted by diminishing the bromide

TABLE III.
Effect of Sodium Chloride on Thujone Convulsions in Bromide-Fed Rabbits.

No.	Date	Fed	Total Halide as mg. NaCl per 100 cc. blood	Blood Bromide as mg. NaBr per 100 cc. blood	Convulsions
61	4-1	(Start of experiment)	460	0	No attempt made to induce convulsion
	4-1 to 4-11	NaBr, NaCl, aa gr. V			
	4-11		430	90	Severe
	4-11 to 4-20	No feeding of NaCl or NaBr			
	4-20 to 4-28	NaBr gr. V daily			
	4-28		442	105	Moderate
	4-28 to 5-5	NaBr gr. V daily			
	5-5		475	165	No attempt made to induce convulsion
	5-6	NaCl gr. XXX			
	5-7	No feeding	428	115	None

[4] Bernoulli, E., *Arch. f. exp. Path. u. Pharm.*, 1913, **73**, 355.

[5] von Bunge, G., *Lehrbuch der Physiologie des Menschen*, 1901, **2**, 103.

[6] Curtis, G. M., *Proc. Inst. Med. Chicago*, 1930, **8**, 110.

content of the blood to a concentration where convulsions could be produced experimentally, if no additional chloride was administered. (Table III.)

7643 C

Effect of Heavy Administration of Viosterol on Metabolism of the Rat.

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In a previous communication[1] it was shown that when large doses of irradiated ergosterol were administered to normal dogs there was a very great increase in metabolic rate. Since it appears that the rat is relatively insensitive to toxic effects of this substance, it seemed advisable to investigate its effect on the metabolism of the rat. Three rats of each sex were selected and trained for several months in a metabolism chamber. They were kept in separate cages and fed on the Wistar normal diet. The cages were kept in the same room where the apparatus was operated during a period of nearly 10 months, and the rats were handled only by the operator. It is believed, therefore, that extraneous factors were eliminated as completely as possible.

The apparatus used consisted of a closed circuit with a motor-driven hydraulic pump that delivered approximately 90 cc. of air each half minute. The respiration chamber consisted of a glass jar. Volume change was recorded on a kymograph by means of a writing needle attached to the bell of a small spirometer cut into the circuit. There was no new principle introduced into the arrangement.

The surface area was calculated by the formula derived by Lee,[2] $S = KW^{0.60}$ in which $K = 12.54$, $W =$ weight in gm., and $S =$ surface area in cm^2. It was mentioned in the earlier publication that one of the difficulties in calculating the surface area in the dog was the varying weight. Since the rat weight also varied it was thought necessary at first to use Lee's modification of Cowgill's formula,[3] $S = KW^{0.61} \times \frac{0.31}{Nobs}$ but comparisons of surface area calcu-

[1] Reed, C. I., Thacker, E. A., Dillman, L. M., and Welch, J. W., *J. Nutrition*, 1933, **6**, 355.

[2] Lee, M. O., *Am. J. Physiol.*, 1929, **89**, 24.

[3] Cowgill, G. H., and Drabkin, D. I., *Am. J. Physiol.*, 1927, **81**, 36.