

found to cause a marked reduction in the blood pressure of dogs made hypertensive by proprioceptor depressor neurotomy. 2. No significant changes were observed in the blood pressure of normal dogs given an amount of

this chemical sufficient to cause a marked effect in hypertensive dogs.

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Ineffectiveness of Sodium Succinate in Control of Duration of Barbiturate Anesthesia

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Recently Soskin and Taubenhaus¹ have reported the effectiveness of sodium succinate in shortening the duration of barbiturate anesthesia in rats. Succinate was also reported to be of some benefit as an antidote for lethal doses of pentobarbital. The impetus for their experimental work was the observation of Quastel and Wheatley² that barbiturates depress the respiration of brain tissue *in vitro* when glucose, pyruvate, or lactate are the substrates, but that succinate oxidation is not inhibited. We had found³ that in tissue preparations which rapidly oxidized succinate *in vitro* the oxidation was not coupled with phosphorylation. Coupling of oxidation with phosphorylation is, as far as is known, the only mechanism by which the organism may derive energy from the oxidation of metabolites. While we have no reason to doubt that succinate oxidation *in vivo* is coupled with phosphorylation the results with tissue preparations suggested that the alterations in tissue during the preparation for manometric experiments are such that the rate of oxidation of substrates *in vitro* does not necessarily indicate the relative importance of that substrate as an energy source *in vivo*.

The observations of Soskin and Taubenhaus seemed of sufficient importance to merit

further investigation. Upon repetition of their work we were unable to confirm their conclusion that the administration of sodium succinate shortens the duration of both pentobarbital and amytal anesthesia in rats.

Experimental and Results. Male rats of the Sprague-Dawley strain, weighing from 200 to 250 g and maintained on stock rations, were the experimental subjects. The sodium salts of the barbiturates in aqueous solution were injected intraperitoneally. Where succinate was administered it was injected as an aqueous solution containing 200 mg of sodium succinate per cc. Equivalent amounts of malate were given some animals. Both succinate and malate were injected 1 to 5 minutes after the barbiturate. Duration of anesthesia was measured from the time of disappearance of the eyelid reflex until the animal arose and moved about the cage. Other experimental conditions and the results obtained are shown in Table I.

In Experiment 1 neither succinate nor malate, administered intramuscularly following the intraperitoneal injection of pentobarbital, significantly affected the duration of anesthesia. Similar results were obtained in Experiment 2 with pentobarbital and in Experiment 3 with amytal.* The experimental conditions in these experiments were very similar to those under which Soskin and Taubenhaus obtained the most dramatic

¹ Soskin, S., and Taubenhaus, M., *J. Pharm.*, 1943, **78**, 49.

² Quastel, J. H., and Wheatley, A. H. M., *Proc. Roy. Soc. London*, 1932, **B112**, 60.

³ Boyer, P. D., Lardy, H. A., and Phillips, P. H., unpublished data.

* We are indebted to Dr. O. S. Orth for supplying the amytal used in these experiments.

TABLE I.
Effect of Succinate and Malate on the Duration of Barbiturate Anesthesia in Rats.

Exp. No.	Barbiturate	Nutritive state	No. of rats	Further treatment			Duration of anesthesia* min.
1	Na Pentobarbital 3.2 mg/100 g wt	Fasted 24 hrs	16	Control			28 ± 11
			16	Succinate,	50 mg/100 g	I.M.†	33 ± 10
			15	Malate,	55	" " "	26 ± 7.4
2	Na Pentobarbital 3.2 mg/100 g	" 16 "	14	Control			18 ± 6.9
			14	Succinate,	50	" " "	18 ± 3.1
3	Na Iso-amyl Ethyl Barbiturate 5 mg/100 g	" 16 "	13	Control			21 ± 9.9
			13	Succinate	50	" " "	26 ± 10
4	Na Pentobarbital 3.2 mg/100 g	Well fed	3	Control			32 ± 13
			4	Succinate,	100	" " I.P.‡	69 ± 6.2
			4	Malate,	111	" " "	90 ± 4.0
5	Na Pentobarbital 6.5 mg/100 g	" "	2	Control			120
			3	Succinate,	100	" " "	165
			2	Malate,	111	" " "	187

* Mean and standard deviation of the mean.

† I.M.—Intramuscularly.

‡ I.P.—Intraperitoneally.

response with succinate. The animals had been fasted and comparatively large doses of succinate were administered.

In Experiments 4 and 5 succinate and malate were administered intraperitoneally. Although it is recognized that metabolites injected intraperitoneally are apt to be absorbed into the portal circulation and deposited in the liver before they can reach the brain, experimental conditions were arranged to have this deposition at a minimum. The animals were well fed and, in addition, large doses of the metabolites were injected. In no case did succinate shorten the duration of anesthesia. The apparent prolongation of

the anesthesia by succinate and malate in experiments 4 and 5 is probably not significant because of the limited number of animals.

Summary. The intramuscular administration of sodium succinate to fasted rats under pentobarbital or amytal anesthesia did not significantly shorten the duration of the anesthesia. Similarly the intraperitoneal administration of succinate or malate to a limited number of fed rats under pentobarbital anesthesia did not significantly influence the duration of anesthesia. We were unable to confirm Soskin and Taubenhaus' observations that succinate is an effective agent in the control of barbiturate anesthesia.

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Influence of Sulfadiazine on Plasma Lipids in Pneumonia.*

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In preceding communications,^{1,2} the author has presented evidence to indicate that in acute infections such as pneumonia in children, there is a definite depression of the plasma levels for total and ester cholesterol, total

fatty acids and phospholipids together with a fall in the iodine numbers of the total fatty acids and the phospholipid fatty acids. Adequate treatment of the pneumonia patients with specific immune serum prevents the fall