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Effects of Ephedrine Upon Blood Lactic Acid and Respiratory Metabolism in Man

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The work of Cori and others has definitely established the ability of epinephrine materially to increase the blood lactic acid and blood sugar. Cori and Buchwald[1] produced positive increments in blood lactic acid and sugar in man by continuous intravenous injections of epinephrine. Similar results were obtained in rabbits by subcutaneous injections.

Ephedrine has produced results similar to those given by epinephrine. Himwich, *et al.*,[2] and Nitzescu and Munteanu[3] report work upon amytalized dogs in whom they obtained increases in blood lactic acid after ephedrine injections of 40-50 mg. per kilo. Wilson[4] found a hyperglycemia in dogs and rabbits after the subcutaneous injection of ephedrine in doses of 10-30 mg. per kilo.

The experiments herein reported were performed upon normal students. Ephedrine sulfate was ingested in aqueous solution in doses of 60-90 mg. Venous blood samples were drawn at intervals without stasis and the blood lactic acid determined by the method of Friedemann and Kendall.[5] Blood sugar was determined by Benedict's method. (Table I.)

TABLE I.

	Subject E.D.		Subject G.D.		Subject G.S.C.		Subject G.D. (Epinephrine)		
Time	mg.% Lactic Acid	mg.% Blood Sugar	mg.% Lactic Acid	mg.% Blood Sugar	mg.% Lactic Acid	mg.% Blood Sugar	mg.% Lactic Acid	mg.% Blood Sugar	Time for Epinephrine
Normal	20.8	98.8	29.2	117.5	23.3	77.7	13.8	102.2	Normal
45 min.	27.3	106.0	29.7	125.0	21.7	84.1	23.0	102.2	15 min.
75 ”	35.2	106.5	38.0	112.0	18.8	100.7	30.7	131.5	30 ”
105 ”	18.8	106.5	83.6	123.0	29.6	112.5	34.0	148.1	45 ”
145 ”			21.4	114.0	18.8	110.2	30.0	129.0	75 ”

1 Cori and Buchwald, *Am. J. Physiol.*, 1930, **45**, 71.

2 Himwich, *et al.*, *J. Biol. Chem.*, 1930, **85**, 571; PROC. SOC. EXP. BIOL. AND MED., 1930, **28**, 331; *Ibid.*, 1930, **28**, 333.

3 Nitzescu and Munteanu, *Comp. Rend. des Seances de la Soc. de Biol.*, 1931, **106**, 1173.

4 Wilson, J. Allen, *J. Pharm. Exp. Therap.*, 1926, **30**, 209.

5 Friedemann and Kendall, *J. Biol. Chem.*, 1929, **82**, 23.

In view of the calorigenic action of epinephrine and the similar effects of epinephrine and ephedrine upon blood lactic acid, it was decided to study the effect of ephedrine upon the respiratory metabolism. The Benedict-Universal metabolism machine was used in following the changes in oxygen consumption and CO_2 output after ephedrine ingestion. The metabolic rate was determined in the post-absorptive or "basal" state after at least 30 minutes rest in bed. Immediately after the basal run a blood sample was taken for lactic acid analysis. Ephedrine, in doses of 1 mg. per kilo was then ingested and after the effects had become pronounced (as indicated by heart rate) the metabolism was again determined. Positive increments of blood lactic acid and oxygen consumption were obtained. (See Table II.)

TABLE II.

	Normal				After 1 mg. Ephedrine per kilo			
Subject	liters O_2/HR	liters CO_2/HR	R.Q.	mg. Lac. Acid	liters O_2/HR	liters CO_2/HR	R.Q.	mg. Lac. Acid
L. C. M.	13.35	11.03	.825	13	14.20	13.35	.94	29
K. G. M.	13.39	11.40	.82	24	15.80	13.90	.88	40.5
K. G. M	11.50	11.40	.99	12.8	9.76	12.10	1.24	28.5
G. S. C.	11.70	11.65	.995	29.2	8.87	13.70	1.55	49.5
G. D.	14.79	12.78	.81		16.37	12.0	.95	
E. D.	13.13	9.83	.749		13.80	14.46	1.06	
L. C. M.	15.70	12.82	.815		16.20	14.6	.90	

Tainter[6] classifies ephedrine pharmacologically with tyramine and phenylaminoethanol, both musculotropic in action, and not with epinephrine, a sympathomimetic drug. He bases his classification upon the antagonism of cocaine towards ephedrine as compared to sensitization of epinephrine action under similar conditions. De Eds and Butt[7] could not obtain the well-known "reversal" phenomenon in the uterine muscle preparation after ergotoxine and ergotamine, when using ephedrine.

On the other hand, Chen and Schmidt,[8] Curtis,[9] and others maintain ephedrine to be sympathomimetic, perhaps not exclusively, but predominantly. Curtis showed that De Eds had used too large a dosage of ephedrine to produce the reversal action on the isolated uterus. He obtained reversal actions with both ephedrine and epinephrine in equi-molecular quantities. Swanson[10] studied the effects

[6] Tainter, M. L., *J. Pharm. Exp. Therap.*, 1929, **36**, 569.

[7] De Eds and Butt, PROC. SOC. EXP. BIOL. AND MED., 1927, **24**, 550.

[8] Chen and Schmidt, Ephedrine and Related Compounds. Monograph.

[9] Curtis, *J. Phar. Exp. Therap.*, 1928, **34**.

[10] Swanson, E. E., *J. Pharm. Exp. Therap.*, 1929, **36**, 541.

of ephedrine and epinephrine on the bronchioles in cocainized and normal animals. He concluded that ephedrine is both bronchoneurotropic and bronchomusculotropic.

Epinephrine, admittedly a sympathomimetic drug, produces an increase in blood lactic acid, blood sugar, and oxygen consumption. Ephedrine, whose mode of action is debated, produces effects comparable to those of epinephrine in (1) increasing the blood lactic acid and blood sugar, and (2) increasing the oxygen consumption and metabolic rate, hence is it not reasonable to assume that its action in these instances at least, is sympathomimetic?*

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Production of Renal Insufficiency by Surgical Procedure.

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This communication describes a method which has been developed to produce renal insufficiency by surgical procedure. Rabbits were used. The method is carried out by putting a loop of thread about one renal artery, when the animal is about 10 days old. This is done by placing a wire of 0.4 mm. diameter alongside the artery and tying a silk thread down upon the 2 together, and then withdrawing the wire. This leaves a loop about the artery of a diameter little larger than the artery. The artery soon grows up to this size and then any increase in the blood flow and size of that kidney is prevented. The other kidney overdevelops and so takes care of the increased renal demands of the animal. When the animal is 3 to 4 months of age, this large kidney is removed, leaving the animal with a small kidney, which cannot hypertrophy because of the tie about the artery. Too much time must not elapse before the second operation, lest atrophy of the small kidney supervene.

In this way any degree of kidney insufficiency can be produced. If the reduction in renal tissue be large (four-fifths) we find a rise in blood non protein nitrogen to 50-80 mg. per 100 cc. of blood, and a large volume of dilute urine is excreted. Greater reduction in kidney tissue results in higher blood non protein nitrogen (120-150

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