

Table I. Creatine produced perosis, which was prevented when choline was also added. Almquist and Mecchi⁵ showed that a dietary deficiency of creatine or its precursors results in muscular dystrophy in chicks. It may be speculated that the tension exerted on the bones by the muscles plays a part in causing the distortion of the bones which characterizes perosis. If the tension is reduced by muscular dystrophy as in creatine deficiency, the tendency towards perosis may be lessened.

Summary. In contrast to turkeys, chicks on a simplified diet, deficient in choline, did not develop perosis unless gelatin or creatine was added. Choline prevented the perosis at a level of 0.1%, but lower levels were only partially effective. A possible explanation for the perosis-producing effect of gelatin or creatine is advanced.

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Vago-Insulin and Sympathetico-Adrenal Systems, Their Mutual Relationship. II. Reaction to Cocaine and Bulbocapnine.*

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For over 60 years (Von Anrep¹) the action of cocaine on the sympathetic nervous system has been known. Several studies (Bömer,² Oelkers and Schutze³) have shown that in normal animals subcutaneous injection of cocaine produces hyperglycemia. The reactions of bulbocapnine, on the other hand, suggest marked parasympathetic stimulation (Molitor,⁴ Kolb and Langworthy⁵) yet here also hyperglycemia is produced in normal animals (Sarno⁶).

In the first paper of this series (Feldman, Cortell and Gellhorn⁷) we have shown that under the influence of anoxia and metrazol both sympathetic and parasympathetic centers are stimulated. It seemed

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¹ Von Anrep, B., *Pflug. Arch. ges. Physiol.*, 1880, **21**, 38.

² Bömer, M., *Arch. exp. Path. Pharmacol.*, 1930, **149**, 247.

³ Oelkers, H. A., and Schutze, G., *Klin. Wschr.*, 1938, **17**, 871.

⁴ Molitor, H., *J. Pharm.*, 1938, **62**, 16.

⁵ Kolb, L. C., and Langworthy, O. R., *J. Pharm.*, 1938, **63**, 108.

⁶ Sarno, D., *Bull. Soc. Ital. Biol. Sper.*, 1931, **6**, 714.

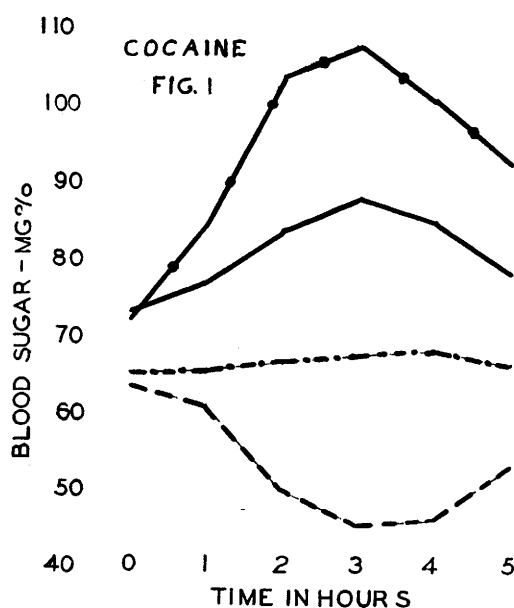
⁷ Feldman, J., Cortell, R., and Gellhorn, E., *Am. J. Physiol.*, 1940, **131**, 281.

to us of interest to determine whether cocaine and bulbocapnine act similarly.

Methods. Rats weighing 200-250 g were used. Four groups of rats were studied. The first group comprised the control, in the second the medulla of the adrenals had been removed, in the third the vagi had been cut below the diaphragm, in the fourth these operations had been combined. Adrenalectomized and adrenalectomized-vagotomized rats received a 2% solution of NaCl instead of drinking water. All animals were fasted 18 hours. Blood sugar was determined by the Somogyi modification of the Shaffer-Hartman method. Fifty mg/kg of cocaine hydrochloride was injected subcutaneously in 6 rats in each of the above series. Blood sugar was determined prior to the injection and at hourly intervals over a period of 5 hours. The animals exhibited no marked symptoms with this dose, only a mild degree of excitement being observed in about one-fourth of the animals.

With bulbocapnine 2 experimental procedures were used. In the first, the effect of subcutaneous injection of 50 mg/kg of bulbocapnine phosphate (Merck) was studied in 7 normal, 6 adrenalectomized and 6 adrenalectomized-vagotomized rats over a period of 2 hours, blood sugar being determined at half hour intervals. In the second, the effect of the same dose of bulbocapnine phosphate was studied on 6 normal and 6 vagotomized rats over a period of 4 hours, blood sugar being determined at hourly intervals. In all cases, the animals showed akinesia and catalepsy, maintaining abnormal positions and hanging from a bar for periods of 1 to 3 minutes. Akinesia developed within 10 minutes after injection and lasted for approximately 1 hour.

Results. With cocaine hydrochloride, normal rats show a rise in blood sugar from a mean of 74.1 mg % to a maximum of 89.0 mg % at the end of 3 hours. By the end of 5 hours this has returned to a mean value of 79.2 mg %. With adrenalectomized rats, on the other hand, one observes a fall in blood sugar from a mean of 64.5 mg % to a minimum of 46.7 mg % at the end of 3 hours and a return to 54.1 mg % at the end of 5 hours. These results indicate that cocaine acts similarly to anoxia and to metrazol in stimulating the vago-insulin as well as the sympathetico-adrenal systems. If this hypothesis is correct, sectioning of the vagi in the adrenalectomized rats should, by elimination of the secretion of insulin *via* the vagi, eliminate the hypoglycemia. This is actually the case, cocaine having no significant effect on the blood sugar of adrenalectomized-vagotomized rats. Moreover, when the vagi are sectioned subdia-

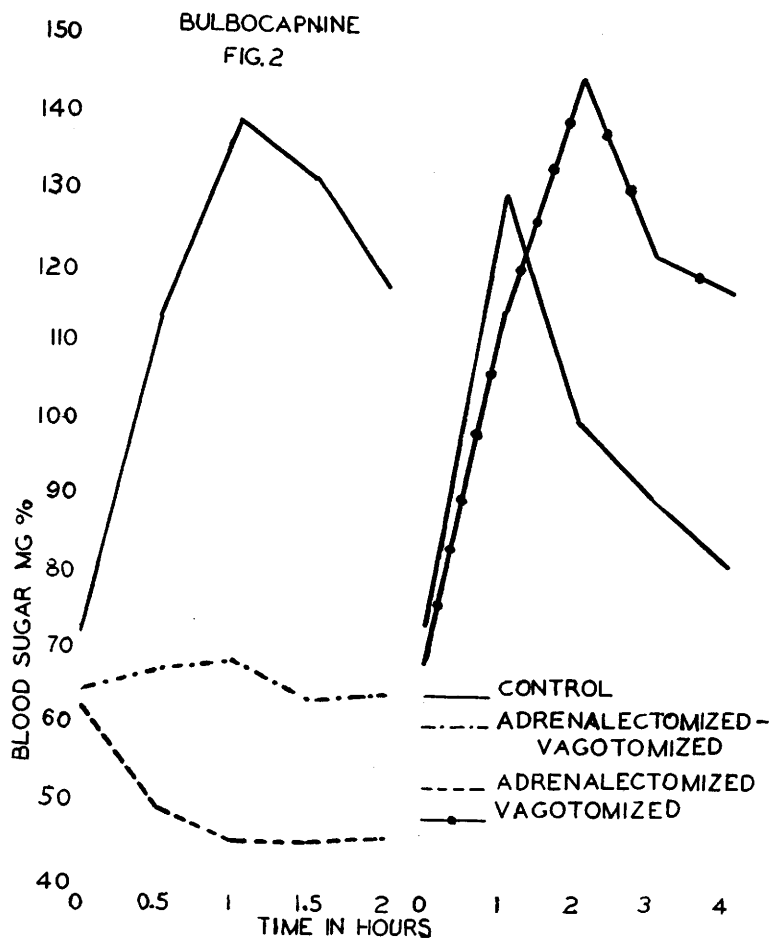


Influence of 50 mg/kg cocaine hydrochloride on the blood sugar of rats. Cocaine injected subcutaneously immediately after the first blood sample was taken.
 — Control; --- adrenalectomized; ···· adrenalectomized-vagotomized;
 —●— vagotomized.

phragnatically in normal rats, one observes a greater hyperglycemic response than in control animals (Fig. 1). This we attribute to the elimination of the vagally controlled insulin secretion.

With bulbocapnine phosphate similar results are obtained (Fig. 2). Here again the normal animals show an increase in blood sugar even greater than with cocaine hydrochloride, the adrenalectomized a fall and the adrenalectomized-vagotomized no significant change. With the vagotomized animals, the rise in sugar is not as rapid as in the controls, but the maximum is higher and the effect much more prolonged. It seems safe, therefore, to conclude that here again we have a stimulation of both sympathetic and parasympathetic centers, and that the reaction of each of these centers may be demonstrated by selection of the proper conditions.

Summary. 1. Subcutaneous injection of cocaine hydrochloride causes hyperglycemia in normal rats and hypoglycemia in adrenalectomized rats. If the vagi are sectioned subdiaphragmatically in the adrenalectomized rats, there is no significant change in blood sugar. If the vagi are cut subdiaphragmatically in normal animals, there is a greater increase in blood sugar than in animals with intact vagi. 2. Similar results are obtained with bulbocapnine phosphate. 3. These results are interpreted to mean that cocaine and bulbocapnine although



Influence of 50 mg/kg bulboCAPNINE phosphate on blood sugar of rats. BulboCAPNINE was injected immediately after the first blood sample was taken. Designation as in Fig. 1.

acting quite differently on the somatic nervous system have a similar action on the autonomic system. They stimulate both the vago-insulin and the sympathetico-adrenal system. The effect on the latter predominates in the normal animal.