

TABLE I. Fecal Enzymes of Normal Dogs and of Dogs with Pancreatic Separation.

	No. of samples	Lipase			Chymotrypsin			Trypsin		
		Mean	Range	S.D.	Mean	Range	S.D.	Mean	Range	S.D.
Normal	22	51	13-212	57	306	50-703	260	171	41-625	185
Pancreatic separation										
Dog A	10	10	5- 20	5	6	4- 11	2	6	3- 14	4
Dog B	10	11	3- 18	5	12	4- 23	6	9	8- 14	3
Dog C	10	5	2- 7	2	3	1- 5	1	3	1- 4	1

All values expressed as micromoles substrate split per minute per gram feces.

S.D., standard deviation.

Difference between means of samples from normal dogs and of samples from each dog with pancreatic separation statistically significant for each enzyme ($P < 0.05$).

mal dogs and dogs with pancreatic separation; for chymotrypsin and trypsin there was no overlap.

Discussion. These studies show that a major portion of the enzymatic activity of the feces for the substrates studied is of pancreatic origin. While it is undoubtedly true that most of the pancreatic enzymes are autodigested and reabsorbed, behaving in this respect like ordinary food protein(2), apparently enough of the enzymes escape destruction to be readily detected in the feces. The source of the enzymatic activity that remains after pancreatic exclusion is uncertain; none of the substrates used is completely specific

for pancreatic enzymes.

The results suggest that study of fecal enzymes might be helpful in detecting pancreatic insufficiency in patients.

Summary. The feces of 3 dogs in which entry of pancreatic juice into the intestine had been excluded by separation of the pancreas from the duodenum had much lower lipase, chymotrypsin, and trypsin activity than did the feces of normal dogs.

1. Pelot, D., Grossman, M. I. *Am. J. Physiol.*, in press.

2. Borgstrom, B., Dahlquist, A., Lundh, G., Sjoval, J., *J. Clin. Invest.*, 1957, v36, 1521.

Received February 19, 1962. P.S.E.B.M., 1962, v110.

Effect of Oxytocin on Plasma Free Fatty Acids of Non-Diabetic and Diabetic Dogs.* (27416)

I. ARTHUR MIRSKY

(With the technical assistance of Edward C. Krimmer and Louisa C. Linn)

Department of Clinical Science, University of Pittsburgh, School of Medicine, Pittsburgh, Pa.

Synthetic oxytocin and related disulfide peptides with oxytocic activity exert an insulin-like action *in vitro* on rate of glucose utilization and rate of lipogenesis from glucose by rat epididymal adipose tissue(1,2,3). Since the *in vitro* action of insulin on adipose tissue(4,5,6,7) is reflected *in vivo* by a reduction in concentration of free fatty acids (FFA) of the plasma(8,9,10,11), it became

pertinent to determine whether oxytocin exerts a similar effect *in vivo*.

Methods. Seven mongrel male healthy dogs and 7 alloxan-diabetic dogs were trained to be in a hammock while samples of venous blood were drawn from an indwelling needle at intervals before and after injection of synthetic oxytocin.[†] The dogs were fasted overnight; the alloxan-diabetic dogs were deprived of exogenous insulin for 24 hours. The

* Aided by grants from U. S. Public Health Service, the Foundations' Fund for Research in Psychiatry, and the Commonwealth of Pennsylvania.

[†] We are indebted to Mr. Sidney Gimpel of Sandoz Pharmaceuticals for generous supplies of synthetic oxytocin (Syntocinon).

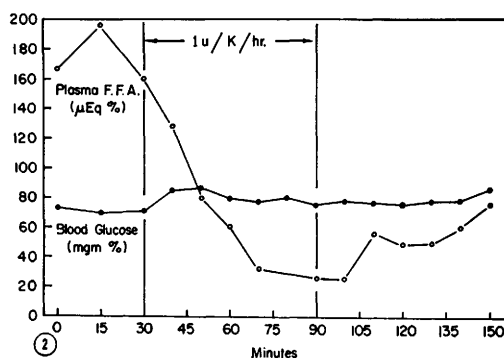
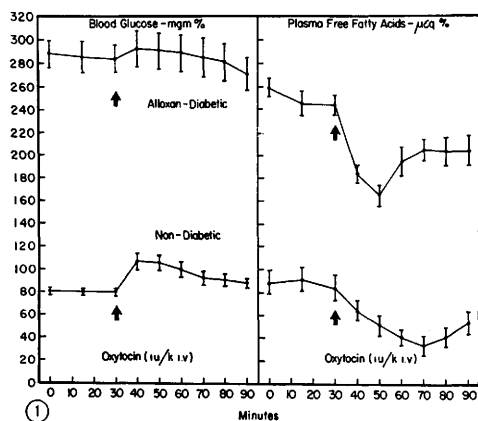


FIG. 1. Effect of synthetic oxytocin on blood sugar and plasma free fatty acids of the dog.

FIG. 2. Effect of slow inj. of synthetic oxytocin on plasma free fatty acids of the dog.

first sample of blood was drawn in from 30 to 60 minutes after the animal was placed in the hammock. A second and third sample was taken in 15 and 30 minutes, and immediately thereafter one unit oxytocin per kilo body weight was injected intravenously within one minute. Thereafter samples were drawn at 10-minute intervals for 60 minutes. In some instances the same dose of oxytocin was injected intravenously over a period of one hour by means of a constant injection pump. After removing an aliquot for determination of whole blood glucose by the Nelson(12) or ferricyanide Autoanalyzer method (13), the sample was centrifuged at 4°C and the plasma kept at that temperature until analyzed for FFA by the Trout *et al.*(14) modification of the Dole procedure(9).

Results. The effect of intravenous injection of one unit of oxytocin per kilo body weight on concentration of glucose in the

blood and of FFA in the plasma of healthy and alloxan-diabetic dogs is depicted in Fig. 1. It is evident that the injection of this quantity of oxytocin produces an immediate statistically significant increase in blood sugar concentration (+ 33%) of the non-diabetic dogs but only an insignificant increase in that of the alloxan-diabetic animals (+ 9%). Concentration of FFA in the plasma of both sets of animals is significantly reduced; a maximum decrease of 65% occurs in 40 minutes in the non-diabetic dogs while the diabetic dogs exhibit a decrease of 66% in 20 minutes.

That smaller quantities of oxytocin are effective is revealed in the rapid decrease in concentration of plasma FFA which occurs when one unit of oxytocin per kilo body weight is administered during a period of one hour (Fig. 2). Thus an appreciable decrease occurred within 10 minutes after onset of the injection by which time 0.166 unit/kg had been introduced into the circulation.

Discussion. Administration of insulin to animal or man results in a decrease in concentration of the FFA in the plasma(8,9,10,11). Since insulin does not influence the rate at which FFA are removed from the circulation (11), the decrease in their concentration in the plasma is attributable to a decrease in the release of FFA from the adipose tissues such as occurs *in vitro* in presence of insulin (4,5,6,7). The effect of oxytocin on concentration of FFA in the plasma of both healthy and alloxan-diabetic dogs is in accord with the demonstration that this hormone exerts an insulin-like action on adipose tissue *in vitro*(3).

The lack of an insulin-like action on concentration of glucose in the circulation is in accord with the observation that oxytocin does not influence *in vitro* utilization of glucose by the isolated rat diaphragm(3). Since oxytocin does not influence the output of glucose by the liver(15), the hyperglycemic response of the non-diabetic dog must be due to some peripheral effect. The nature of the peripheral effect cannot now be evaluated.

Although the dose of oxytocin employed in this study is beyond physiological concen-

trations, it is pertinent that similar, but more evanescent, changes in plasma FFA are induced by doses as low as 0.1 unit per kilo body weight. Even if smaller quantities of oxytocin were effective in reducing plasma FFA, the physiological significance of this systemic effect would remain obscure in view of the rapidity with which this hormone is destroyed *in vivo* (16). It is quite possible, however, that the effect on the circulating FFA reflects an action at or near the site of secretion of oxytocin in the nuclei of the hypothalamus.

Irrespective of the physiological significance of the action of oxytocin on circulating FFA, the present findings provide a tool for dissociating the effects of insulin which are dependent upon utilization of glucose by the muscles from those which are dependent upon utilization of glucose by adipose tissue.

Summary. Intravenous injection of oxytocin results in a decrease in concentration of free fatty acids in the plasma of non-diabetic and alloxan-diabetic dogs.

1. Mirsky, I. A., Perisutti, G., *Biochim. Biophys. Acta*, 1961, v50, 603.

2. Pittman, J. A., Boshell, B. R., Williams, B. H., Hamner, D., Hill, P., *Biochem. Biophys. Res. Comm.*,

1961, v6, 29.

3. Mirsky, I. A., Perisutti, G., *Endocrinology*, in press.

4. Gordon, R. S., Jr., Cherkes, A., *Proc. Soc. Exp. Biol. and Med.*, 1958, v97, 150.

5. Cahill, G. F., Jeanrenaud, B., LeBoeuf, B., Renold, A. E., *Ann. N. Y. Acad. Sci.*, 1959, v82, 403.

6. Raben, M. S., Hallenberg, C. H., *J. Clin. Invest.*, 1960, v39, 435.

7. Lynn, W. J., McLeod, R. M., Brown, R. H., *J. Biol. Chem.*, 1960, v235, 1904.

8. Estes, E. H., Jr., Bogdonoff, M. D., Friedberg, S. J., Harlan, W. R., Trout, D. L., *J. Clin. Invest.*, 1959, v38, 2131.

9. Dole, V. P., *ibid.*, 1956, v35, 150.

10. Gordon, R. S., Jr., Cherkes, A., *ibid.*, 1956, v35, 206.

11. Bierman, E. L., Schwartz, I. T., Dole, V. P., *Am. J. Physiol.*, 1957, v191, 359.

12. Nelson, N., *J. Biol. Chem.*, 1944, v153, 375.

13. Grady, H. J., Lamar, M. A., *Clin. Chem.*, 1959, v5, 542.

14. Trout, D. L., Estes, E. H., Jr., Friedberg, S. J., *J. Lipid Res.*, 1960, v1, 199.

15. Bergen, S. S., Jr., Sullivan, R., Hilton, J. G., Willis, S. W., Jr., Van Itallie, T. B., *Am. J. Physiol.*, 1960, v199, 136.

16. Ginsburg, M., Smith, M. W., *Brit. J. Pharmacol.*, 1959, v14, 327.

Received February 23, 1962. P.S.E.B.M., 1962, v110.

Interaction of Growth Hormone with ACTH, TSH, and FSH in the Hypophysectomized Rat.* (27417)

CHRISTOPHER LONGCOPE[†] AND JOSEPH W. JAILER[‡]
(Introduced by Nicholas P. Christy)

*Departments of Medicine and Obstetrics and Gynecology, College of Physicians and Surgeons,
Columbia University, New York City*

Whereas purified ACTH is extremely effective in depleting adrenal ascorbic acid and in stimulating adrenal steroidogenesis, it is not so effective as the less pure substance in increasing adrenal weight in the hypophysectomized animal (1). This dichotomy of effect has been demonstrated by Li (2), Cater and Stacke-Dunne (3), and Dixon, Young *et al.* (4). The latter investigators prepared pituitary fractions relatively rich in adrenal weight-maintaining activity and others which were noted to be more active in depleting adrenal ascorbic acid. The nature of the adrenal weight-maintaining substance is not clear.

* This investigation was supported by grants from Nat. Inst. Health.

† Fellow of the Dazian Foundation for Medical Research, 1959-1960. Present address: Dept. of Medicine, Univ. of Washington, School of Med., Seattle.

‡ Deceased.

Jailer, Longson and Christy (5) have demonstrated the presence of a factor in the