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Received May 11, 1962. P.S.E.B.M., 1962, v110.

Effect of Catecholamines on the Individual Free Fatty Acids of Plasma.* (27604)

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Previous studies from this laboratory dealt with the removal and mobilization of individual free fatty acids in normal and diabetic dogs(1,2). The present report extends these observations to include the effects of administration of epinephrine and norepinephrine on plasma individual free fatty acids.

Methods. Normal dogs of both sexes were employed after fasting for 16 hours. All experiments were carried out under nembutal anesthesia. Blood was sampled from the femoral artery through a cannula in a small side branch. After a control sample, epinephrine or norepinephrine was infused intravenously at the rate of 10 μg/kg/min. A second sample was withdrawn after 20 minutes of infusion. Total concentration of free fatty acids (FFA) was determined by Dole's method(3), free fatty acids were separated from other lipid fractions on silicic acid and ion exchange columns and the individual fatty acids analyzed by gas liquid chromatography, as described previously(1).

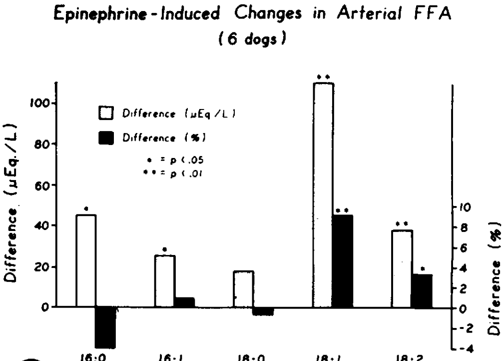
Results. The effect of epinephrine administration on arterial individual FFA is shown in Fig. 1. Total arterial concentration of FFA increased (mean increase = .268 meq/l) due to a rise in concentration of most major fatty acids. The percentage composition of the elevated FFA was also different; oleic and linoleic acids represented a significantly higher percentage. Although the percentage concentration of palmitic and stearic acids decreased, these changes were not statistically significant.

The arterial change in individual FFA after administration of norepinephrine is illustrated in Fig. 2. The rise in total arterial concentration of FFA (mean increase = .611 meq/l) is accompanied by an elevated concentration of the major 5 fatty acids, while the percentage concentration of oleic acid increased and that of stearic acid decreased significantly. Thus, it appears from the above findings that catecholamine-induced mobilization of FFA from the adipose tissue is characterized by a relative increase of oleic acid (and possibly linoleic acid) in the plasma. Since catecholamines have also been assumed to regulate the release of FFA from adipose tissue under physiological conditions, it could be of value to demonstrate a correlation between the normal arterial FFA level and its fractional content of oleic acid. The existence of such a correlation (which has a correlation coefficient of .618 and is significant at $p < .01$ level) is shown in Fig. 3. Each of the 38 points on the scattergram represents a different normal dog under anesthesia. No such relationship could be shown for palmitic or linoleic acids.

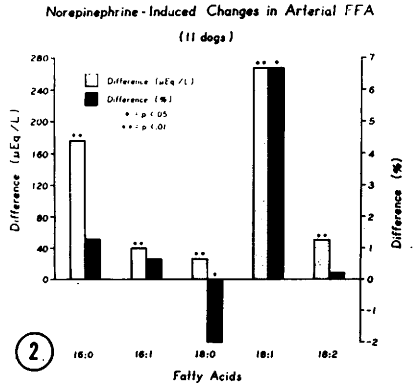
A similar scattergram for 29 alloxan-diabetic dogs is shown in Fig. 4. This slope also indicates a significant positive correlation (correlation coefficient = .555, $p<.01$). Thus, as the blood level of FFA rises, oleic acid comprises an increasing percentage of the total FFA.

Discussion. Previous studies have indi-

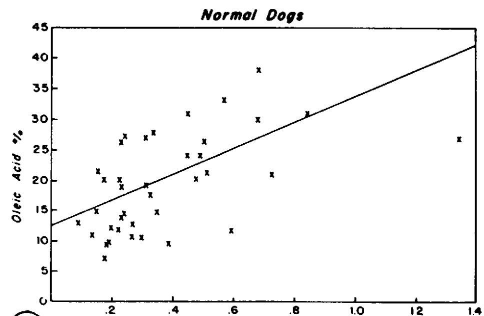
* Supported by grants from Nat. Science Foundation and Nat. Heart Inst.



(1)



(2)



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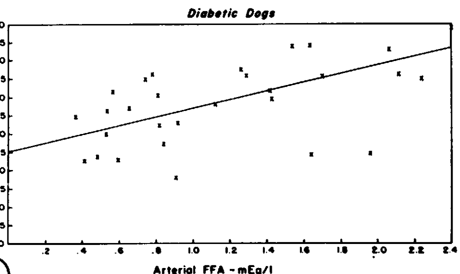

(4)

FIG. 1. Effect of epinephrine administration on individual FFA. "Difference (μeq/l)" refers to the absolute change in individual fatty acids during infusion of the hormone as compared to the control sample. "Difference (%)" refers to the difference in percentage composition of fatty acids during infusion of hormone, compared to % composition before hormone was administered.

FIG. 2. Effect of norepinephrine administration on individual FFA. See explanation in Fig. 1.

FIG. 3. Correlation between normal arterial FFA level and its fractional content of oleic acid.

FIG. 4. Correlation between arterial FFA level and its fractional content of oleic acid in diabetic dogs.

cated(1) that the fatty acid composition of adipose tissue in normal dogs is different from that which is released from the adipose tissue under *in vivo* conditions. The major difference is that oleic acid is released in a relatively smaller percentage of the total FFA, than is present in the adipose tissue. This is found to be altered in diabetic dogs(2). It has also been reported recently(4,5) that catecholamines stimulate release of a high percentage of oleic acid into the medium from the epididymal fat pad of the rat under *in vitro* conditions.

Results of the present study indicate that an increased formation of FFA in the adipose tissue cell (whether due to the influence of catecholamines or to development of diabetes) tends to foster a closer equilibrium with the FFA of blood, in terms of the percentage makeup of FFA.

Uptake of FFA is regulated by arterial concentration at least as far as the liver(6), kidney(7) and the myocardium(8) are concerned. No known influences exist (with the possible exception of exercise) that directly regulate the uptake of FFA by tissues. Thus, the importance of epinephrine and/or norepinephrine in regulating FFA metabolism becomes even more pronounced, since these hormones through their influence in releasing FFA from adipose tissue indirectly affect the removal of FFA from the blood and presumably also its utilization.

Summary. The effect of epinephrine and norepinephrine on the individual free fatty acids of plasma was investigated in anesthetized dogs. The increased arterial FFA after administration of catecholamines was due to a rise in concentration of most major fatty acids. The percentage contribution of oleic and linoleic acids to total arterial FFA was also increased. A direct relationship was found, both in normal and in diabetic dogs, between the resting arterial FFA level and percentage of oleic acid in FFA. An attempt was made to relate these findings to the selective release of FFA from adipose tissue that occurs in the normal animal.

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Received May 14, 1962. P.S.E.B.M., 1962, v110.

Quantitative Response of Rat Mammary Glands to Mammogens. I. Estrogen Alone and with Progesterone.* (27605)

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Silver(1) reported that 17 β-estradiol dipropionate (0.25 and 1.0 μg) induced no extension of the mammary duct system of suckling, ovariectomized, hooded Norway rats. In our laboratory these doses of estrogen have stimulated mammary growth in suckling rats of 3 strains, including hooded Norway rats. Lyons *et al.*(2), Kirkham and Turner(3), and Smith(4) have shown that the optimal estrogen to progesterone ratio for lobule-alveolar growth is 1:400, 1:3000-5000, and 1:5000, respectively. Since the ratio of estrogen to progesterone is important in lobule-alveolar growth it was of interest to determine whether estrogen and progesterone, when injected at various ratios, were more effective in stimulating mammary duct growth than estrogen alone.

Methods. Two or 3 pups per litter were taken at random for ovariectomy at 8 days of age from litters of 10 pups divided as equally as possible by sex. Hormone injections (sbc) were begun on the 11th day of age and were continued through the 19th day with sacrifice on the 21st day.

Eleven ovariectomized pups received no treatment and served as controls. Additional ovariectomized pups were injected with: either 1.0 μg (10), 2.0 μg (12), or 4.0 μg (11) of estradiol dipropionate (ED) every other day alone, or with 0.5 μg ED every other day and 1.0 mg progesterone (P) daily (6); 0.5 μg ED plus 2.5 mg P every other day (8); 1.0 μg ED every other day plus 1.0 mg P on 11th and 15th day of age (11); or 1.0 μg ED plus 1.0 mg P every other day (12). This provided ED:P ratios of: 1:4000, 1:5000, 1:400, and 1:1000.

After sacrifice on the 21st day, right abdominal mammary glands were removed, stained, and mounted in balsam. Mammary gland area was determined by the method of Macdonald and Reece(5) and expressed as mm^2 per 100 cm^2 of body surface area ($W^{2/3} \times 10$).

Results. Mammary areas of pups which received 1.0, 2.0, or 4.0 μg ED were 37.5,

* Paper of the Journal Series, N. J. Agri. Exp. Station, Rutgers, The State University, New Brunswick.