tanol in varying degree in the presence of human plasma. Only serotonin and tryptamine of the substances tested were significantly influenced in their fat solubilization in the presence of plasma by addition of an excess of Ca^{++} or Mg^{++} and/or chelators to the *in vitro* system. Solubilization of both serotonin and tryptamine in benzene-butanol in presence of plasma was decreased somewhat by addition of Ca^{++} or Mg^{++} or disodium EDTA in excess to the system. It was eliminated by addition of disodium EDTA (but not disodium calcium EDTA) and either Ca^{++} or Mg^{++} to the system, also by prolonged prior dialysis of the plasma against balanced buffered salt solution plus disodium EDTA. The overall findings supported the hypothesis that divalent cations bound to a substance or substances present in human plasma formed a complex with serotonin or tryptamine to solubilize these usually lipid-insoluble materials in benzene-butanol, in the absence of competing chelators.

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Influence of Epinephrine and Fasting on Free Fatty Acid Mobilization in Goldthioglucose-Induced Obesity. (26803)

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Regulatory and metabolic types of obesity in mice have been described by Mayer(1). In the former, accelerated rates of lipogenesis are considered to be a consequence of hyperphagia resulting from hypothalamic damage. In the latter, it is suggested that hyperphagia is secondary to hyperlipogenesis arising from an inherent metabolic defect.

Recently it was reported that obese-hyperglycemic mice (O-H), representing metabolic obesity, exhibit an impairment in their ability to mobilize free fatty acids (FFA) *in vitro*, from adipose tissue in response to fasting and epinephrine stimulation(2).

To determine whether the defect is related to the etiology of the obese-hyperglycemic syndrome, or if it is a nonspecific consequence of obesity *per se*, the influence of fasting and epinephrine stimulation was investigated in goldthioglucose† obese (GTG) mice, an example of regulatory obesity.

Materials and methods. 50-60 mg portions of epididymal adipose tissue were obtained from goldthioglucose-induced obese CBA mice in the dynamic phase of obesity and from lean controls. Obese mice were approximately 5 months old, weighed 42-50 g, had been obese for 2 months, and were still actively gaining weight. Lean mice were the same age and weighed 27-37 g. Tissues were incubated in a Krebs-Ringer bicarbonate medium containing 0.1% glucose and 2% bovine serum albumin. FFA content of adipose tissue and release into the medium were measured 3 hours following addition of either epinephrine* or, as in the case of controls, water. Analytical methods used are identical with those reported earlier(2).

Results and discussion. Adipose tissue from fed goldthioglucose obese mice and lean controls produced equivalent amounts of FFA during incubation without hormonal stimulation (Fig. 1). In the lean group, epinephrine induced an increase in FFA content of both tissue and medium which amounted to a 6-fold increase in total FFA production ($p<.001$). Similarly, epinephrine

* Adrenalin, Parke Davis Co., Detroit, Mich.

† Goldthioglucose, courtesy Schering Corp., Bloomfield, N. J.

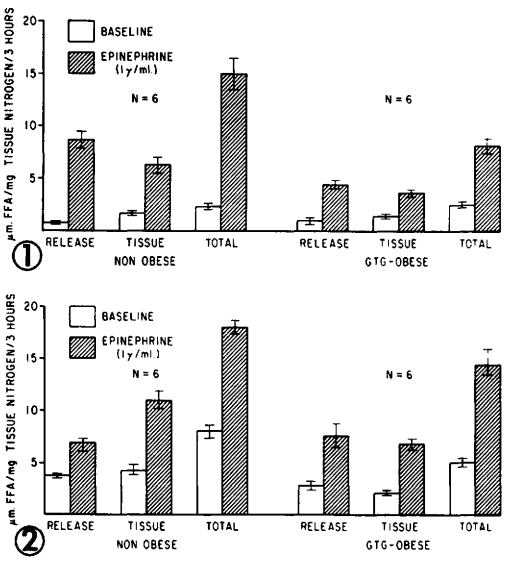

FIG. 1. The influence of epinephrine on epididymal adipose tissue content and release of FFA in fed goldthioglucose induced obese mice during dynamic phase of obesity and in lean CBA mice.

FIG. 2. The influence of epinephrine on epididymal adipose tissue content and release of FFA in fasted goldthioglucose induced obese mice during dynamic phase of obesity and in lean CBA mice.

stimulation in the obese group resulted in a 3-fold increase in total FFA production ($p < .001$).

Results obtained with 16-18 hr fasted animals are represented in Fig. 2. Baseline FFA production in adipose tissue of lean and obese mice was increased significantly ($p < .001$) in response to fasting; the response of the former, however, was greater than the latter. In both groups, epinephrine evoked an equivalent increase in FFA mobilization ($p < .001$).

These results reveal that adipose tissue from goldthioglucose obese mice, unlike that of O-H mice(2), significantly increases FFA production in response to fasting and epinephrine stimulation. Moreover, the response of tissue obtained from fasted GTG mice was of similar magnitude as that of tissue from lean animals. An impaired response was, however, observed in tissue from fed GTG obese mice; also, tissues from lean mice gave a greater response to fasting than did tissue from obese mice.

Accelerated rates of lipogenesis have been reported for fed and fasted obese-hyperglycemic mice and for fed (but not fasted) goldthioglucose obese mice(3). Since tissues from fed and fasted O-H mice and fed GTG obese mice also show an impairment in FFA mobilization, it is suspected that the diminished response to fasting and epinephrine stimulation may be in part a reflection of hyperlipogenesis.

FFA concentrations of adipose tissue and incubation medium are influenced by 2 processes: a) rate of lipolysis of tissue triglyceride and b) rate of esterification of FFA(4). Esterification of FFA by adipose tissue has been shown to be dependent upon the nutritional state of the animal in that adipose tissue from fasted rats incorporates less FFA into triglyceride than does tissue from fed animals (5). It is possible that FFA released from triglyceride in response to epinephrine stimulation are more rapidly re-esterified in tissues actively synthesizing lipid (*viz.*, fed and fasted O-H and fed GTG mice), thus suggesting an apparent diminished mobilization of FFA. Accelerated rates of re-esterification of FFA, therefore, may account for the diminished response of adipose tissue from fed GTG mice to the lipolytic influence of epinephrine, and may also be a component in the impaired mobilization of FFA in adipose tissue from O-H mice.

Summary. Epididymal fat pad adipose tissue obtained from goldthioglucose obese mice mobilized free fatty acids (FFA) when incubated with epinephrine and in response to a 16-hr fast. FFA production was similar in adipose tissues of fasted lean and obese mice; however, the response of adipose tissues of fed obese mice was less than that of fed lean animals. It is suggested that rate of re-esterification of FFA may be a factor in the apparent mobilization of FFA in adipose tissue.

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Effects of Valine-5 Angiotensin II on Excretion of Water and Salt in Primary and Secondary Hypertension.* (26804)

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Intravenous administration of angiotensin in hypertensive subjects promotes an increased excretion of water and salt(1). In contrast, a similar infusion in normal subjects usually results in sodium retention and antidiuresis(2). Whether angiotensin causes natriuresis in subjects with hypertension by acting directly on the kidney, or by some other mechanism is not clear. Since hypertensives seem to ingest more salt than normotensives (3), it may well be that this dietary factor conditions their response to angiotensin.

The present study deals with the effects of intravenous angiotensin under conditions of high and low salt intake on renal excretion of sodium, potassium and water in subjects with hypertension due to primary aldosteronism, advanced essential hypertension and chronic glomerulonephritis.

Material and methods. Six subjects were studied. One (H.M.) had primary aldosteronism, 2 (H.F., O.J.) advanced essential hypertension, and 3 (S.J., B.E., R.D.) chronic glomerulonephritis. Resting diastolic blood pressure ranged between 110 and 130 mm Hg in H.M., H.F. and O.J., and from 90 to 100 mm Hg in S.J., B.E. and R.D. Degree of renal disease varied from severe (S.J., B.E., R.D., H.F.) to moderate (O.J.) or no impairment (H.M.). None of the subjects presented symptoms or signs of congestive heart failure.

All subjects were maintained on a fixed Na (30 to 90 mEq/day) and K (50 to 90 mEq/day) intake for one to 6 weeks. Daily urines were measured and samples of the individual diets saved. After establishing Na retention (urinary Na 20 to 80 mEq/day below intake for at least 10 days) in H.M., H.F. and O.J., and Na depletion (urinary Na exceeding intake by 20 to 30 mEq/day for 2 weeks) in S.J., B.E. and R.D. an intravenous infusion of 300 cc of 5% D/W was given over 6 to 24 hours. On the following day, 100 to 200 μg of synthetic valine-5 angiotensin II (angiotensin II)† diluted in 300 cc 5% D/W was administered intravenously during 6 to 24 hours.

In one of the subjects (R.D.) on each of the following 2 days the effects of intravenous aldosterone‡ alone, 0.5 mg diluted in 300 cc 5% D/W, and in combination with angiotensin II were also studied.

Observations similar to the above were repeated in the subject with primary aldosteronism (H.M.) after removal of an adrenal cortical adenoma, in one subject (O.J.) with advanced hypertension after 3 weeks of reduced Na intake (20 mEq/day), and in 2 subjects (B.E., R.D.) with chronic glomerulonephritis after Na depletion had been corrected by provision of additional salt in tablet form (65 and 100 mEq Na/day).

All subjects were kept recumbent throughout the infusions. Blood pressure was determined at 5 to 30 minute intervals during administration of angiotensin II, and less frequently during infusion of 5% D/W. Blood was drawn before and at termination of infusions.

Pooled diet samples and urines were analyzed for sodium and potassium by flame

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† Hypertensin Ciba, lot E6429

‡ d-aldosterone Ciba, lot E6403.