initiated inflammation as did lymph from dogs undergoing thoracic duct obstruction alone, pancreatic duct obstruction alone or neither one of these procedures. Whether or not components of bile reached thoracic duct lymph was therefore not critical.

Role of the lymphatic system in the pathogenesis of pancreatic inflammatory disease in man is obscure. Recent experimental data indicate that flow capacity in the thoracic duct in man is limited and that lymph does not flow continuously through the lymphatic venous junction in the neck(13). Further, data acquired from experiments still in progress indicate that when the pancreatic exocrine system is obstructed thoracic duct lymph flow is an important mechanism regulating intraductal pressure. It seems reasonable to speculate that in patients actively secreting acinar fluid against exocrine flow resistance the normal impairment of thoracic duct lymph flow at the lymphatic venous junction may be a critical factor in the control of pancreatic interstitial pressure and release of substances capable of initiating inflammation.

*Summary.* Sudden distension of the pancreatic exocrine system by excess pancreatic secretion releases substances into thoracic duct lymph which initiate an acute inflammatory reaction when injected into rats. Lymph becomes more potent in this respect when either the exocrine duct system or the thoracic duct is obstructed and especially when these two maneuvers are combined.

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## Effects of Hypophysectomy on Lipolytic Response of Adipose Tissue To Pituitary Hormones.* (30681)

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An intact pituitary gland appears to be required for normal responsiveness of adipose tissue to hormones. Hypophysectomy increases the sensitivity of adipose tissue to the insulin-like actions of growth hormone(1). Similarly, pituitary ablation decreases the effects of epinephrine on free fatty acid (FFA) mobilization(2,3,4). The present report describes the effects of hypophysectomy on the sensitivity of adipose tissue to the lipolytic actions of corticotropin (ACTH) and thyrotropin (TSH).

*Materials and methods.* Male rats weighing 100-120 g were obtained from the Charles River Breeding Laboratories and were maintained on Purina Lab Chow. Hypophysectomized rats were studied 2-4 weeks postopera-

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TABLE I. Effects of Corticotropin on FFA Production by Adipose Tissues from Normal and Hypophysectomized Rats.

| Incubation medium | μEq/g fresh tissue/hr FFA released | P | Hormone effect | P |
|---|---|---|---|---|
| | Normal rats | | | |
| Control | −.22 ± .07* | | | |
| 1 μg/ml ACTH | 4.69 ± .43 | <.001 | 4.91 ± .34 | <.001 |
| | Hypox rats | | | |
| Control | −.40 ± .12 | | | |
| 1 μg/ml ACTH | .36 ± .09 | <.001 | .76 ± .10 | <.001 |

* Means ± S.E.M., 8 observations; negative value denotes FFA uptake.

tively. The rats were killed by cervical dislocation and the epididymal fat bodies excised and halved. The 4 tissues obtained from each rat were incubated in vials of 1 ml of Krebs-Ringer phosphate buffer containing 4% bovine serum albumin (Armour) and 1 mg/ml of glucose for 3 hours at 37°C. Each rat contributed both control and experimental tissues. The corticotropin, prepared by Organics, Inc. (lot No. 2u 27563) contained 130 μ/mg, and was kindly provided by Dr. E. B. Astwood. The thyrotropin used was Armour Thytropar (A 7002).

FFA released into the medium was determined by the method of Dole(5). Glycerol production was determined enzymatically(6). Statistical evaluation of the data was made using Student's t test.

TABLE II. Effects of Thyrotropin on FFA Production by Adipose Tissues from Normal and Hypophysectomized Rats.

| mU TSH/ml incubation medium | μEq/g fresh tissue/hr FFA released | P | Hormone effect | P |
|---|---|---|---|---|
| | Normal rats | | | |
| 0 | −.39 ± .04* | | | |
| .25 | −.41 ± .06 | N.S. | — | |
| 2.5 | .59 ± .08 | <.001 | .98 ± .09 | <.001 |
| 25 | 1.50 ± .08 | <.001 | 1.89 ± .09 | <.001 |
| | Hypox rats | | | |
| 0 | −.34 ± .05 | | | |
| .25 | −.29 ± .05 | N.S. | — | |
| 2.5 | −.25 ± .04 | N.S. | .09 ± .02 | <.01 |
| 25 | .08 ± .08 | <.01 | .42 ± .08 | <.01 |

* Means ± S.E.M., 8 observations; negative value denotes FFA uptake.

*Results.* Hypophysectomy reduced the effects of both corticotropin and thyrotropin on FFA production by adipose tissues from fed rats (Tables I and II). The increments in FFA production were significantly greater ($p<.01$) in the normal tissues for each dose of hormone tested. Fasting for the 24 hr preceding the experiment increased the production of FFA by the tissues of hypophysectomized rats in response to both ACTH and TSH (Table III). However, fasting did not increase the effects of these hormones on glycerol production, nor did fasting abolish the difference between hypophysectomized and normal rats on FFA production in response to these pituitary hormones. Fasting did, however, increase the release of FFA from adipose tissues of hypophysectomized as well as normal rats, although the increase was less pronounced in the hypophysectomized rats. In the present experiments, no significant increase in glycerol production was

TABLE III. Effects of Hypophysectomy and Fasting Response of Adipose Tissues to Corticotropin and Thyrotropin.

| Incubation medium | FFA release μEq/g/hr | P | Glycerol production μM/g/hr | P |
|---|---|---|---|---|
| | Hypox rats | | | |
| Fed | | | | |
| Control | .05 ± .15* | | 2.30 ± .24 | |
| .1 μg/ml ACTH | .14 ± .19† | N.S.‡ | 2.86 ± .41 | N.S. |
| 25 mU/ml TSH | .93 ± .15† | <.001 | 3.66 ± .29 | <.01 |
| Fasting | | | | |
| Control | .50 ± .09§ | | 2.44 ± .20 | |
| .1 μg/ml ACTH | 1.37 ± .22 | <.001 | 2.75 ± .23 | N.S. |
| 25 mU/ml TSH | 1.74 ± .16 | <.001 | 3.85 ± .31 | <.01 |
| | Normal rats | | | |
| Fasting | | | | |
| Control | 1.94 ± .44‖ | | 3.81 ± .43¶ | |
| .1 μg/ml ACTH | 5.36 ± .21 | <.001 | 5.69 ± .25 | <.01 |
| 25 mU/ml TSH | 6.71 ± .72 | <.001 | 7.46 ± .71 | <.01 |

* Mean ± S.E., 8 observations.
† 9 observations.
‡ Not statistically significant ($p>.05$).
§ Significantly different from fed controls ($p<.05$).
‖ Significantly different from fasting hypox ($p<.01$).
¶ Significantly different from fasting hypox ($p<.05$).

found for the tissues of fasting hypophysectomized animals.

*Discussion.* Hypophysectomy decreases the sensitivity of adipose tissue to the lipolytic effects of both corticotropin and thyrotropin. Comparable effects have been described previously with respect to epinephrine(4). In the latter case, pretreatment of the hypophysectomized rats with triiodothyronine, adrenal steroids, or growth hormone restored the sensitivity of adipose tissue to epinephrine. Similar hormonal treatment presumably would be effective in restoring sensitivity to pituitary lipolytic hormones as well. Indeed, a requirement of adrenal steroids for the lipolytic effect of corticotropin has been demonstrated(7). Similarly, the lipolytic actions of corticotropin, thyrotropin, and glucagon are reduced by thyroidectomy(8).

The dependence of both catecholamines and pituitary hormones on the presence of the pituitary gland (as well as the thyroid and adrenal glands) for a normal lipolytic response suggests that these lipolytic hormones may all act through some common mechanism. This suggestion is strengthened by the observation that adrenergic blocking drugs also block the response of adipose tissue to the lipolytic actions of ACTH, TSH, and glucagon(9,10,11), although endogenous norepinephrine probably is not an intermediate in the lipolysis induced by pituitary hormones(12).

The tissues of hypophysectomized rats also had a reduced lipolytic response to fasting. In fact, in the present studies, glycerol production was not altered by the 24-hour fast, suggesting that the small increment in FFA production seen was due to decreased reesterification rather than to increased lipolysis. Reduced fat mobilization in hypophysectomized rats is usually ascribed to a deficiency of pituitary lipid-mobilizing hormones, although a physiological role for pituitary lipolytic agents has not been firmly established. However, an alternative explanation is suggested by the present experimental findings. Rather than depriving the animal of hormonal mediators of lipolysis, hypophysectomy may simply reduce the sensitivity of adipose tissue to physiological stimuli for fatty acid mobilization. Thus an important role of the pituitary in prompting lipolysis may be that of maintaining sensitivity of adipose tissue to adipokinetic agents. The manner in which this critical function is achieved remains to be elucidated.

*Summary.* Hypophysectomy reduces the *in vitro* output of FFA by adipose tissue in response to both corticotropin and thyrotropin. Fasting slightly enhances the effects of these hormones on FFA output, but does not alter their effect on glycerol production, suggesting that the enhancement is due to decreased reesterification rather than increased lipolysis. Hypophysectomy also reduces FFA and glycerol production in response to fasting. It is suggested that the reduced fat mobilization usually found in hypophysectomized rats may be due to reduced sensitivity of adipose tissue to physiological stimuli for FFA mobilization rather than to a deficiency of lipolytic agents.

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