Mar) serum cholesterol level averaged 366 mg % during the pre-treatment period and fell to average 279 mg % while on neomycin. The patient received 2 g of neomycin daily for the first 2 weeks, 1 g daily for the next 2 weeks, and finally 0.5 g daily for 2 weeks. The fall in the serum cholesterol was maintained although amount of medication was reduced. In Fig. 2 (Patient Walk) it can be seen that increasing the amount of neomycin from 0.5 g daily to 1 g daily resulted in a further decrease in serum cholesterol level.

The esterified fraction of serum cholesterol decreased in the serum in proportion to the total serum cholesterol in the 3 patients studied. Total serum lipids decreased in each patient, average fall for the group being 23% during the neomycin period. C/P ratio remained approximately unchanged during the study.

Two patients were subsequently given 60 mg of neomycin intramuscularly daily for 2 weeks without appreciable change in serum cholesterol level. This amount of neomycin was calculated to exceed that proportion of oral neomycin (3%) which is absorbed from the gastrointestinal tract(4).

No significant side effects occurred as the result of oral neomycin but mild transitory diarrhea occurred in 4 of the 10 patients at the 2 g dosage. Otherwise, the patients' clinical status remained unchanged during the period of study. The renal status as measured by urinalysis and blood urea nitrogen determinations and liver function as determined by cephalin flocculation and serum bilirubin tests were unaltered.

Comment. The mechanism of action of neomycin in lowering serum cholesterol concentration is unexplained. It is known that 97% of the orally administered drug is eliminated unchanged in the stool. It is possible that the effect of neomycin on the intestinal bacterial flora or upon certain enzyme systems of the gastro-intestinal tract may be responsible for the decrease in serum cholesterol level. Further studies utilizing antibiotics other than neomycin are in progress.

Summary. Oral administration of neomycin was associated with a significant decrease in serum cholesterol concentration of all of the 10 patients studied. On 1.5 to 2 g of neomycin daily, mean serum cholesterol level in each patient was decreased from 17 to 29%, average fall for the group was 22%. The fall in serum cholesterol level was maintained for the duration of drug administration which varied from 3 to 16 weeks. At a daily dose level of 0.5 to 1 g of neomycin similar but less marked falls in the serum cholesterol level resulted.

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Mobilization of Fatty Acids by Epinephrine in Normal and Hypophysectomized Rhesus Monkeys.*† (24570)

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The demonstration by Dole(1), Gordon and Cherkes(2) and others(3) that epinephrine markedly increases the concentration of circulating non-esterified fatty acids

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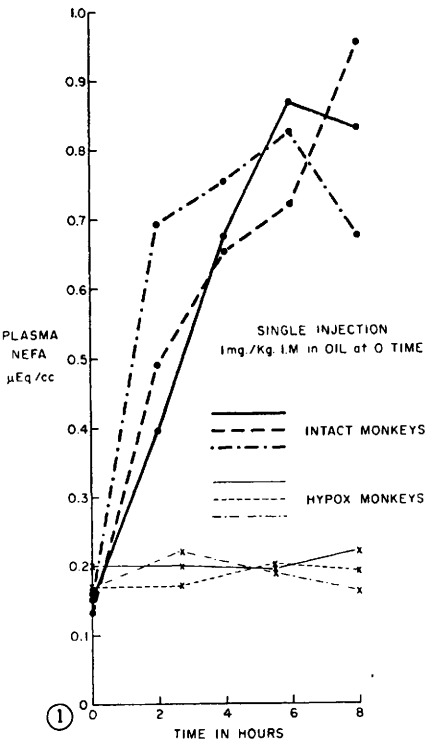
(NEFA) was confirmed in *in vitro* systems (4,5) suggesting a direct effect of epinephrine on adipose tissue with a resultant release of NEFA to the perfusing medium. In the course of studies designed to investigate possible interrelations between this effect of epinephrine and the previously described action of fasting(1,2,6) and growth hormone administration(3), on plasma NEFA concentrations the unexpected observation was made that epinephrine, in contrast to growth hormone, was ineffective in the hypophysectomized rhesus monkey. The following report deals with the role of various endocrine factors in the NEFA mobilizing action of epinephrine.

Materials and methods. Normal and hypophysectomized rhesus monkeys (*Macaca mulatta*) of both sexes were utilized in this study. Hypophysectomy, using the parapharyngeal approach, was performed at least 2 months before initiation of experiments. All animals were maintained on a natural diet supplemented by a commercial monkey ration(7). A 10% glucose solution was available to hypophysectomized monkeys in addition to tap water except during experimental periods. Epinephrine (1 mg/kg I.M.) was administered in oil as a single injection. Control animals received an intramuscular injection of an equal volume of peanut oil. Epinephrine injections were made one hour following a standardized feeding, the animals being fasted throughout the remainder of the experiment. Plasma NEFA concentrations were determined by the method of Dole(1) and blood glucose by the method of Nelson(8) from samples drawn from the femoral vein into heparinized syringes.

Results. A single intramuscular injection of epinephrine (1 mg/kg in oil) produced a 5- to 6-fold increase in plasma NEFA concentration in the intact animals. In sharp contrast, the same dose of epinephrine, administered under identical experimental conditions, was without effect in hypophysectomized monkeys (Fig. 1). The hyperglycemic effect of epinephrine, on the other hand, was noted in both groups of animals.

Comparable findings have been reported with reference to the hyperglycemic action of epinephrine. The hyperglycemic response to epinephrine is attenuated in hypophysectomized and adrenalectomized animals. Pretreatment of such animals with adrenal corti-



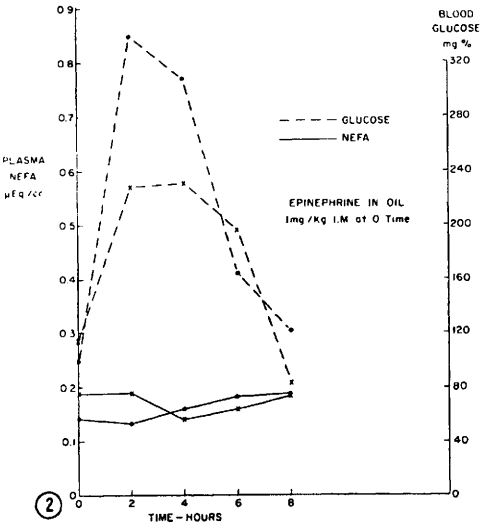


FIG. 1. Effect of epinephrine on plasma NEFA concentrations in intact and hypophysectomized rhesus monkeys.

FIG. 2. Effect of cortisol acetate pretreatment (3 mg/kg/day for 6 days) on NEFA response to epinephrine in hypophysectomized rhesus monkeys.

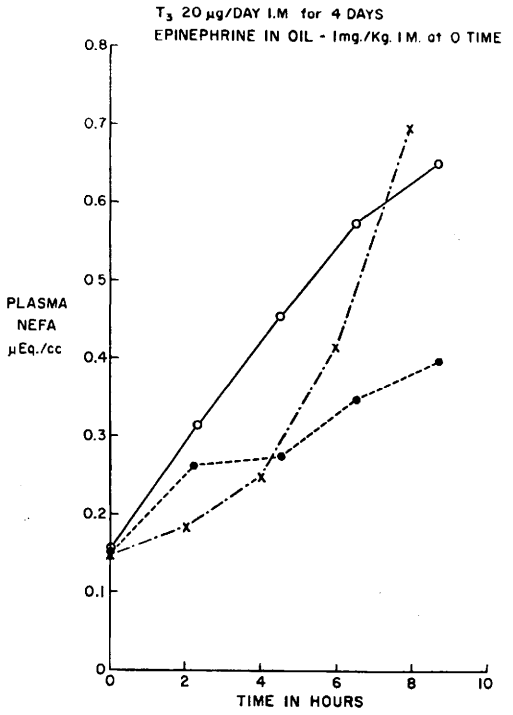


FIG. 3. Response of hypophysectomized monkeys to epinephrine following pretreatment with l-triiodothyronine.

cal steroids restores the hyperglycemia following epinephrine administration to normal (9). With these observations in mind, hypophysectomized monkeys were given daily injections of cortisol acetate (3 mg/kg I.M.) for 6 days and NEFA response to epinephrine determined on the seventh day. While the hyperglycemic effect of epinephrine was fully evident, no rise in plasma NEFA concentration was observed (Fig. 2).

Pretreatment of hypophysectomized monkeys with prolactin (200 I.U. per day for 4 days) and ACTH (40 units per day for 4 days in gelatin) similarly failed to restore NEFA response to epinephrine. Pretreatment with monkey growth hormone (1 mg/kg per day for 4 days), however, caused a slight rise in plasma NEFA concentrations when epinephrine was administered.

The known TSH contamination of the monkey growth hormone and the hypothyroid state of the hypophysectomized monkeys suggested pretreatment with TSH and thyroid hormone. Pretreatment with 5 units of TSH per day for 4 days preceeding the epinephrine injection partially restored the NEFA response. Pretreatment with 20 μg-l-triiodothyronine per day for 4 days restored ability of hypophysectomized monkeys to respond to epinephrine in terms of an increase in plasma NEFA concentrations (Fig. 3). This was sustained for several weeks following cessation of thyroid therapy.

These observations suggest that the inability of hypophysectomized rhesus monkeys to respond to epinephrine by a mobilization of NEFA can best be explained in terms of the hypothyroid state of these animals and that optimal thyroid function is requisite for the NEFA mobilizing action of epinephrine. As mentioned above, such does not appear to be the case for growth hormone and fasting since both hypophysectomized and intact animals respond to these experimental situations.

Summary. Mobilization of NEFA by epinephrine in rhesus monkeys is abolished by hypophysectomy while the hyperglycemic response is retained. Pretreatment of hypophysectomized monkeys with cortisol acetate, ACTH, prolactin and growth hormone fails to restore response to epinephrine in terms of NEFA mobilization. Pretreatment with TSH or triiodothyronine, however, produced a restoration of the response. It is concluded that optimal thyroid function is requisite for the NEFA mobilizing action of epinephrine *in vivo*.

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